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High-resolution ultrasonography of the sural nerve in diabetic peripheral neuropathy

Kunwar Pal Singh, Kamlesh Gupta, Nilanshu Kataria,
Vijinder Arora, Nimisha Nagpal

Department of Radiodiagnosis and Imaging, Sri Guru Ram Das University of Health Sciences,
Sri Amritsar, Punjab, India

Correspondence: Dr Kunwar Pal Singh, e-mail: kpsdhami@gmail.com

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Abstract

Aim of the study: To study the cross-sectional area, the maximum thickness of the nerve fascicle and the thickness/width ratio of the sural nerve in patients with diabetes mellitus and non-diabetic subjects using high-resolution ultrasonography and to correlate the results with nerve conduction studies. **Material and methods:** This prospective study was conducted among 60 patients divided into two groups: A and B. Group A consisted of 30 patients >18 years of age with a history of type 2 diabetes mellitus, and Group B consisted of 30 non-diabetic patients >18 years of age. High-resolution ultrasonography was performed using a linear transducer with the frequency of 5–18 MHz in all the patients in the prone position with the transducer placed in a transverse position at the junction of the middle and lower thirds of the calf. Nerve conduction studies were performed using Aleron 201 (RMS) in all the patients. **Results:** As compared to the control group, the sural nerve in the diabetic group showed increased cross-sectional area, maximum thickness of the nerve fascicle and thickness/width ratio ($p < 0.05$). Nerve conduction studies showed decreased amplitude, increased latency and decreased velocity in the cases as compared to controls ($p < 0.05$). The cross-sectional area, maximum thickness of the nerve fascicle and thickness/width ratio showed statistical significance when compared with amplitude, latency and velocity in the cases as well as controls ($p < 0.001$). **Conclusion:** This study suggests that high-frequency ultrasound of the sural nerve is a useful tool for evaluating changes typical of peripheral neuropathy in patients with diabetes mellitus.

Introduction

Diabetes mellitus is a group of metabolic disorders characterized by hyperglycemia resulting from impairment in insulin secretion, insulin action, or both. Chronic hyperglycemia in the course of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Long-term complications of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers,

amputations, and Charcot joints; and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction⁽¹⁾.

Diabetic peripheral neuropathy (DPN) is the most common neuropathic syndrome seen in persons with diabetes. DPN is described as a symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and microvessel alterations as a result of exposure to chronic hyperglycemia and cardiovascular risk covariates. Irregularities in nerve conduction tests, which are frequently subclinical, appear to be the first objective quantitative indication of the condition⁽²⁾.

