Original Article

Role of Nerve Ultrasound in the Assessment of Peripheral Neuropathy

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Abstract

Background: Peripheral neuropathy (PN) is a group of disorders that affects peripheral nerves with variable pathologic and etiologic mechanisms. **Objective:** The aims of this research are to find the role of assessing nerve cross-sectional area (CSA) and echogenicity in patients with different PNs classified according to pathology (A: axonal, D: demyelinated and M: mixed (axonal and demyelinating) (PN). **Materials and Methods:** This is a case–control conducted at Imam Al-Sadiq Teaching Hospital in Hilla Governorate. It includes 135 patients diagnosed with PN by an experienced neurologist. Electrodiagnostic studies are used to classify patients according to their pathology into axonal, demyelinating, and mixed polyneuropathies. We matched 138 controls for age and sex. The patient is examined "by high-resolution ultrasound" for nerve CSA by tracing the nerve inside the hyperechoic epineurium; also, echogenicity was assessed subjectivity. The nerves assessed are median and ulnar, tibial, peroneal, and sural nerves. Results are compared between cases and controls and then matched between different types of polyneuropathies according to pathology. **Results:** The study indicated that there were statistically significant differences in the average CSA between patients and controls. The demyelinating group had more mean CSA than other groups, followed by the mixed group and, lastly, the axonal group. Also, there is a significant difference in echogenicity between different groups, with a demyelinating group show a hypoechoic appearance of all examined nerves more than other groups (axonal, mixed). **Conclusion:** Nerve ultrasound is a useful and complementary test for assessing patients with PN and differentiating between its variable pathologies.

Keywords: Axonal, CSA, demyelinating and mixed peripheral neuropathy, echogenicity, neuromuscular ultrasound, peripheral neuropathy

Introduction

Peripheral neuropathy (PN) and polyneuropathy are terms that describe syndromes that cause subsequent diffuse lesions of peripheral nerves, usually presenting through weakness, pain, sensory loss, and autonomic disturbance.[1] Neurological disorders have a wide variety of causes and clinical presentations. The main causes of neurological disorders are systemic diseases, toxins, infections and autoimmune disorders, genetic disorders, ischemia, deficiency states, and paraneoplastic conditions.[2]

PN is a major cause of morbidity worldwide, and its prevalence is increasing due to an excessive increase in the prevalence of diabetes and the use of neurotoxic drugs such as antiretrovirals and chemotherapy. Diagnosis of PN is usually based on neurological diagnosis, a careful review of the existing condition, and electrodiagnostic testing.[3] Nerve conduction study (NCS) is considered the gold standard for the diagnosis of PN because of its advantages of being objective, sensitive, and reliable.[4] It can identify the distribution of neuropathy and recognize whether the neuropathy involves single or multiple nerves, distal or proximal, identifying the type of damaged nerve. Only the functions of large myelinated nerve fibers can be assessed in NCS, while small nerve fibers' function cannot be evaluated, which may result in a misdiagnosis. Also, it

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does not provide any information about the anatomical aspect of the nerve and its surrounding structures.[5]

Nerve ultrasound examination is a safe, promising method for the assessment of peripheral nerve morphology; it has a growing role in the diagnosis of PN in recent years.[6]

High-resolution ultrasound (HRUS) has been shown to be a simple, relatively low-cost, rapid, accurate, and noninvasive method for the evaluation of the Median nerve.[7]

It is an available tool that is able to visualize peripheral nerves with great resolution and accuracy. It can distinguish the nerve alterations that occur in different types of neuropathies.[8] It offers a real-time dynamic examination of the entire limb efficiently. The valuable information offered by ultrasound is considered complementary to clinical and NCS findings.[9] In this study, we explored the role of neuromuscular ultrasound in cross-sectional area (CSA) measurement to demonstrate the presence and pattern of nerve size in various PN disorders and to determine the association of CSA and echogenicity with each disease.

