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ULTRASONOGRAPHIC TIBIAL NERVE CROSS-SECTIONAL AREA AND ITS CORRELATION WITH NERVE CONDUCTION PARAMETERS AND CLINICAL SEVERITY IN DIABETIC PERIPHERAL NEUROPATHY: A CROSS-SECTIONAL STUDY OF 140 CASES

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ABSTRACT

Background: Diabetic peripheral neuropathy (DPN) is a common microvascular complication of diabetes mellitus. High-resolution ultrasonography (HRUS) has emerged as a non-invasive tool to assess peripheral nerve morphology.**Objective:** To evaluate tibial nerve cross-sectional area (CSA) and its correlation with nerve conduction study (NCS) parameters and clinical severity (mTCNS), and to determine diagnostic performance using ROC analysis.**Materials and Methods:** A cross-sectional study was conducted on 140 patients with type 2 diabetes mellitus. Tibial nerve CSA was measured at the ankle using HRUS. NCS parameters (amplitude, latency, conduction velocity) were recorded bilaterally. Clinical severity was assessed using modified Toronto Clinical Neuropathy Score (mTCNS). Statistical analysis was performed using SPSS v26. Pearson correlation, ROC curve analysis, and multivariate logistic regression were applied.**Results:** Mean age was 56.8 ± 8.4 years. Mean tibial nerve CSA was 16.82 ± 3.12 mm² (right) and 16.54 ± 3.05 mm² (left). CSA positively correlated with mTCNS ($r = 0.46$, $p < 0.001$). Negative correlation was observed between CSA and tibial CMAP amplitude ($r = –0.42$, $p < 0.001$). ROC analysis showed AUC 0.82 (95% CI: 0.75–0.88). Optimal CSA cut-off was 17.1 mm² (Sensitivity 81%, Specificity 74%). Multivariate regression showed CSA independently predicted DPN (OR 1.28; 95% CI 1.12–1.47; $p < 0.001$).**Conclusion:** Tibial nerve CSA is significantly associated with electrophysiological abnormalities and clinical severity. Ultrasonography may serve as an adjunct diagnostic tool in DPN.

KEYWORDS

Diabetic peripheral neuropathy, Ultrasonography, Cross-sectional area, mTCNS, ROC curve, Logistic regression

INTRODUCTION

Diabetic peripheral neuropathy (DPN) is one of the most common and debilitating long-term complications of diabetes mellitus, affecting almost half of all patients with the disease.[1]. The worldwide increase in type 2 diabetes has consequently elevated the incidence of neuropathic complications, resulting in considerable morbidity, diminished quality of life, foot ulceration, and heightened risk of lower-limb amputation.[2] Diabetic peripheral neuropathy (DPN) is characterized by a progressive, length-dependent sensorimotor polyneuropathy stemming from chronic hyperglycemia-induced metabolic and microvascular changes.[3]

Activation of the polyol pathway, oxidative stress, accumulation of advanced glycation end products (AGEs), activation of protein kinase C, and mitochondrial dysfunction are all part of the multifactorial pathogenesis of DPN.[4] Axonal degeneration and segmental demyelination eventually follow from these metabolic disruptions, which also cause endothelial dysfunction and reduced nerve blood flow.[5] Loss of nerve fibers, damage to Schwann cells, and thickening of the endoneurial microvasculature are examples of structural alterations.[6]

Nerve conduction studies (NCS), which mainly evaluate large myelinated fibers and identify variations like decreased conduction velocity, prolonged distal latency, and decreased compound muscle action potential (CMAP) amplitude, are currently regarded as the gold standard for objective diagnosis of DPN.[7] However, NCS may miss early or small-fiber neuropathy because they assess functional impairment rather than morphological changes. Additionally, NCS take a lot of time, rely on the operator, and can cause discomfort for patients.

One promising non-invasive imaging technique for evaluating peripheral nerves is high-resolution ultrasonography (HRUS)[9]. It enables cross-sectional area (CSA) measurement, echotexture, and nerve morphology visualization in real time. It is believed that endoneurial edema, microvascular congestion, and connective tissue proliferation[10] cause nerve enlargement in DPN. Patients with diabetic neuropathy have been consistently found to have higher CSA of the tibial and sural nerves when compared to controls[11].

Significant relationships between elevated nerve CSA and electrophysiological parameters have been shown in a number of studies, indicating a structural-functional relationship in DPN[12]. Despite these results, universal clinical adoption has been hampered by heterogeneity in methodology, small sample sizes, and variation in cut-off values. Additionally, there is still little data on the independent predictive value of nerve CSA after controlling for confounding factors like age and diabetes duration.

To elucidate the diagnostic utility of HRUS in DPN, a thorough assessment that incorporates clinical severity scoring, electrophysiological parameters, and ultrasonographic measurements is necessary.