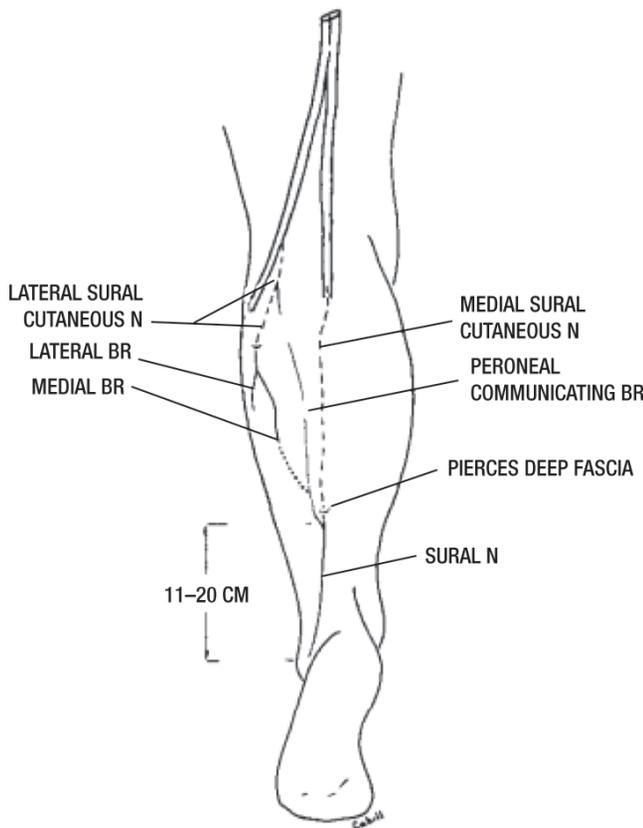


Fig. 1. Anatomy of the sural nerve (right)⁽⁷⁾

DPN severity is highly correlated with the severity and duration of diabetes mellitus⁽³⁾. Chronic hyperglycemia and associated metabolic disorders are assumed to be involved in its pathogenesis⁽⁴⁾. The initial effect of the degenerative process is thought to occur in the cutaneous nerve fiber endings⁽⁵⁾.

Sural nerve involvement is common in diabetic neuropathy, suggesting that long nerves are commonly affected⁽⁶⁾. The nerve usually consists of four named components: the medial sural cutaneous nerve, the lateral sural cutaneous nerve, the peroneal communicating branch, and the sural nerve⁽⁷⁾. The anatomy of the sural nerve is depicted in Fig. 1.

Ultrasonography (USG) is an excellent, cost-effective modality in imaging of peripheral nerves⁽⁸⁾. A high-end sonography unit equipped with a high-resolution broadband linear probe (>12 MHz) and corresponding soft-tissue contrast-enhancing software are the basic requirements for peripheral nerve sonography.

In the transverse section, the nerve is oval to round and has a hyperechoic outer contour corresponding to the outer epineurium. The echotexture has a typical honeycomb pattern.

Sonographic examinations of the sural nerve (SN) are performed with high-frequency linear-array transducers. Patients are placed in the prone position during the examination. The transducer is placed in the transverse position on the lower section of the calf. The thickness divided by width of the SN on the transverse image is defined as the thickness/width

(T/W) ratio and is an indicator of the level of swelling and deformation of the SN. The cross-sectional areas (CSAs) of the SN, which are traced along the outer hyperechoic rim on the transverse sonograms, are calculated using the formula for an ellipse after determination of six optional points along the nerve. The maximum thickness of the nerve fascicles (MTNF) is measured along the short axes⁽⁹⁾.

A sonographic image of the normal sural nerve in the transverse section is depicted in Fig. 2.

Aims and objectives

1. To study the cross-sectional area, the maximum thickness of the nerve fascicle and the thickness/width ratio of the sural nerve in patients with type 2 diabetes mellitus and non-diabetic subjects using high-resolution ultrasonography;
2. To examine bilateral sural nerve conduction in diabetic patients and non-diabetic controls;
3. To correlate the sural nerve ultrasonography findings with nerve conduction studies in patients with diabetes mellitus and non-diabetic controls.

Materials and methods

Study design

This cross-sectional, case-control study was conducted among 60 patients attending an outpatient department (OPD) or admitted to a tertiary care hospital in Amritsar. The patients were divided into two groups: A and B.

Study group A

Group A (cases) consisted of 30 patients >18 years of age with a history of type 2 diabetes mellitus.

Patients with a history of type 2 diabetes mellitus, attending the outpatient department (OPD) or admitted to this tertiary care hospital for ultrasonography were included in the study group A.



Fig. 2. Ultrasonographic appearance of the normal sural nerve adjacent to the short saphenous vein in the transverse view

Inclusion criteria

Patients >18 years of age and of either gender with a history of type 2 diabetes mellitus were included in the study.

Exclusion criteria

1. Patients with peripheral neuropathy due to other causes, such as:
 - alcoholism,
 - drugs,
 - obesity,
 - pregnancy;
2. Non-consenting patients.

Study group B:

Subjects of group B (controls) were selected from individuals of either gender >18 years of age, attending the outpatient department (OPD) or admitted to this hospital for medical/surgical treatment without any history of diabetes mellitus, peripheral neuropathy or trauma to the lower limbs.

Ethical clearance was obtained from the institutional ethics committee for conducting the study.

After obtaining the informed, written consent from each patient, detailed clinical history was recorded and general physical examination was conducted.