Materials and Methods

This case study was conducted in the Department of "Neurophysiology," Imam Al-Sadiq Teaching Hospital, Babylon Province, during the period from October 2020 to December 2021 on 135 patients (58 males and 77 females (with PN were included. All patients were diagnosed by experienced neurologists as having PN with its type according to the pathology is also stated. The diagnosis and disease type are based on a careful history, neurological examination, electrodiagnostic study, and biochemical or immunological test if needed. Variable types of PN like Acquired PN like, diabetic PN, uremic PN, hypothyroid PN, autoimmune PN as well as hereditary PN were included. The patients' ages ranged from 40 to 65 years. An additional 138 adults (63 males and 75 females) also took part as a control group, who were chosen to match patients' age, sex, and demographic data. The patients were divided into subgroups of numbers; 57 patients in Group A (axonal neuropathy) (29 females and 28 males), 35 patients in Group D (demyelinating neuropathy) (24 females and 11 males), and 43 patients in Group M (mixed neuropathy) (24 females and 19 males). We took a complete history from each patient, body mass index (BMI), and a comprehensive physical examination in addition to a complete neurological examination of the upper and lower extremities. Then, an electrodiagnostic study was performed using the Nihon Koheden machine in 2018. Each participant had four motor nerves tested (median, ulnar, tibia, and peroneal) and three sensory nerves (median, ulnar, and sural nerves). Limb temperatures were maintained between 33 and 36°C using a radiant heater when needed, and skin was prepared when necessary using an abrasive skin cleaner. Maximum responses were made using electrical stimuli. Multiple parameters were measured for each nerve, including waveform amplitude, distal latency, and conduction velocity.[10] An ultrasound examination was performed in the ultrasound unit using the Philips device 2017. We use a linear transducer with a frequency of 3–12 MHz to scan the nerve and tune it to a high frequency of 12 MHz.[11] Large amounts of ultrasound gel should be used to remove any air between the skin and the probe. Nerve CSA and echogenicity were evaluated for median and ulnar nerves for upper limbs and tibial, peroneal, and sural nerves for lower limbs. During a nerve ultrasound examination, the ultrasound probe should be perpendicular to the nerve.[12,13] Also, nerves are scanned along their entire length, looking for any focal of CSA. Nerve CSA and echogenicity are examined at multiple predetermined sites if no focal enlargement is found. Median and ulnar nerve CSA was measured at three levels: at the wrist, at the midpoint of the forearm, and at the midpoint of the arm; peroneal nerve CSA measured at three levels: at fibular head (FH), at popliteal fossa (pop), and at ankle (deep peroneal nerve), tibial nerve CSA measured at two levels: at popliteal fossa and at ankle and the sural nerve was examined.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before the sample was taken. The study protocol, the subject information, and the consent form were reviewed and approved by a local ethics committee according to document number MEC-52 on July 24, 2023.

Statistical analysis

Statistical analysis conducted by statistical package for social sciences (SPSS, IBM Statistics, California, USA) version 22. Frequency and percentage were used for the mean, median, and standard deviation of categorical data and continuous data. Chi-square is used for the evaluated association between variables, the person association showing the association between continuous data. *t*-Test for evaluation differences between the mean and the mean for continuous variables. The receiver operator characteristic (ROC) curve is also used to show more specific and sensitive cutoff points. A *P*-value of ≤0.05 is considered significant.

Results

Case–control comparative study of 4 groups, control 138 patients and 57 patients A (axonal), 35 patient's D (demyelinating), and 43 patients M (mixed).

The demographic data of the study groups are illustrated in Table 1 and show that the mean age of total patients is 46 ± 10 years old. The mean age of Group A is 49.719 ± 6.691 years, Group D: 40.68 ± 11.34 years, and Group M: 49.90 ± 6.19 years. The distribution of gender of patients according to groups as Group A: 50.9%

Table 1: The distribution of BMI and demographic data of patients according to groups

Variable	Control	Axonal	Demyelinating	Mixed	*P* value
Age (years)	45.04 ± 11.65	49.71 ± 6.69	40.68 ± 11.34	49.90 ± 6.19	
Gender					
Male	63 (45.7%)	28 (49.1%)	11 (31.4%)	19 (44.2%)	0.39
Female	75 (54.3%)	29 (50.9%)	24 (68%)	24 (55.8%)	
BMI (kg/m^2)					
Low	0 (0.0%)	0 (0.0%)	1 (3.0%)	0 (0.0%)	0.042
Normal	14 (10.1%)	4 (7.0%)	2 (6.1%)	1 (2.4%)	
Overweight	77 (55.8%)	28 (49.1%)	15 (45.5%)	16 (38.1%)	
Obese	47 (34.1%)	25 (43.9%)	15 (45.5%)	25 (59.5%)	
Total no.	138	57	35	43	

