



Original Article

Role of high resolution ultrasound as a screening tool in peripheral neuropathy

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Abstract

Objective: Early detection of nerve dysfunction is important in management of diabetic peripheral neuropathy. Our study was aimed at finding the correlation of cross sectional area and Maximum thickness of nerve fascicle with the presence of peripheral neuropathy.

Materials and Methods: 50 patients with type 2 diabetes clinically diagnosed with diabetic peripheral neuropathy were analysed and severity of peripheral neuropathy was determined using Toronto clinical neuropathic score. 45 diabetic patients with no symptoms of peripheral neuropathy and 50 healthy non-diabetic subjects were taken as controls. The cross sectional area and maximum thickness of nerve fascicles of the tibial nerve were calculated 3cm cranial to medial malleolus in both lower limbs.

Results: The mean cross sectional area ($17.01 \pm 1.31 \text{ mm}^2$) and maximum thickness of nerve fascicle (0.61 mm) of the tibial nerve in patients with peripheral neuropathy compared with both control groups were significantly larger and statistically significant correlation was found with Toronto clinical neuropathic score ($p < 0.001$). the diabetic patients with no signs of peripheral neuropathy had larger mean cross sectional area ($10.77 \pm 1.73 \text{ mm}^2$) and maximum thickness of nerve fascicle (0.25mm) than the healthy non-diabetic subjects ($7.46 \pm 1.77 \text{ mm}^2$ and 0.20 mm respectively).

Conclusion: The cross sectional area and mean thickness of nerve fascicle of the tibial nerve is larger in diabetic patients with or without peripheral neuropathy than in healthy subjects and it showed correlation with severity and high resolution USG can be used as a screening tool in these patients.

Keywords: cross sectional area, maximum thickness of nerve fascicle, tibial nerve, sonography, diabetic neuropathy.

Introduction

According to the World Health Organization, 180 million people worldwide have diabetes. Diabetic peripheral neuropathy is one of the major complications of diabetes mellitus. About half of the patients will develop neuropathy during the course of the disease⁽¹⁾.

Poor glycemic control is a major risk factor in the development of diabetic polyneuropathy. Hyperglycemia leads to osmotic swelling of the nerves with injury to the axons and myelin sheath, which triggers the onset of neuropathy. Advanced DPN causes serious complications like diabetic foot ulcers, gangrene, and neuropathic joint. Patients commonly present with complaints of

tingling, numbness, or prickling sensations affecting the feet. The symptoms are often seen bilaterally and in an asymmetrical distribution. The most common sign is the absence of ankle reflexes. Sensory disturbance is also commonly seen, and the most common is the loss of vibration sense at the toes, followed by pinprick, temperature, and light touch sensations⁽²⁾.

The diagnosis of peripheral neuropathy is primarily based on nerve conduction study. Although imaging is not used as a criteria for diagnosis, High resolution Ultrasonography (US) of the nerve is a fast real time tool for detecting diabetic neuropathy⁽³⁾. There is no patient discomfort, nor any radiation exposure. The nerve conduction studies used by the neurologists for the diagnosis of peripheral neuropathy are not available in every setup. Radiologically, USG and MRI are excellent tools for imaging the nerves. But USG is cost effective and patient co-operation is more when compared with MRI.

Aims and Objectives

Correlation of the cross sectional area and maximum thickness of the nerve fascicles of the tibial nerve with the presence and severity of diabetic peripheral neuropathy.

Materials and Methods

Study Area- Department of Radiodiagnosis, SCBMCH

Study Design - Hospital based observational study

Study Duration - January 2018 to December 2019

Study Population - Patients with type 2 diabetes mellitus

Inclusion Criteria- Diabetic patients with neuropathic symptoms

Exclusion Criteria- Neuropathy due to causes other than diabetes

Methods

The subjects were divided into three groups.

Group 1 - Diabetic patients with clinical signs of peripheral neuropathy.

Group 2 - Diabetic patients with no clinical signs and symptoms of peripheral neuropathy.

Group 3 – Healthy volunteers

Healthy volunteers are recruited as controls for the study. High resolution ultrasonography of the tibial nerve with the patient lying in lateral position for the easy assessment of medial aspect of ankle and distal leg. The cross sectional area and maximum thickness of nerve fascicles of bilateral tibial nerve 3cm above the medial malleolus are measured. The cross sectional area measured by manual tracing, the maximum thickness of the nerve fascicle calculated by measuring the largest antero-posterior diameter of the largest hypoechoic area in the short axis view of the tibial nerve. Neurological and sonological exam are conducted in one visit.

Reference Standard

The peripheral neuropathy status and severity of the patients is determined using Toronto clinical neuropathic score.

Equipment

The values were measured in SAMSUNG MEDISON HS70A ultrasound machine.

Statistical Analysis

The mean cross sectional area and maximum thickness of nerve fascicle of the tibial nerve of all three groups were compared using IBM SPSS 20.0 software, with ANOVA and post hoc tests performed. The correlation of the values with Toronto clinical neuropathic score and HbA1c levels were done using pearson's correlation coefficient.