Sonography technique

In all the patients, high-resolution ultrasonography was performed using a linear transducer with the frequency of 5–18 MHz on the Affiniti 50G system (Philips Healthcare). All of the subjects were examined in the prone position. The transducer was placed in the transverse position at the junction of the middle and lower thirds of the calf.

Nerve conduction studies

In all the cases and controls, nerve conduction studies of the sural nerve were performed using Aleron 201 (RMS) in the nerve conduction study lab in the outpatient department of the hospital by a technician.

High-resolution ultrasonography findings were correlated with nerve conduction studies in the cases and controls. The data thus obtained was statistically analyzed. The duration of diabetes was recorded for all the diabetic patients.

Ultrasonography parameters, including cross sectional area (cm²), maximum thickness of nerve fascicle (cm) and thickness/width ratio, were recorded for all the cases and controls.

Nerve conduction was evaluated using three parameters: amplitude (μ V), conduction velocity (cm/s) and latency, (ms) in the cases and controls.

CSA, MTNF and T/W ratio as well as amplitude, latency and velocity were compared between group A and group B using the *t*-test. Furthermore, the *t*-test was also employed to compare CSA, MTNF and T/W ratio individually with each nerve conduction variable, namely amplitude, latency and velocity, in the cases and controls. *T*-values and *p*-values were calculated as depicted in Tab. 1 and Tab. 2.

Observations and results

Bilateral ultrasound examinations of the sural nerve were conducted in a total of 30 patients with type 2 diabetes mellitus (group A) and in 30 non-diabetic controls (group B).

The mean age of the group A patients was 55.13 ± 12.58 years and of the group B patients: 52.00 ± 11.77 years. Group A comprised 18 males and 12 females, while group B consisted of 16 males and 14 females. The mean duration of diabetes in group A was 5.55 ± 4.28 years. The mean HbA_{1c} value in the diabetic patients was 11.01 ± 2.03 .

The inner part of the sural nerve, consisting of the fascicle, perineurium and epineurium, was identified in all the participants.

The CSA, MTNF and T/W ratio of the right sural nerve in the diabetic group were: 0.034 ± 0.010 cm², 0.041 ± 0.010 cm and 0.510 ± 0.153 , respectively, as compared with 0.030 ± 0.010 cm², 0.037 ± 0.008 cm and 0.497 ± 0.117 , respectively, in the controls ($p < 0.05$).

The CSA, MTNF and T/W ratio of the left sural nerve in the diabetic group were: 0.035 ± 0.010 cm², 0.043 ± 0.010 cm and 0.571 ± 0.047 , respectively. The respective values in the controls were 0.030 ± 0.010 cm², 0.040 ± 0.009 cm and 0.530 ± 0.151 ($p < 0.05$).

In this study, 16 participants (53%) in group A were found to have unstimulable sural nerves on nerve conduction studies.

In the right sural nerve, nerve conduction studies in the diabetic patients revealed amplitude, latency and velocity of 22.686 ± 6.866 μ V, 2.194 ± 0.682 ms and 41.010 ± 11.581 m/s, respectively, as compared to controls where amplitude, latency and velocity reached 23.660 ± 5.090 μ V, 2.070 ± 0.430 ms and 54.830 ± 12.340 m/s, respectively ($p < 0.05$).

In the left sural nerve of the diabetic patients, nerve conduction studies revealed amplitude, latency and velocity of 23.350 ± 6.973 μ V, 2.184 ± 0.624 ms and 42.986 ± 12.387 m/s, respectively. In the controls, amplitude, latency and velocity were: 23.780 ± 5.120 μ V, 2.070 ± 0.430 ms and 54.960 ± 12.090 m/s, respectively ($p < 0.05$).

Ultrasonography findings in a non-diabetic and a diabetic patient are depicted in Fig. 3 and Fig. 4.