Table 2: Differences in CSA mean according to types in nerves of upper limbs

Nerves of upper limbs		*N*	Mean	SD	*P* value
CSA. med. N. wrist	Control	138	8.340	0.6183	
	A	57	11.298	3.2280	0.0001
	D	35	18.383	6.0651	
	M	43	13.723	5.0627	
CSA. med. N. mid forearm	Control	138	6.103	0.8388	
	A	57	8.272	3.3942	
	D	35	24.983	14.9664	0.0001
	M	43	12.647	12.4429	
CSA. Mid arm	Control	138	7.846	0.9491	
	A	57	11.868	3.5162	0.0001
	D	35	47.991	79.0439	
	M	43	17.860	17.5605	
CSA. ulnar. N. wrist	Control	138	5.183	0.6926	
	A	57	7.423	2.1562	0.0001
	D	35	13.051	5.4563	
	M	43	9.065	3.9286	
CSA. ulnar. N. mid forearm	Control	138	4.838	0.5966	
	A	57	8.014	7.0628	
	D	35	19.594	11.3283	0.0001
	M	43	9.677	7.1043	
CSA. Ulnar. N. mid arm	Control	138	5.442	0.6321	
	A	57	8.086	2.6037	0.0001
	D	35	25.611	16.8409	
	M	43	11.805	11.5263	

SD: standard deviation

P value ≤ 0.05 (significant)

females and 49.1% males. Group D: 68.6% are females and 41.4% are males. Group M: 55.8% are females and 44.5% are males.

Table 1 shows the distribution of BMI of patients according to Group A: 49.1% of patients are overweight; Group D: 45.5% of patients are overweight and obese; Group M: 59.5% of patients are obese with significant association.

As shown in Tables 2 and 3, there is a significant difference in the mean of CSA CSA. Median (med.) nerve (N.) at the wrist, CSA. med. N.at mid forearm, CSA. Med. at mid-arm, CSA. ulnar. N. at the wrist, CSA. ulnar. N. at mid-forearm, CSA. Ulnar. N. at the mid-arm, CSA Tibia N. at the ankle, CSA tibia N. at popliteal fossa(pop), CSA deep peroneal N. at the ankle, CSA peroneal N. at fibular head (F.H), CSA peroneal N. at pop according to groups. In all nerves, Group D (demyelinating) has more mean than other groups, then Group M (mixed), and lastly, Group A (axonal) all groups have a mean more than the control group.

In Table 4 and Figure 1, more sensitive and specific cutoff points for CSA. of Median N. at arm is 9.1 (84%, 100%).

In Table 5 and Figure 2, more sensitive and specific cutoff points for CSA of peroneal N. at F.H is 14.15 (80%, 100%).

Table 3: Differences in mean according to types in nerves of lower limbs

Nerves of lower limbs		*N*	Mean	SD	*P* value
CSA Tibia n. at ankle	Control	138	12.399	1.1109	
	A	57	19.093	6.7735	0.0001
	D	35	27.477	6.4503	
	M	43	21.423	8.1726	
CSA tibia n. at pop	Control	138	30.158	4.4935	
	A	57	42.211	10.1017	0.0001
	D	35	59.134	11.7185	
	M	43	48.902	14.1928	
CSA deep peroneal n. at the ankle	Control	138	2.975	.5561	
	A	57	3.826	1.4330	0.0001
	D	35	7.223	2.2108	
	M	43	4.321	1.9899	
CSA peroneal n. at F.H	Control	138	11.981	2.1839	
	A	57	17.732	6.4437	0.0001
	D	35	25.880	6.9741	
	M	43	19.491	4.4620	
CSA peroneal n. at pop	Control	138	14.117	4.6374	
	A	57	20.000	8.0315	0.0001
	D	35	39.449	9.4952	
	M	43	25.021	11.7361	
CSA sural nerve	Control	138	2.0712	.22129	
	A	57	4.0553	1.22047	0.0001
	D	35	8.9071	3.48506	
	M	43	4.8991	2.10065	