OBJECTIVES

1. To assess CSA of the tibial nerve in individuals with type 2 diabetes.
2. To compare tibial nerve CSA and NCS parameters.
3. To compare tibial nerve CSA and clinical severity (mTCNS).
4. To assess CSA's diagnostic performance
5. To evaluate independent predictors of DPN.

MATERIALS AND METHODS

A Hospital-based cross-sectional study was conducted among 140 patients with type 2 diabetes mellitus in the Department of Radiodiagnosis, RajaRajeswari Medical College and Hospital, Bangalore, over a period of 24 months.

Patients with type 2 diabetes mellitus with age more than thirty years, presenting with symptoms suggestive of peripheral neuropathy and referred to the Department of Radiodiagnosis for ultrasonographic evaluation and were willing to give consent were included in the study.

Patients with other known causes of peripheral neuropathy, Patients with amputated lower limbs were excluded from the study.

Method of data collection

Patients who met the inclusion criteria were told about the study and given signed consent after a thorough clinical evaluation. According to the proforma, pertinent clinical information was documented. High-frequency linear transducers on SAMSUNG RS80A and ESAOTE MyLab Class-C ultrasound equipment were used to perform the ultrasonographic examination.

In both axial and sagittal planes, the posterior tibial nerves of both lower limbs were assessed at the level of the medial malleolus. The posterior tibial vessels were located next to the nerve.

The posterior tibial nerve's cross-sectional area was measured as part of the quantitative evaluation. The evaluation of fascicular (honeycomb) pattern, general nerve shape, and echogenicity were all part of the qualitative assessment.

RESULTS

Graph 1: Gender distribution

When applicable, associated abnormalities of the surrounding circulatory structures and soft tissues were also evaluated.

Severity of neuropathy was assessed using the Modified Toronto Clinical Neuropathy Score.[13] Nerve conduction study parameter[7], wherever available, were recorded and correlated with ultrasonographic findings.

All observations were systematically recorded, compiled and analysed.

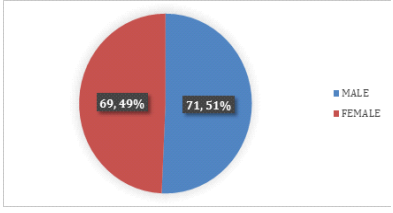
Nerve Conduction Study [7]

Parameters recorded:

- Tibial CMAP amplitude
- Distal latency
- Conduction velocity

Statistical Analysis

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software, version 26.0 (IBM Corp., Armonk, NY, USA). While categorical data were shown as frequencies and percentages, continuous variables were given as mean ± standard deviation (SD). Before inferential analysis, the distribution's normality was evaluated. The association between tibial nerve cross-sectional area (CSA) and clinical and electrophysiological characteristics was assessed using Pearson's correlation coefficient. To test the diagnostic efficacy of CSA in identifying diabetic peripheral neuropathy and to define the ideal cut-off value based on maximal sensitivity and specificity, receiver operating characteristic (ROC) curve analysis was carried out. To determine independent predictors of neuropathy, multivariate logistic regression analysis was conducted by adjusting for relevant covariates. A p-value of less than 0.05 was considered statistically significant for all analyses.



The study included 51% of males and 49% females. (Graph 1)

Table 1: Baseline Characteristics

Variable	Mean ± SD
Age (years)	56.8 ± 8.4
Duration of DM (years)	15.11 ± 4.3
mTCNS score	14.8 ± 4.1
Right Tibial CSA (mm²)	16.82 ± 3.12
Left Tibial CSA (mm²)	16.54 ± 3.05

The mean age of the study participants was 56.8 ± 8.4 years, indicating that the majority of patients belonged to the middle-aged to elderly group. The average duration of diabetes mellitus was 15.11 ± 4.3 years, suggesting long-standing disease in most cases. The mean modified Toronto Clinical Neuropathy Score (mTCNS) was 19.8 ± 4.1, reflecting mild to moderate neuropathy severity within the study population.

On ultrasonographic evaluation, the mean cross-sectional area (CSA) of the tibial nerve was 16.82 ± 3.12 mm² on the right side and 16.54 ± 3.05 mm² on the left side. The comparable values on both sides indicate symmetrical nerve involvement, which is characteristic of diabetic peripheral neuropathy. (Table 1)

Table 2: USG features

USG feature		Right Limb	Left limb
Echogenicity	Increased	87	86
	Normal	53	54
Honey comb pattern	Lost	72	64
	Normal	68	76
Other USG features	Hyperechoic foci	7	4
	Hyperechoic rim	4	5
	Normal	129	132

On ultrasonographic evaluation, increased echogenicity of the tibial nerve was observed in 87 (62.1%) right limbs and 86 (61.4%) left limbs, while normal echogenicity was seen in 53 (37.9%) and 54 (38.6%) limbs respectively. The predominance of increased echogenicity suggests structural alteration of the nerve, likely reflecting intraneural fibrosis, endoneurial edema, or chronic metabolic injury associated with diabetic peripheral neuropathy.