Results

Table demonstrating demographic, clinical, biochemical and USG findings of all groups are summarised below:

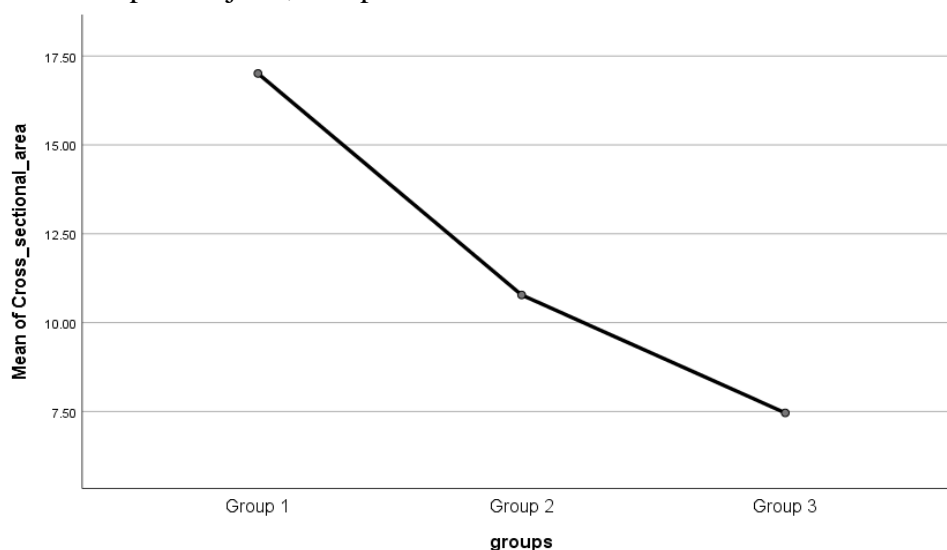
Clinical & Biochemical characteristics	Group 1	Group 2	Group 3
Age in yrs (mean+/- SD) Range	57.64+/-9 (41-80)	46.6+/-5.93 (30-60)	40.52+/-11.18 (24-70)
Duration of diabetes in yrs (Mean+/- SD) Range	13.38+/-5.8 (5-29)	7.22+/-3.36 (3-17)	-
Male:Female	32:18	24:21	28:22
Weight in Kg (Mean+/-SD) Range	68.38+/-10.39 (51-88)	66.51+/-6.01 (80-54)	60.64+/-5.76 (52-72)
Systolic BP in mmHg (Mean+/-SD) Range	141.3+/-29.89 (120-170)	128.8+/-18.49 (110-150)	118.6+/-8.57 (110-140)
Diastolic BP in mmHg (Mean+/-SD) Range	81.4+/-7.82 (65-90)	74.33+/-5.17 (65-80)	73.6+/-4.84 (70-80)
HbA1c % (Mean+/- SD) Range	8.43+/-1.0 (7.0-11.1)	6.97+/-0.33 (6.5-8.4)	6.44+/-0.25 (5.0-6.0)
CSA of Tibial nerve in mm ² (Mean+/-SD) Range	17.01+/-1.31 (15-20)	10.77+/-1.73 (7-13)	7.46+/-1.77 (3-10)
MTNF of tibial nerve in mm (Mean+/-SD) Range	0.61+/-0.07 (0.4-0.7)	0.25+/-0.06 (0.1-0.4)	0.204+/-0.07 (0.1-0.3)
TCNS (Mean+/-SD) Range	10.28+/-2.11 (8-16)	1.52+/-1.10 (0-3)	-

CSA- Cross Sectional Area; MTNF – Maximum thickness of nerve Fascicle; TCNS – Toronto clinical neuropathic score

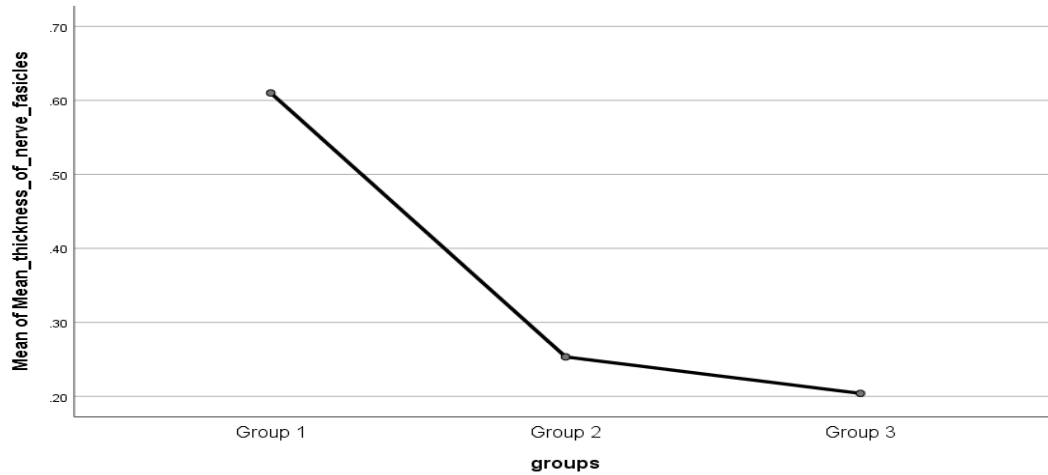
Table 1 Clinical and biochemical characteristics of patients, CSA, MTNF, TCNS results. Group 1 – Diabetic patients with peripheral neuropathy, Group 2 – Diabetic patients without symptoms of peripheral neuropathy, Group 3- Non-diabetic subjects

Male predominance was observed in all 3 groups. Weight, Systolic blood pressure and Diastolic blood pressure were highest in Group 1. The mean Cross sectional area of tibial nerve was appreciably raised in Group 1 subjects, compared

with Groups 2 and 3 with p<0.001 (table 7). The mean Cross sectional value of tibial nerve was also larger in Group 2 when compared with group 3, with p<0.001.