Tab. 1. Comparison between various ultrasonographic parameters and nerve conduction study parameters in the right and left sural nerves in the cases

Findings	Right		p-value	t-value	Left		p-value	t-value
	Mean	SD			Mean	SD		
CSA (cm²)	0.034	0.010			0.035	0.010		
Amplitude (µV)	22.686	6.866	0.001	-26.36	23.350	6.973	0.001	-28.31
Latency (ms)	2.194	0.682	0.001	-23.28	2.184	0.624	0.001	-36.46
Velocity (cm/s)	41.010	11.581	0.001	-41.80	42.986	12.387	0.001	-34.99
MTNF (cm)	0.041	0.010			0.037	0.008		
Amplitude (µV)	22.686	6.866	0.001	-26.36	23.350	6.973	0.001	-28.99
Latency (ms)	2.194	0.682	0.001	-23.32	2.184	0.624	0.001	-36.10
Velocity (cm/s)	41.010	11.581	0.001	-41.81	42.986	12.387	0.001	-34.98
T/W ratio	0.510	0.153			0.497	0.117		
Amplitude (µV)	22.686	6.866	0.001	-25.46	23.350	6.973	0.001	-27.66
Latency (ms)	2.194	0.682	0.001	-15.23	2.184	0.624	0.001	-27.22
Velocity (cm/s)	41.010	11.581	0.001	-41.25	42.986	12.387	0.001	-34.51

SD – standard deviation

Tab. 2. Comparison between various ultrasonographic parameters and nerve conduction study parameters in the right and left sural nerves in the controls

Findings	Right		p-value	t-value	Left		p-value	t-value
	Mean	SD			Mean	SD		
CSA (cm²)	0.030	0.010			0.030	0.010		
Amplitude (µV)	23.660	5.090	0.001	-47.65	23.780	5.120	0.001	-48.01
Latency (ms)	2.070	0.430	0.001	-55.20	2.070	0.430	0.001	-57.38
Velocity (cm/s)	54.830	12.340	0.001	-40.73	54.960	12.090	0.001	-43.28
MTNF (cm)	0.043	0.010			0.040	0.009		
Amplitude (µV)	23.660	5.090	0.001	-47.67	23.780	5.120	0.001	-47.96
Latency (ms)	2.070	0.430	0.001	-54.99	2.070	0.430	0.001	-57.43
Velocity (cm/s)	54.830	12.340	0.001	-40.73	54.960	12.090	0.001	-43.24
T/W ratio	0.571	0.047			0.530	0.151		
Amplitude (µV)	23.660	5.090	0.001	-46.76	23.780	5.120	0.001	-47.30
Latency (ms)	2.070	0.430	0.001	-42.86	2.070	0.430	0.001	-35.30
Velocity (cm/s)	54.830	12.340	0.001	-40.32	54.960	12.090	0.001	-42.67

SD – standard deviation

Discussion

Peripheral neuropathy is a highly complex and prevalent disease. This condition is observed in over 8% of the general population, and this number increases to 15% in individuals of 40 years of age or older⁽¹⁰⁾.

The most common causes of peripheral neuropathy in the United States and Europe are prediabetes and type 2 diabetes. At least a half of all diabetic patients, including patients with type 1 diabetes, develop some form of neuropathy during their lifetime. Pre-diabetes and type 2 diabetes are recognized as a global epidemic, with an incidence that continues to rise, particularly in countries adopting a more Westernized diet⁽¹¹⁾.

This study demonstrates that high-frequency ultrasonography is a useful diagnostic technique to evaluate

morphological changes in the sural nerves of diabetic patients. Because the inner parts of the SN can be clearly identified, it is possible to accurately measure morphological parameters.

The SN is commonly used to study distal sensory polyneuropathy in diabetic patients.

In this study, sural nerve morphology was examined using a linear transducer with the frequency of 5–18 MHz on a Philips Affiniti 50G system at the junction of the middle and lower thirds of the leg in the prone position. The transducer was placed in the transverse position. Minimal pressure was applied with the probe to avoid compression of the sural nerve and short saphenous vein.

