The role of ultrasound in the diagnosis and evaluation of diabetic neuropathy in nerve roots of the foot

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Background Neuropathies are characterized by a progressive loss of nerve fiber function. Diabetic peripheral neuropathy is the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes. The diagnosis of diabetic neuropathy is based primarily on characteristic symptoms and is confirmed with nerve conduction studies (NCS), which are time-consuming, slightly invasive, and occasionally not well tolerated for repeated evaluations. In contrast, ultrasonographic (US) examinations can be performed to assess peripheral nerves with less discomfort and have already been used for the evaluation of several disorders of the peripheral nervous system such as carpal tunnel syndrome.

Patients and methods A total of 50 patients were included in the study, with 40 patients with type 2 diabetes and 10 controls. All cases underwent clinical history, local clinical examination, NCS, and real-time high-resolution US.

Ultrasound examination The patients were examined in supine position, and the foot was bolstered with a pillow to expose the anterior and medial portion of the lower leg and foot. The transducer was placed immediately above the medial malleolus to locate the tibial nerve in the transverse (short axis) and the longitudinal (long axis) views. The 5.0–12.0-MHz multifrequency linear array probe was used for tibial nerve scanning. The instrument used was Philips HD3 ultrasound scanner.

Result There was a statistically significant difference between case and controls regarding US cross-sectional area done for right and left tibial nerves, with high mean among cases (0.18±0.02 and 0.17±0.02, respectively). There was a statistically significant difference between US and NCS. There was no statistically significant difference between the two groups regarding the other measurements.

Conclusion High-resolution US can be used as adjuvant tool for the NCS for diabetic patients suspected to have neuropathy.

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Background

Management of diabetic neuropathy should begin at the initial diagnosis of diabetes. The primary care physician needs to be alert for the development of neuropathy – or even its presence at the time of initial diabetes diagnosis – because failure to diagnose diabetic polyneuropathy can lead to serious consequences, including disability and amputation. In addition, the primary care physician is responsible for educating patients about the short-term and long-term complications of diabetes [1].

The diagnosis of diabetic neuropathy is based primarily on characteristic symptoms and is confirmed with nerve conduction studies (NCS), which are time-consuming, slightly invasive, and occasionally not well tolerated for repeated evaluations [2].

In contrast, ultrasonographic (US) examinations can be performed to assess peripheral nerves with less discomfort and have already been used for the evaluation of several disorders of the peripheral nervous system such as carpal tunnel syndrome [3]. Abe *et al.* 2004 [4–6].

US can be used to determine the location, extent, type of lesion as well as the presence of nerve swelling and inflammation [7].

Major peripheral nerves in the extremities, such as the median, ulnar, radial, sciatic, and posterior tibial nerves can be seen using conventional US performed with 5–12-MHz probes [7].

In controls, peripheral nerves are seen as hypoechoic neuronal fascicles surrounded by echogenic connective tissue. The basic units of the peripheral nerve consist of a neural fiber embedded in the endoneurium. Because the endoneurium is too thin to reflect the sound beam,

it is hypoechogenic on the US scan. The neural fascicle consists of several neural fibers and is embedded in a capsule called the perineurium. This capsule consists of connective tissue, vessels, and lymphatic ducts and is thick enough to reflect the sound beam, resulting in hyperechoic lines on the US scan. The trunk of the peripheral nerve consists of several neural fascicles and is embedded in a thicker membrane called the epineurium, which is seen as bold echogenic lines on the US. Therefore, a peripheral nerve is seen as several parallel hyperechoic lines and bold hypoechoic lines on longitudinal images and as a faveolate pattern on transverse images [8].

It appears that the percentage of the hypoechoic area of the peripheral nerves was significantly greater in patients with lower motor nerve conduction velocity and diabetes mellitus (DM) than in controls or patients with higher motor nerve conduction velocity and DM [9].

Aim

This aim of this work was to evaluate the role of US in the diagnosis of diabetic neuropathy of nerve roots of the foot.

Patients and methods

Patients

A total of 40 diabetic patients were included in this study. The study was conducted in the Internal Medicine Clinic of the Fayoum General Hospital and in Fayoum University Hospital. It was performed between June 2013 and January 2015. There were 20 male and 20 females patients, with age ranging from 45 to 70 years. All patients had diabetic neuropathy, which means that diabetic neuropathy is more predominant after the age of 40 years.

Inclusion criteria

Diabetic patients who attend the Internal Medicine Clinic of the Fayoum General Hospital and were diagnosed as diabetics and complained of neuropathic pain were included in this study.

Exclusion criteria

The patients with causes of neuropathic pain other than DM, such as follows, were excluded from the study:

Amyloid polyneuropathy.
Chronic inflammatory demyelinating polyradiculo neuropathy.
Nutritional neuropathy.
Sarcoidosis and neuropathy.
Spinal cord tumors.
Thyroid disease.
Toxic neuropathy.
Uremic neuropathy.
Vasculitic neuropathy.
Vitamin B_{12} deficiency.
Alcohol (ethanol)-related neuropathy.