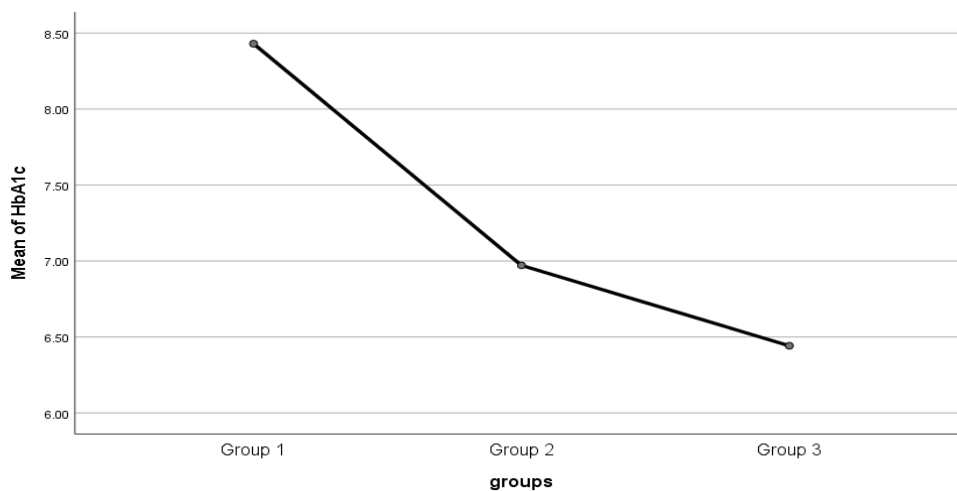


The mean Maximum thickness of tibial nerve fascicle was higher in Group 1 than Groups 2&3, with p<0.001.



MTNF of tibial nerve was higher in Group 2 when compared to group 3, with $p < 0.001$ (significant) Mean HbA1c value in Group 1 was higher in group 1 than other groups, with significant

statistical correlation with Cross sectional area ($r = 0.924$; $p < 0.001$) and Mean thickness of nerve fascicle ($r = 0.763$; $p < 0.001$)



On comparison with group 2, subjects of group 1 showed highest mean of Toronto clinical neuropathic score with a good correlation with

Cross sectional area ($r = 0.876$; $p < 0.001$) and Mean thickness of nerve fascicle ($r = 0.922$; $p < 0.001$) of the tibial nerve.

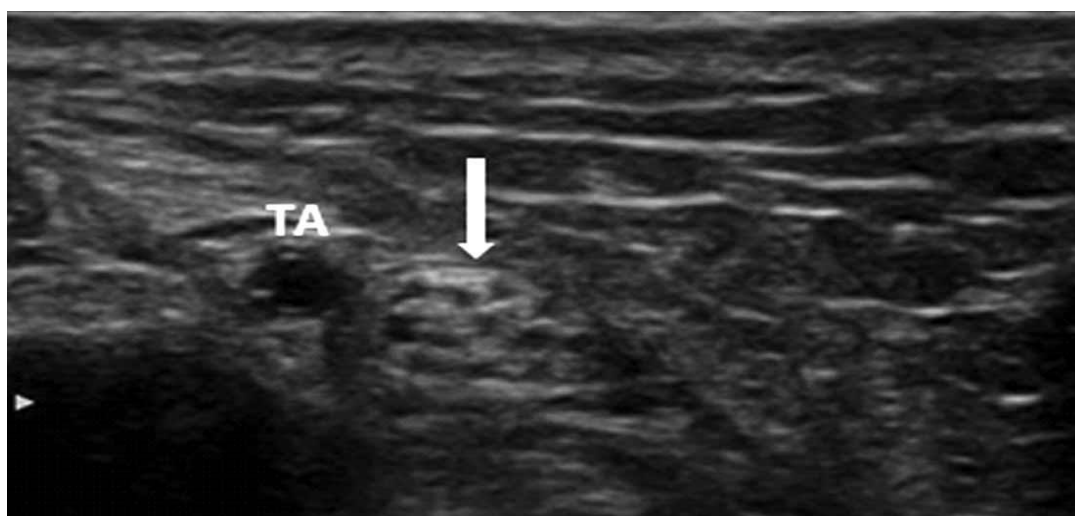


Figure 1 transverse image showing tibial nerve above the ankle adjacent to the tibial artery