SD: standard deviation
P value ≤ 0.05 (significant)

Table 4: Sensitivity and specificity and cut off point of cross-sectional area of median nerve at the forearm in the diagnosis of peripheral neuropathy

Cutoff point of CSA.mearm	Sensitivity (%)	Specificity (%)
8.95	86	82
9.1	84	100
9.35	80	100

Discussion

Results did not appear to be a significant Effect of Gender on Ultrasound Measurements Study (US). The distribution of gender of patients according to Group A: 50.9% females and 49.1% males; Group D: 68.6% are females and 41.4% are males; Group M: 55.8% are females and 44.5% are males. This finding was consistent with other studies like.[6,10,13] On the other hand, some other studies disagree with this finding and conclude that gender plays a role in changing different parameters like NCS parameters ultrasound (US) measurements.[14,15]

"There were statistically insignificant differences ($P > 0.05$) "in the age between the study mean age of total patients 46 ± 10 years old. The mean age of Group A is

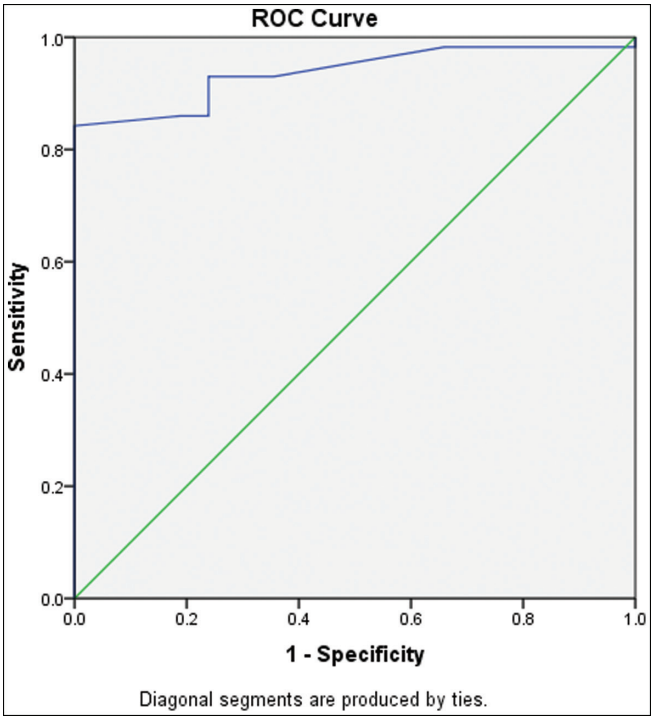

Figure 1: Receiver operator characteristic of cross-sectional area of median nerve at the forearm in the diagnosis of peripheral neuropathy

Table 5: Sensitivity and specificity and cut off point of cross-sectional area of peroneal nerve at the fibular head in the diagnosis of peripheral neuropathy

Cutoff point of CSA. CSAperonealn. atF.H	Sensitivity (%)	Specificity (%)
14.15	80	100
14.65	78	100
15.15	73	100

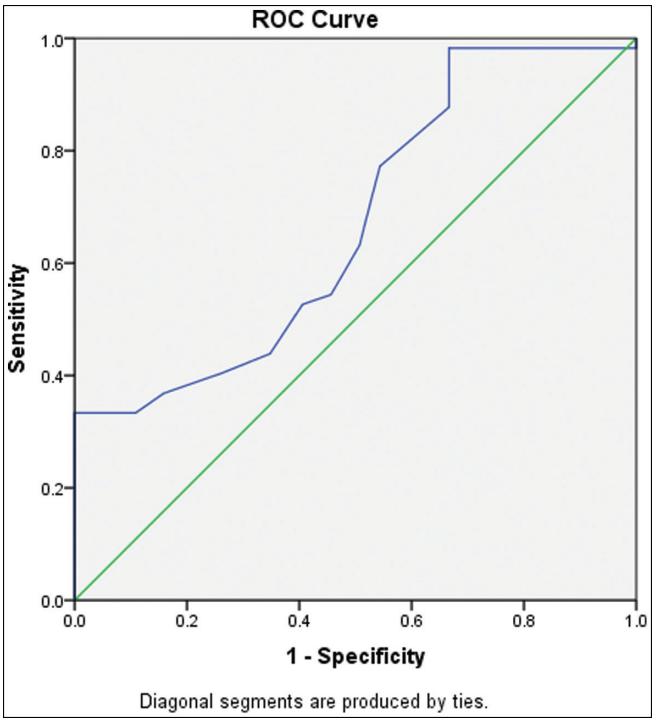

Figure 2: Receiver operator characteristic of cross-sectional area of peroneal nerve at the fibular head in the diagnosis of peripheral neuropathy