All patients underwent clinical history, local clinical examination, real-time high-resolution US, and NCS.

Ultrasound examination

The patients were examined in supine position, and the foot was bolstered with a pillow to expose the anterior and medial portion of the lower leg and foot. The transducer was placed immediately above the medial malleolus to locate the tibial nerve in the transverse (short axis) and in the longitudinal (long axis) views. The 5.0–12.0-MHz multifrequency linear array probe was used for tibial nerve scanning. The instrument used was Philips HD3 ultrasound scanner (FUJIFILM SonoSite, Inc., WA, USA).

Tibial nerve localization

First, the identification of the bony medial malleolus (bony shadow) was done, and then the transducer was moved slightly posteriorly to identify the tibial is posterior and flexor digitorum longus tendons. Both tendons are found within the flexor retinaculum of the ankle. They display a sliding movement with ankle flexion and are often hyperechoic. Then, the pulsatile posterior tibial artery (Doppler use is optional) is identified. The tibial nerve at the ankle is often round to oval with a honeycomb appearance. It is expected to lie posterior to the posterior tibial artery. The tibial nerve is traced proximally. The nerve is larger, and it is easy to identify it more cephalad in the leg. It is also easy to image the nerve longitudinally by rotating the transducer 90°.

Sonographic features to be evaluated were the morphology of the nerve and the cross-sectional area.

Nerve conduction study

NCS was performed in Fayuom University Hospital using Cadwell EMG equipment. The patients had bilateral nerve conduction testing done to the motor tibial nerves for latencies, amplitudes, and conduction velocities. Moreover, the patients had unilateral nerve conduction testing done to sensory and motor median

nerve for latencies, amplitudes, and conduction velocities. Electrophysiological abnormality was defined by at least one abnormal NCS parameter in both tibial and median nerves.

Results

The study included 40 diabetic patients (type 2). The study was conducted at the Internal Medicine Clinic of Fayoum General Hospital. It was performed between June 2013 and January 2015. Of the 40 patients, 20 were male and 20 female, and their ages ranged from 45 to 70 years. All patients had diabetic neuropathy by NCS examination. All of them presented with pain in the form of tingling, numbness, and hotness in the foot.

Table 1 illustrates the mean disease duration in the cases (7.2±4.6 years).

There is a statistically significant difference, with *P* value of less than 0.05, between different NCS and US diagnosis regarding the age, with higher mean age among neuropathic patients (Table 2).

There is a statistically significant difference with *P* value of less than 0.05), between case and controls regarding motor NCS velocity of conduction in left tibial nerve with high mean among controls (51.08±16.7). On the contrary, there is no statistically significant difference, with *P* value more than 0.05, regarding latency and amplitude of conduction (Table 3).

Table 1 Description of disease duration among neuropathic cases

Variable	Minimum	Maximum	Mean±SD
Disease duration (years)	3	20	7.2 (4.6)

Table 2 Comparisons of age among neuropathic and non-neuropathic subjects

Variables	Age (*n*=50) (mean±SD)	*P*-value	Significance
Diagnosis by nerve conduction study			
Non-neuropathy (*n*=10)	50.5 (2.3)	**0.01**	S
Neuropathy (*n*=40)	54.2 (8.4)		
Diagnosis by ultrasound			
Non-neuropathy (*n*=16)	50.1 (8.2)	**0.03**	S
Neuropathy (*n*=34)	55 (7)		

S, significant.

There is a statistically significant difference, with *P*-value less than 0.05, between case and controls regarding US cross-sectional area done for right and left tibial nerve, with high mean among cases (0.18±0.02 and 0.17±0.02, respectively) (Table 4).

There was 84% total agreement and 16% disagreement in the diagnosis of neuropathy between US and NCS. ($P<0.05$).

Sensitivity and specificity test for US in comparison with NCS illustrates probability of being true positive is 86.3%, which is more than being false positive when repeat test 100 times, with sensitivity of 82.5% and specificity of 90%. US can predict 97.1% from truly positive cases, and predict 56.3% from truly negative healthy persons (Tables 5 and 6).

Table 3 Comparisons of motor nerve conduction study to left tibial nerve among different study groups

Left tibial nerve	Case (*n*=40) (mean±SD)	Control (*n*=10) (mean±SD)	*P*-value	Significance
Latency	4.89 (1.4)	3.87 (1.8)	0.06	NS
Amplitude	5.56 (2.6)	5.04 (1.5)	0.5	NS
Velocity	37.78 (7.9)	**51.08** (16.7)	**0.001**	HS

HS, highly significant.

Table 4 Comparisons of ultrasound cross-sectional area of right and left tibial nerves among the different study groups

US cross-sectional area	Case (*n*=40) (mean±SD)	Control (*n*=10) (mean±SD)	*P*-value	Significance
Right tibial nerve	**0.18** (0.02)	0.12 (0.02)	<**0.001**	HS
Left tibial nerve	**0.17** (0.03)	0.12 (0.02)	<**0.001**	HS

HS, highly significant; US, ultrasonography.