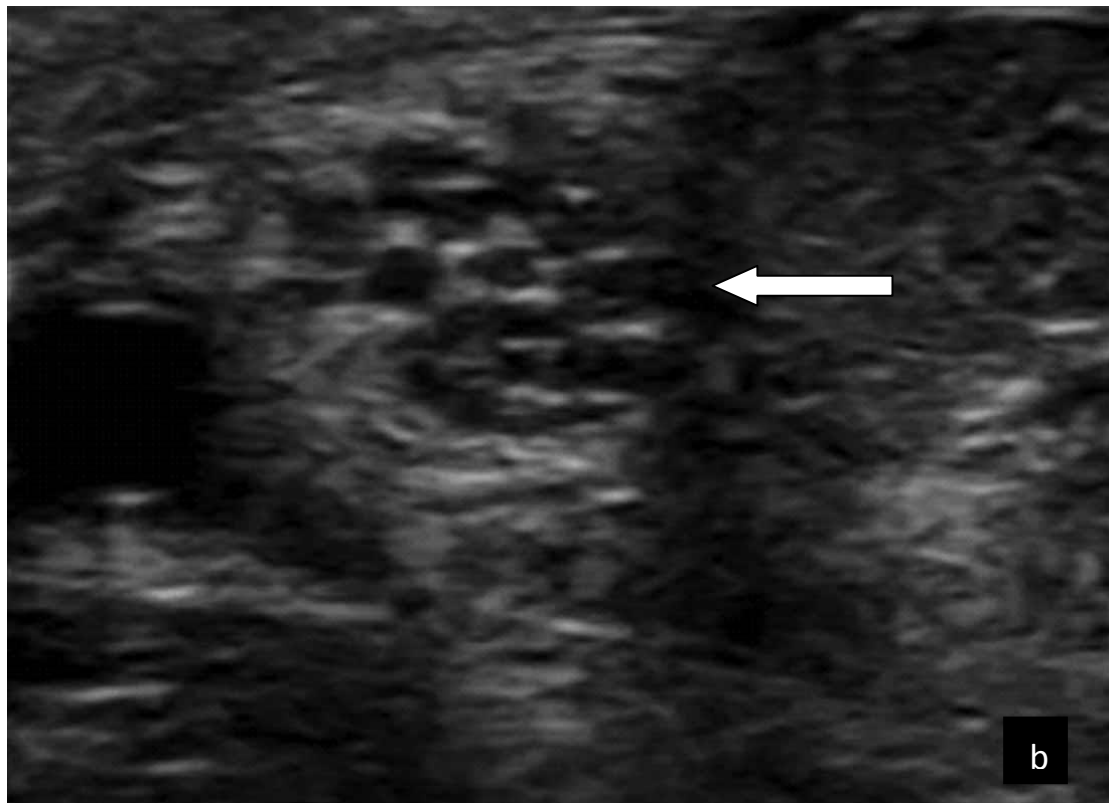
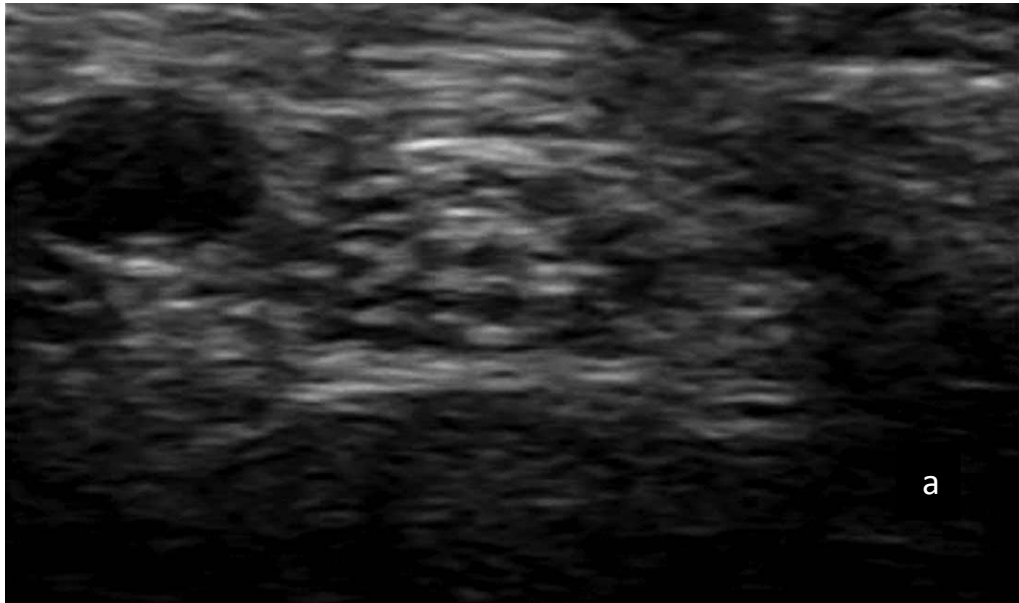


Figure 2 transverse images of the tibial nerve in a normal patient and a patient(a) with diabetic neuropathy (b).Note the enlarged hypoechoic fascicles in (b) [arrow]