Singh K *et al.* studied high-resolution ultrasonography of the tibial nerve in diabetic peripheral neuropathy and found that the cross-sectional area and maximum

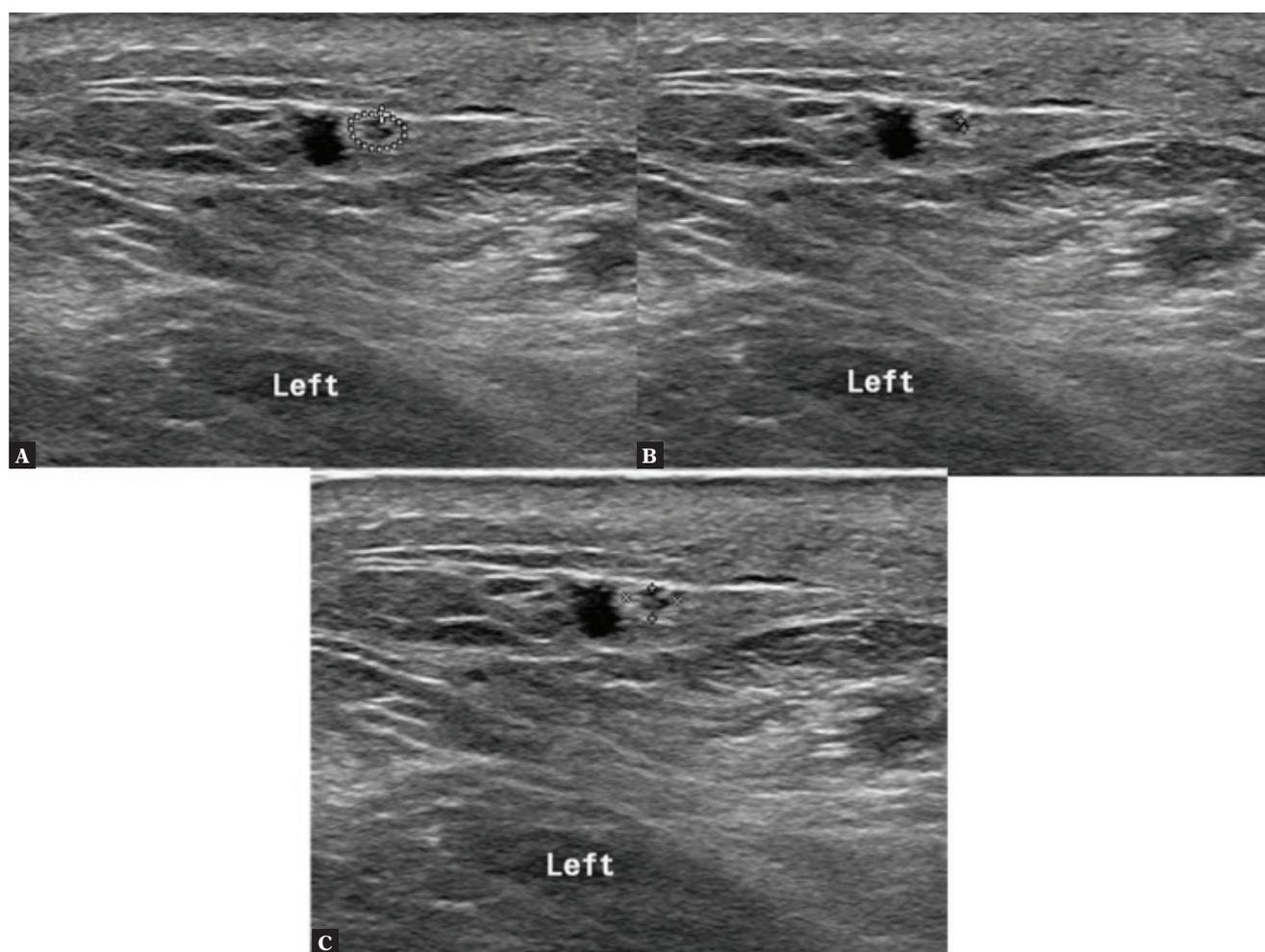


Fig. 3. Ultrasonography of the left sural nerve in a non-diabetic patient showing: A. cross-sectional area of 0.027 cm^2 , B. maximum thickness of nerve fascicle of 0.035 cm , and C. thickness/width ratio of 0.429 . The nerve conduction studies in this patient revealed amplitude of $21.2 \mu\text{V}$, maximum velocity of 59.34 cm/s and latency of 2.34 ms

thickness of nerve fascicles of the tibial nerve were larger in diabetic patients with or without peripheral neuropathy than in control subjects. They concluded that ultrasonography could be a good screening tool in these patients⁽¹²⁾.