Table 5 Comparisons of ultrasound diagnosis with the nerve conduction study in the study group

Diagnoses by ultrasound	Diagnoses by nerve conduction study [*n* (%)]		*P*-value	Significance
	Negative	Positive		
Negative	**9** (18)	7 (14)	<**0.001**	HS
Positive	1 (2)	**33** (66)		

HS, highly significant.

Table 6 Sensitivity and specificity of ultrasound in comparison with nerve conduction study in the diagnosis of neuropathy

Variable	Sensitivity (%)	Specificity (%)	Positive predictive (%)	Negative predictive (%)	Accuracy (%)
Ultrasound	82.5	90	97.1	56.3	86.3

Discussion

The aim of the present study is to evaluate the role of US in the diagnosis of diabetic neuropathy of nerve roots of the foot and to evaluate whether the sonographic finding in the tibial nerve corresponded to the results of NCS in diabetic patients. We found that the CSA of tibial nerve in diabetic patients was larger than those in controls. This is similar to Watanabe and colleagues, who found that the CSA of both median and tibial nerves in diabetic patients was significantly larger than those in controls.

The diagnosis of diabetic neuropathy is based on its characteristic symptoms and can be confirmed with NCS [10,11]. However, NCS is time consuming, slightly invasive, and generally not well tolerated for repeated evaluations [2]. In contrast, sonographic examinations can be performed to assess peripheral nerves with less discomfort and have already been used for the evaluation of disorders of the peripheral nervous system (Wiesler and colleagues and Watanabe and colleagues) [12].

In this study, we used high-resolution US for measurement of cross-sectional area of posterior tibial nerve to diagnose diabetic neuropathy, and the results were compared with NCS results.

The current study was conducted in 40 patients, with 20 male and 20 female patients. The average age was 54.2±8.4 years, which is similar to Watanabe and colleagues, whose mean patients' age was 59.8±10.2 years.

All patients in had type 2 DM, and this goes with a study by Watanabe and colleagues, whereas in the study by Riazi *et al*. [13], the patients had both type 1 and type 2 DM.

The posterior tibial nerve was imaged at each of three separate levels, specifically1, 3, and 5 cm proximal to the cephaled border of the medial malleolus [13]. In our study, similar technique was used but the PTN was imaged at only 5 cm distance proximal to the cephaled border of the medial malleolus.

In our study, we examined the posterior tibial nerve above the medial malleolus in both longitudinal and transverse scans using a linear array transducer with a frequency of 5–12 MHz (Philips HD3 ultrasound machine), whereas [14] examined the posterior tibial nerve above the medial malleolus in both longitudinal and transverse scans using a linear array transducer with a frequency of 6–14 MHz (Aplio XG; Toshiba Medical Systems ultrasound machine; KPI HEALTHCARE INC., Yorba Linda, CA, USA), and [13] examined the posterior tibial nerve above the medial malleolus in both longitudinal and transverse scans using a linear array transducer with a frequency of 6–13 MHz (SonoSite M-Turbo ultrasound machine).

In our study, the mean normal value of PTN cross-sectional are a above the medial malleolus was 0.12± 0.02 cm^2, which was greater than the mean normal value of PTN cross-sectional area above the medial malleolus (0.08 cm^2) in the study performed by Watanabe and colleagues, but matches with the results of Cartwright *et al*. [15] where the mean normal value of PTN cross-sectional are a above the medial malleolus was 0.13 cm.

In this study, the mean CSA of the tibial nerve was 0.18±0.02 cm^2.

In neuropathic patients, the CSA had low motor conduction velocity, which is similar to Watanabe and colleagues, whose CSA was 0.15±0.06 cm^2 in low tibial motor conduction velocity, and to Riazi *et al*. [13], whose CSA above the medial malleolus was 0.22 cm^2.

Riazi *et al*. [13] reported that compared with the control subjects, the DSP subjects demonstrated slower motor and sensory nerve conduction velocities, and longer distal motor, sensory, and F-wave latencies. This agreed with our study as there is a statistically significant difference, with *P*-value of less than 0.05, between cases and controls regarding motor NCS of velocity, with high mean among controls (51.08±16.7). On the contrary, there is no statistically significant difference, with *P*-value of more than 0.05, regarding latency and amplitude of conduction.

In our study, US in comparison with NCS detected sensitivity of 82.5% and specificity of 90% in the diagnosis of neuropathy, and this agreed with Watanabe and colleagues, who indicated the possibility of using US for the diagnosis of DPN as it reported sensitivity of 80% and specificity of 94%. However, the study performed by Riazi *et al*. [13] detected lower sensitivity and specificity (69 and 77%, respectively).

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Conflicts of interest

There are no conflicts of interest.

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