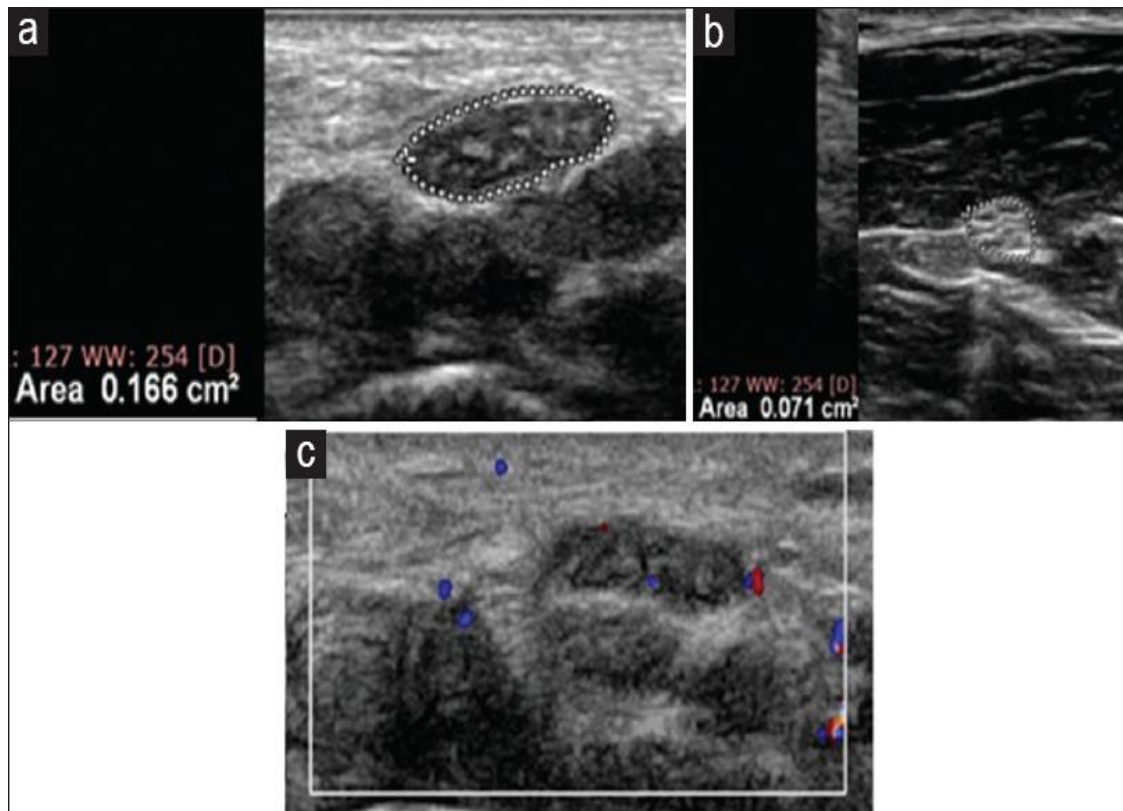


Figure 3 Three images showing the measurement of CSA of tibial nerve. (a) shows increased calibre of the nerve. (b shows nerve with normal calibre)

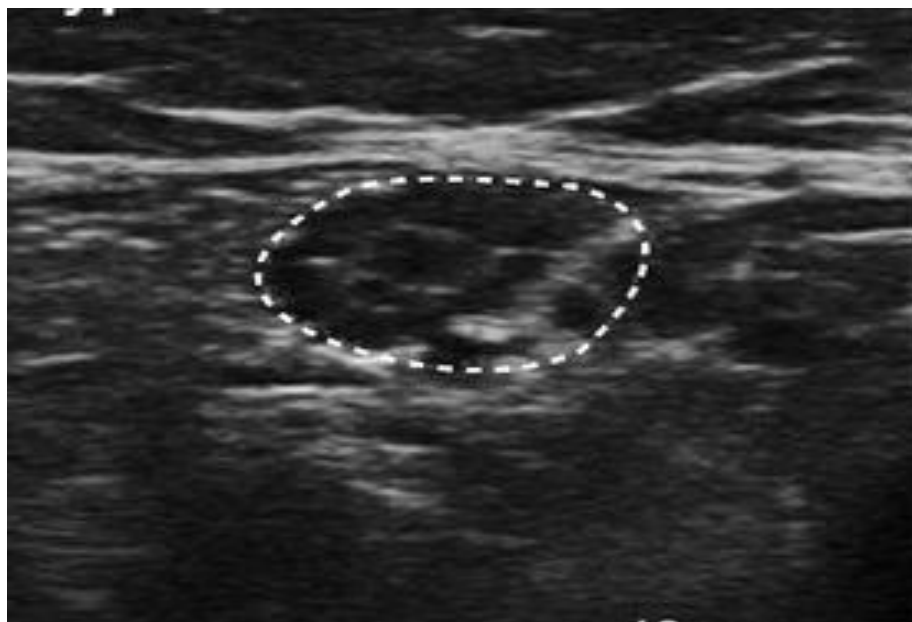


Figure 4 Axial image of tibial nerve with heterogeneously hypoechoic enlarged fascicles

Discussion

Before the introduction of imaging methods, the diagnostic work-up of peripheral nerve disorders was based only on the evaluation of the clinical history, neurological examination and other diagnostic tests, such as nerve conduction studies,

F-waves and electromyography⁽¹⁾. Nerve imaging has become an important method in patient management by providing information on lesion morphology, anatomical location, relationship of the lesions to the adjacent structures, and evaluation of areas not accessible with

electrodiagnostic tests. Imaging can also identify peripheral nerve space-occupying lesions that are not apparent on electrodiagnostic tests⁽⁷⁾.