We found that the CSA and MTNF were sensitive predictors of diabetic neuropathy. In the present study, CSA maybe the most commonly used for evaluation of nerve swelling from among the ultrasonographic criteria for nerve swelling assessment.

Similar results were obtained by Ebadi H *et al.*⁽¹³⁾ who found the mean CSA of the sural nerve in diabetic patients was $3.2 \pm 0.8 \text{ mm}^2$ and in controls: $2.7 \pm 0.6 \text{ mm}^2$ (p , 0.0070), and this was independent of sex. There was no difference in the thickness-to-width ratio or echogenicity of the nerves in their study.

In the study carried out by Kang S *et al.*, ultrasonographic features of multiple peripheral nerves in the upper and lower extremities of DPN patients were investigated and compared with those of controls. The CSAs for the sural

nerve were significantly larger in the DPN group and significantly correlated with electrophysiologic findings. The sural nerve CSA revealed significant correlation with HbA_{1c} ⁽¹⁴⁾.

In the current study, mean HbA_{1c} in group A was found to be 11.01 .

In our study, the maximum thickness of nerve fascicle was slightly higher in the diabetic patients compared to the controls ($p < 0.05$). This is in corroboration with studies conducted by Wei *et al.*⁹ The MTNF may be therefore considered an indicator of the level of nerve fascicle swelling.

The thickness-to-width ratio (TW) was calculated by dividing the thickness by the width as described by Wei *et al.*⁽¹⁵⁾ In our study, T/W ratio was found to be slightly higher in the diabetic patients than in the controls ($p < 0.05$).

Chen J *et al.* studied the feasibility of high-resolution ultrasonography to assess the ulnar nerve in patients with diabetes mellitus and found that the cross-sectional area was