49.719 ± 6.691 years, Group D: 40.68 ± 11.34 years, and Group M: 49.90 ± 6.19 years. This is consistent with other studies[6,16-18] and against other studies.[15,19,20]

There was a statistically insignificant difference between study groups regarding BMI, as shown in Table 1.[1] the distribution of BMI of patients according to Group A: 49.1% of patients are overweight; Group D: 45.5% of patients are overweight and obese; Group M: 59.5% of patients are obese. This result is consistent with other studies,[6,21] which found that BMI did not indicate any risk in the development of neuropathy. While disagree with other studies,[21] which found that BMI plays an important role in the development of PN.[23]

This study is a detailed ultrasound diagnosis of patients with demyelinating and axonal nerve disorders and an evaluation of modulation of major nerves of the upper and lower extremities. Zeidman was the first to compare disorders of demyelinated nerves and axons with ultrasound in a large number of patients and found that nerve volume parameters were generally greater in demyelinating than in multiple neurodegenerative disorders. However, only the median and ulnar nerves, which contain the demyelinated group, were examined on both hereditary and acquired types. Similarly, in the recent report by.[23] As shown in Tables 2 and 3, there is a significant difference between CSA. Median N. At the wrist, CSA. median. N.at mid forearm and CSA median N. at mid arm, CSA. ulnar. N. Wrist, CSA. ulnar. N. at mid-forearm, CSA. ulnar. N. mid-arm, CSA tibial N. At the ankle, CSA tibia n. In popliteal fossa (pop), CSA deep peroneal n. In the ankle, CSA peroneal N. In fabular head (F.H), CSA peroneal N.at (pop), and sural nerve. By groups, in all tested nerves, Group D (demyelination) has more on average than the other groups, then Group M (mixed), and finally, Group A (axon). All groups mean more than the control group, confirming similar results already reported in the literature by Hwajin.[24]

Nerve enlargement, especially in proximal median nerve segments, distinguished patients with demyelinating groups reliably from those with axonal neuropathies. This study is consist with Hannaford and his study group in 2021 and Zaidman and his colleagues in 2013.[3,24] Test characteristics of sonography were excellent, more sensitive, and specific cutoff points for CSA. of Median N. at arm is 9.1 (84%, 100%) with sensitivity reaching 84% and even better specificity (100%). Our data suggest that HRUS is a valuable diagnostic tool to identify potential neuropathies and discriminate them from axonal neuropathies. This agrees with the study of Catwright and his study group in 2020.[25,26]

Also, in our study, peroneal nerve CSA at the fibular head was accurate for PN diagnosis (more sensitive and specific cutoff points for CSA of peroneal N. at F.H is 14.15 (sensitivity 80%, specificity 100%).

Based on the ROC curve analysis of our study, all results had high sensitivity and specificity, suggesting that ultrasound has good diagnostic accuracy for the detection of PN, suggesting that using nerve sonographic examination as a safe available tool in the diagnosis of PN is consistent with other authors like Kadhim and Alkhafaji in 2021[27] and Huand in 2021.[28-30] authors. "Some other interesting aspects of this study are that the pathological ultrasound changes were detected at several proximal and distal sites in the course of the peripheral nerves. This finding highlights the immunohistochemically incomplete multifocal demyelination occurring along nerve fibers in the PN."

Conclusions

Neuromuscular ultrasound can be used because it is an economical, convenient, painless, and available instrument for the examination of PN with some limitations. Neuromuscular ultrasound findings help to

prove the pathophysiological mechanism resulting in PN (demyelinating from those with axonal neuropathies).

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Conflicts of interest

There are no conflicts of interest.

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