Sonography of the peripheral nerve is not essentially new. As early as 1988, Bruno Fornage reported on the feasibility of peripheral nerve imaging (Fornage 1998). The progress of nerve sonography in the subsequent years, however, was slow, and this was mainly due to the fact that nerves are small structures and were not easy to approach with the then available technique.

The lacking of high-resolution transducers was the main problem and therefore it took until the late 1990s and the first years of the new millennium for sonography of the peripheral nerve to experience a real boost, which still continues. High resolution ultrasound (HRUS) and magnetic resonance imaging (MRI) are the most commonly used methods for visualizing peripheral nerves. US is used as an adjuvant in the neurological assessment even in day-to-day practice, and this confirms the increasing interest in US for the evaluation of the peripheral nervous system disorders⁽⁷⁾.

US examination is currently increasingly used for the imaging of peripheral nerves, supplementing the physical examination. An important breakthrough in the ultrasound diagnostics of peripheral nerves occurred with the introduction of US probes with high frequencies (greater than 12–15 MHz).

Contrast and resolution are the basic physical principles that matter with sonography. Therefore, high-resolution transducers are a must for nerve imaging. Currently available transducers for clinical imaging reach frequencies of up to 18 MHz which results in an axial resolution of 250–500 μ m.

The vessels accompanying the nerves are taken as anatomical reference points during US examination. The tibial nerve is the thicker terminal branch of the sciatic nerve. At the level of the medial malleolus, it is accompanied by the posterior tibial artery and veins, proximally on its anterior side, and distally along its medial

aspect⁽¹³⁾. The symptoms of DPN usually first appear in the toes or the soles of the feet^(16,17). This is one reason why we used the tibial nerve as the studied structure in our study.

The diagnosis of diabetic neuropathy can be confirmed with NCS, however it is time-consuming and not widely available in all centres. US, on the other hand, can be performed at the patient's little or no discomfort, and has already been used for evaluating peripheral neural pathologies^(14,15).

As it is the case for sonographic examinations in general, nerves must be imaged in two perpendicular planes. Nerves are tubular structures with hypoechoic fascicular bundles interspersed by echoic connective tissue^(8,24). This is why on longitudinal scans nerves are not easily distinguished from close-lying muscle tissue or tendons.

On transverse scans, this is much easier achieved, as nerves run along fascial planes embedded in fat and connective tissue – often together with vessels – and the honeycomb appearance of a nerve on a transverse scan is quite characteristic and easily distinguished from other anatomical structures.

In general the presentation of nerves on high resolution sonograms is exquisite and nicely correlates with the anatomical ultra structure. Fascicles are the smallest structure to be discerned by modern sonography and are groups of nerve fibers surrounded by a common outer epi- and perineurial sheath⁽⁸⁾.

The single nerve fibers composed of axons, myelin sheaths, and Schwann cells are still beyond the resolution of sonographic imaging. An individual amount of fascicles comprises a peripheral nerve, which is surrounded by outer epineurium. How many fascicles combine to a peripheral nerve is variable and depends on the type of nerve (amount of motor and sensory fibers), its location in the body (distance from its origin, type of surrounding tissue), and its size.

The fascicles and the epineurial tissue are important features, as changes in these two elements are the hallmark of distinct

pathophysiological entities of peripheral nerve disease.

Marked swelling of fascicles and loss of inner and outer hyperechoic epineurial borders, for example, may result from venous congestion and edema and are characteristic for acute or subacute compression neuropathy. So when performing peripheral nerve sonography, attention to the microanatomic texture of a nerve is important.

A cross-sectional study of diabetic neuropathy reported by Dyck et al²¹ found that polyneuropathy was the most common form of diabetic neuropathy, followed by CTS. It is well known that diabetic neuropathies are frequently asymptomatic

Severinsen and Andersen²² reported that the nerve conduction velocity may be reduced not only because of loss of the fastest conducting axons but also because of demyelination and acute metabolic dysregulation, which may cause lower nerve conduction velocity

Suzuki et Al²³ reported that sorbitol itself and secondary sodium accumulation caused by an increase in sorbitol may be major contributors to the increase in intracellular hydration using a ¹Hnuclear magnetic resonance study.

It has further been hypothesized that the peripheral nerve is swollen in individuals with diabetes mellitus because of increased water content related to increased aldose reductase conversion of glucose to sorbitol. We hypothesize that an increased hypoechoic area of the peripheral nerve in diabetic patients may occur because of increased water content, which is also a cause of an enlarged peripheral nerve.

Diabetes mellitus is becoming a major cause of premature disability, and peripheral neuropathy is a common complication of diabetes. The diagnosis of diabetic neuropathy is based on its characteristic symptoms and can be confirmed with NCS²¹.

However, NCS is time consuming, and generally not well tolerated for repeated evaluations. 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.⁴

Fukashi Ishibashi *et al.* ⁽¹⁷⁾ studied CSA, hypoechoic area and MTNF of the median and posterior tibial nerves in patients with or without diabetic neuropathy. CSA was measured by direct tracing. They concluded that the morphological changes in peripheral nerves of type 2 diabetic patients were seen even prior to the clinical onset of neuropathy, and were closely correlated with the severity of the disease. Moreover, CSA and MTNF in patients with neuropathy were larger than those in the controls, with significant *p*-values⁽¹⁷⁾.