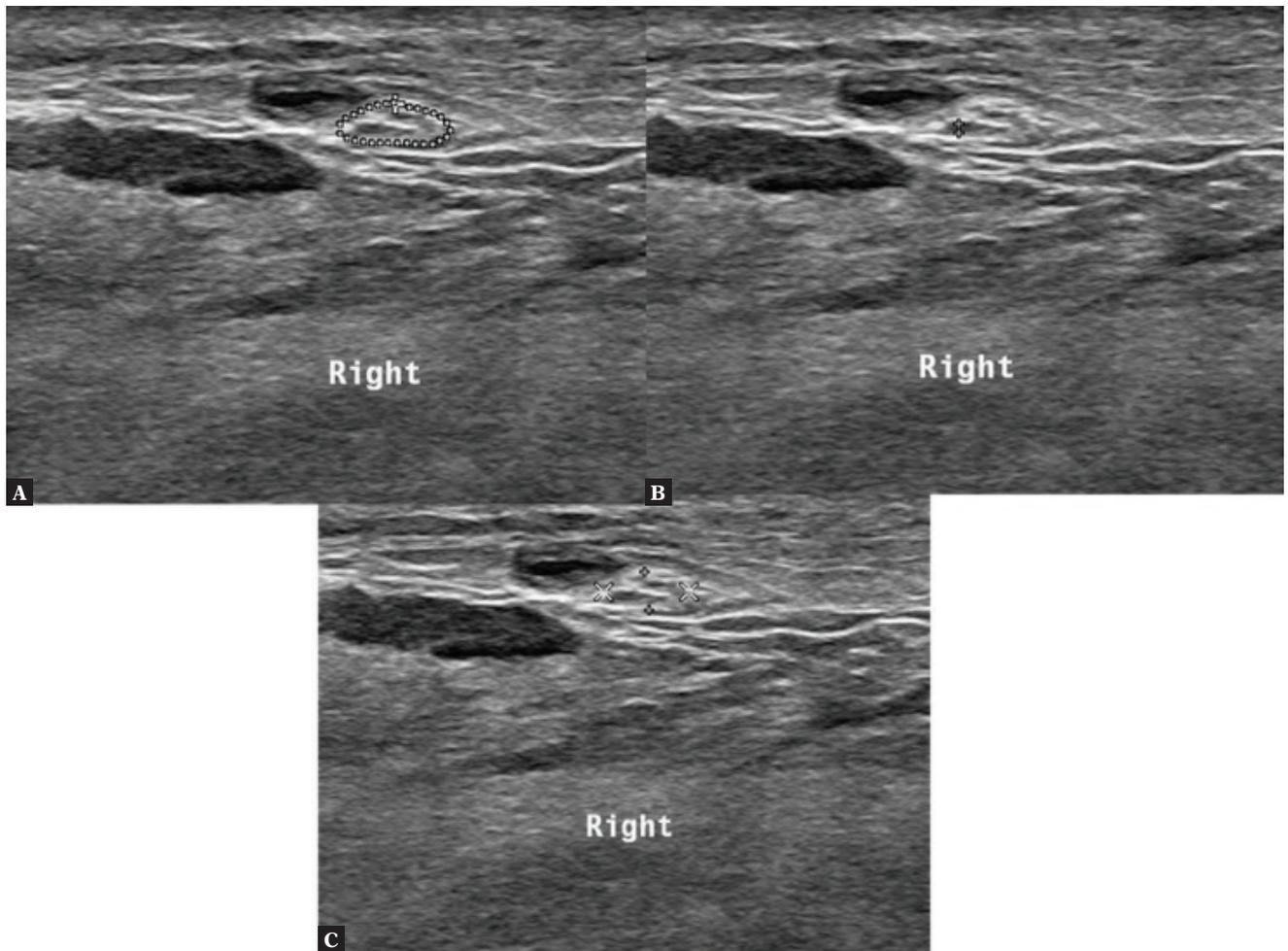


Fig. 4. Ultrasonographic image of the right sural nerve in a diabetic patient showing: A. cross-sectional area of 0.052 cm²; B. maximum thickness of nerve fascicle of 0.037 cm, and C. thickness/width ratio of 0.555. On nerve conduction studies, the right sural nerve was found to be unstimulable

larger in the diabetic peripheral neuropathy group compared with the control group⁽¹⁶⁾.

On nerve conduction studies, three parameters, namely amplitude, latency and velocity, were calculated. Amplitude was found to be slightly lower in the diabetic group as compared to the control group ($p < 0.05$). Latency was higher and velocity was lower in the diabetic patients ($p < 0.05$) compared to controls ($p < 0.05$). In this study, 16 participants (53%) in group A were found to have unstimulable sural nerves on nerve conduction studies.

The results from sonography and nerve conduction studies were statistically analyzed using the t-test. Statistically significant results were found for CSA, MTNF and T/W ratio when compared with velocity of nerve conduction, latency and amplitude in the cases as well as controls ($p < 0.05$).

Our study is in contradiction with the study conducted by Hobson-Webb LD *et al.*, which was performed to establish the sonographic characteristics of lower extremity nerves in DPN and correlate them with electrodiagnostic (EDx)

findings. The authors found that ultrasound measurements of lower extremity nerves in DPN do not differ from controls and do not correlate with EDx findings⁽¹⁷⁾.

Conclusions

This study suggests that high-frequency ultrasound of the sural nerve is a useful tool for evaluating changes typical of peripheral neuropathy in patients with diabetes mellitus. The cross-sectional area, which is altered in diabetic peripheral neuropathy, is the most sensitive parameter. Nerve conduction studies suggest that velocity is the most significantly affected parameter.

Conflict of interest

Authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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