The findings were similar in our study, where CSA and MTNF in Group I patients were larger than in the other two groups, with *p* < 0.001. There was also a statistically significant difference between MTNF of Group II and Group III, with *p* < 0.05. Hence, the morphological changes in the tibial nerve can be detected on HRUS even before the onset of neuropathy.

There was no statistically significant difference between CSA and MTNF of the tibial nerves in right (respectively) and left lower limbs (respectively). Also, CSA of the tibial nerve was larger in males than in females, both in the affected patients as well as controls. Similar findings were observed in the study conducted by FukashiIshibashiet *al.*, where there was no difference in CSA of the median nerve between right and left hands, neither in controls, nor in diabetic patients, and CSA was larger in men than in women⁽¹⁷⁾. As far as HbA1c is concerned, it is an index of the average blood glucose level over the preceding weeks to months. Quarterly HbA1c determination is an important measure of glycemic control of the patient. Poor glycaemic control can result in the onset as well as progression of diabetic peripheral neuropathy⁽¹⁸⁾.

Watanabe *et al.*⁽⁴⁾ studied the role of ultrasonography in diabetic peripheral neuropathy, concluding that there was no statistically significant correlation between HbA1c levels and CSA of the peripheral nerves⁽⁴⁾. The likely reason may be the small sample size in their study. In our

study, a significant correlation was observed between these two parameters, with $p < 0.001$ in Group I and <0.001 in Group II.

The size of the nerve fascicles is one of the determinants of the hypoechoic area in CSA of peripheral nerves. MTNF in non-neuropathic diabetic patients was larger compared with control subjects, with statistically significant correlation between MTNF and the severity of neuropathy, as observed by Ishibashi.

The morphological changes in the peripheral nerves of diabetic patients were detected even before the onset of neuropathy, and were closely correlated with the severity of the disease⁽¹⁷⁾.

Similar findings were observed in our study, as CSA of the tibial nerve was at its maximum in the diabetic patients with diabetic neuropathy, followed by diabetic patients without neuropathy and the non-diabetic healthy volunteers (Table 1). Thus, CSA of the tibial nerve may be used as a marker for detecting DN and also in the grading of its severity.

Sheila Riazi *et al.* studied 98 diabetic patients classified by NCS. The severity of neuropathy was determined using TCNS. The cross-sectional area of the tibial nerve was measured at 1, 3, and 5 cm proximal to the level of the medial malleolus.

They concluded that CSA measured at 3 cm above the medial malleolus had an optimal threshold value for diagnosing diabetic peripheral neuropathy, with a sensitivity and specificity of 0.69 and 0.77 respectively⁽⁵⁾. In our study, we measure CSA at the level of 3cm proximal to the medial malleolus.

Kang *et al.*⁽¹⁹⁾ evaluated the role of multiple peripheral nerves in twenty diabetic neuropathy patients with twenty patients as controls. They concluded that CSAs of sural, tibial and median nerves show significant correlations with electrophysiological findings. CSA of sural nerve revealed a significant correlation with HbA1c levels⁽¹⁹⁾. In our study, CSA of the tibial nerve correlated significantly with TCNS and HbA1c levels, at $p < 0.001$.

Cartwright *et al.*²⁰ evaluated the CSA reference value studied for nerve sonography. In their study, the mean area of the tibial nerve at the ankle was 13.7 mm², which was greater than the value that we obtained. They also reported that age and height showed weak correlations with the nerve CSA, whereas weight and BMI showed stronger correlations with the nerve CSA. Their study participants' mean BMI and weight were 26.5 and 74.5 kg, respectively, which were markedly greater than those of our participants, explaining the discrepancy with our findings

A study by kunwarpal singh⁽²⁶⁾ and colleagues on High resolution ultrasonography of tibial nerve in diabetic peripheral neuropathy showed results similar to our study.

Conclusion

The main aim of this study is to find the usefulness and validity of high resolution ultrasound to detect the cases of diabetic peripheral neuropathy. In diabetic peripheral neuropathy, nerves become swollen and lose their normal echogenicity and hypoechoic areas develop within the nerves. So for this study, cross sectional area of the nerve and maximum thickness of the hypoechoic area in the nerve was taken as criterias and the values were measured and compared within the groups.

Demographic and biochemical data of the patients were also collected and compared within the groups so as to solidify the validity results.

Tibial nerve was selected as the nerve of choice as it is one the earliest nerves to get affected in diabetic neuropathy. And on comparison of cross sectional area and maximum thickness of nerve fascicles of the tibial nerve, High resolution ultrasound was able to detect almost all patients with diabetic neuropathy and the values were significantly higher than the normal cut off.

And also in diabetic patients without any symptoms of neuropathy, the values were high normal range and also significantly higher than the normal subjects.

Thus concluding that High resolution ultrasound of the peripheral nerve is a valuable tool in the diagnosis and early detection of diabetic peripheral neuropathy even before the onset of symptoms.

Bibliography

- Callaghan BC, Cheng HT, Stables CL, Smith AL, Feldman EL: Diabetic neuropathy: Clinical manifestations and current treatments. *Lancet Neurol* 2012; 11: 521–534.
- Llewelyn JG: The diabetic neuropathies: types, diagnosis and management. *J Neurol Neurosurg Psychiatry* 2003; 74: ii15–ii19.
- Catwright MS, Passmore LV, Yoon JS, Brown ME, Caress JB, Walker FO: Cross-sectional area reference values for nerve ultrasonography. *Muscle Nerve* 2008; 37: 566–571.
- Watanabe T, Ito H, Sekine A, Katano Y, Nishimura T, Kato Y *et al.*: Sonographic evaluation of the peripheral nerve in diabetic patients: the relationship between nerve conduction studies, echo intensity, and cross-sectional area. *J Ultrasound Med* 2010; 29: 697–708.
- Riazi S, Bril V, Perkins BA, Abbas S, Chan VW, Ngo M *et al.*: Can ultrasound of the tibial nerve detect diabetic peripheral neuropathy? A cross-sectional study. *Diabetes Care* 2012; 35: 2575–2579.
- Bril V, Perkins BA: Validation of the Toronto Clinical Scoring System for diabetic polyneuropathy. *Diabetes Care* 2002; 25: 2048–2052.
- Böhm J: High resolution sonography of peripheral nerves: normal values in healthy worth individuals and the role of sonography in rare disorders of peripheral nerves (doctoral dissertation).
- Silvestri E, Martinoli C, Derchi LE, Bertolotto M, Chiaramondia M, Rosenberg I: Echotexture of peripheral nerves: correlation between US and histologic findings and criteria to differentiate tendons. *Radiology* 1995; 197: 291–296.
- Lawande AD, Warriar SS, Joshi MS: Role of ultrasound in evaluation of peripheral nerves. *Indian J Radiol Imaging* 2014; 24: 254–258.
- Perkins BA, Bril V: Diabetic neuropathy: a review emphasizing diagnostic methods. *Clin Neurophysiol* 2003; 114: 1167–1175.
- Arezzo JC: The use of electrophysiology for the assessment of diabetic neuropathy. *Neurosci Res Commun* 1997; 21: 13–23.
- Fantino O, Coillard JY, Borne J, Bordet B: Ultrasound of the tarsal tunnel: Normal and pathological imaging features. *J Radiol* 2011; 92: 1072–1080.
- Bae JS, Kim BJ: Subclinical diabetic neuropathy with normal conventional electrophysiological study. *J Neurol* 2007; 254: 53–59.
- Kowalska B, Sudoł-Szopińska I: Normal and sonography anatomy of selected peripheral nerves. Part III: Peripheral nerves of the lower limb. *J Ultrason* 2012; 12: 148–163.
- Kim WK, Kwon SH, Lee SH, Sunwoo I: Asymptomatic electrophysiologic carpal tunnel syndrome in diabetics: Entrapment or polyneuropathy. *Yonsei Med J* 2000; 41: 123–127.
- Dyck PJ, Kratz KM, Karnes JL, Litchy WJ, Klein R, Pach JM *et al.*: The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester Diabetic Neuropathic Study. *Neurology* 1993; 43: 817–824.
- Ishibashi F, Taniguchi M, Kojima R, Kawasaki A, Kosaka A, Uetake H: Morphological changes of the peripheral nerves evaluated by high-resolution ultrasonography are associated with the

- severity of diabetic neuropathy, but not corneal nerve fiber pathology in patients with type 2 diabetes. *J Diabetes Investig* 2015; 6: 334–342.
18. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ *et al.*: Translating the A1C assay into estimated average glucose values. *Diabetes Care* 2008; 31: 1473–1478.
 19. Kang S, Kim SH, Yang SN, Yoon JS: Sonographic features of peripheral nerves at multiple sites in patients with diabetic polyneuropathy. *J Diabetes Complications* 2016; 30: 518–523.
 20. Cartwright MS, Passmore LV, Yoon JS, Brown ME, Caress JB, Walker FO. Cross-sectional area reference value for nerve ultrasonography. *Muscle Nerve* 2008; 37:566–571.
 21. Dyck PJ, Kratz KM, Karnes JL, et al. The prevalence by staged severity of various types of diabetic neuropathy, retinopathy, and nephropathy in a population-based cohort: the Rochester diabetic neuropathic study. *Neurology* 1993; 43:817–824.
 22. Severinsen K, Andersen H. Evaluation of atrophy of foot muscles in diabetic neuropathy: a comparative study of nerve conduction studies and ultrasonography. *Clin Neurophysiol* 2007; 118:2172–2175.
 23. Suzuki E, Yasuda K, Yasuda K, et al. ¹H-NMR analysis of nerve edema in the streptozotocin-induced diabetic rat. *J Lab Clin Med* 1994; 124:627–637.
 24. M Graif, A.Seton, J.Nerubai, H. Horoszowski, Y, Itzhak. Sciatic nerve: Sonographic evaluation and anatomic considerations.
 25. Duncan I, Sullivan P, Lomas F. Sonography in the diagnosis of carpal tunnel syndrome. *AJR Am J Roentgenol.* 1999;173:681–684
 26. Kunwarpal S, Kamlesh G, Sukhdeep k : HRUSG of tibial nerve in Diabetic neuropathy, 2017; 17:246-252.
 27. Heckmatt JZ, Dubowitz V, Leeman S. Detection of pathological change in dystrophic muscle with B-scan ultrasound imaging. *Lancet.* 1980;1:1389–1390.