Loss of the normal honeycomb pattern, which represents disruption of the normal fascicular architecture, was identified in 72 (51.4%) right limbs and 64 (45.7%) left limbs. Preservation of the normal fascicular pattern was noted in 68 (48.6%) right limbs and 76 (54.3%) left limbs. The relatively high proportion of fascicular pattern loss supports morphological nerve damage consistent with neuropathic involvement. (Table 2)

Regarding additional ultrasonographic features, hyperechoic foci were detected in 7 (5.0%) right limbs and 4 (2.9%) left limbs, while a hyperechoic rim was observed in 4 (2.9%) right limbs and 5 (3.6%) left limbs. The majority of limbs (129 right and 132 left) demonstrated no additional abnormal findings. These focal echogenic changes may represent localized fibrosis or perineural thickening, although they were relatively uncommon in the present cohort. (Table 2)

Overall, ultrasonographic findings demonstrate symmetrical structural abnormalities in both limbs, characterized predominantly by increased echogenicity and partial loss of normal fascicular architecture. These findings support the presence of diffuse, length-dependent neuropathic changes typical of diabetic peripheral neuropathy. (Table 2)

Table 3: Correlation Analysis (Pearson)

Variables	r value	p value
CSA vs mTCNS	0.46	<0.001*
CSA vs CMAP amplitude	–0.42	<0.001*
CSA vs Conduction velocity	–0.39	<0.001*

*-significant

CSA showed moderate positive correlation with clinical severity, negative correlation with electrophysiological function indicates structural enlargement with worsening neuropathy. (Table 3)

Table 4: Mtcns Score comparison across USG features

USG Feature		n	mTCNS score	p value
Echogenicity	Increased	87	11.6 ± 3.8	<0.001*
	Normal	53	7.2 ± 3.1	
Honey comb pattern	Lost	72	12.3 ± 3.9	<0.001*
	Normal	68	7.4 ± 3.2	
Other USG features	Hyperechoic foci	7	13.1 ± 4.0	0.02*
	Hyperechoic rim	4	12.8 ± 3.6	
	Normal	129	9.4 ± 4.0	

*-significant

Significantly higher mTCNS scores ($p < 0.001$) were seen in patients with increased echogenicity and loss of the typical honeycomb pattern, suggesting that structural nerve changes are closely linked to higher clinical severity of diabetic neuropathy. Furthermore, despite smaller subgroup sizes, the presence of hyperechoic foci or rim was associated with higher mTCNS scores ($p = 0.02$), indicating that these focused ultrasonographic alterations may represent advanced neuropathic involvement.(Table 4)

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Table 5: ROC Curve Analysis

Parameter	Value
AUC	0.82
95% CI	0.75–0.88
Optimal Cut-off	17.1 mm²
Sensitivity	81%
Specificity	74%

CSA shows good diagnostic accuracy in detecting DPN at cut off of 17.1mm2 with AUC of 0.82, Sensitivity of 81% and Specificity of 74%. (Table 5)

Table 6: Multivariate Logistic Regression

Variable	B	Std. Error	Wald	p-value	Interpretation

CSA (mm^2)	0.246	0.069	12.71	<0.001	Significant independent predictor; increasing CSA increases odds of DPN
Duration of DM	0.086	0.033	6.80	0.01	Significant predictor; longer duration increases risk of DPN
Age in years	0.020	0.016	1.56	0.21	Not statistically significant predictor

Multivariate logistic regression analysis demonstrated that tibial nerve cross-sectional area (CSA) was a significant independent predictor of diabetic peripheral neuropathy (B = 0.246, p < 0.001). Each 1 mm^2 increase in CSA increased the odds of neuropathy by approximately 28%. Duration of diabetes mellitus was also a significant predictor (B = 0.086, p = 0.01), indicating progressive risk with longer disease duration. However, age did not show a statistically significant association after adjustment (p = 0.21), suggesting that nerve enlargement is more strongly related to disease duration and structural changes rather than chronological age alone. (Table 6)

DISCUSSION

The current study used high-resolution ultrasonography (HRUS) to assess structural changes in the tibial nerve and correlated the results with electrophysiological parameters and clinical severity in patients with diabetic peripheral neuropathy (DPN). Middle-aged people with long-term diabetes (mean duration 15.11 ± 4.3 years) made up the majority of the study sample, which is consistent with the known progressive nature of neuropathy in chronic hyperglycaemia.[3]

Our study's mean tibial nerve CSA (16.82 ± 3.12 mm^2 right; 16.54 ± 3.05 mm^2 left) showed symmetrical expansion in line with the bilateral and length-dependent pattern of DPN. Kerasnoudis et al.11 and Riazi et al.10 showed similar bilateral nerve enlargement and found that diabetes patients had considerably higher tibial nerve CSA than controls. Similar mean CSA values (about 16–18 mm^2) were also seen in more recent data from Singh et al.12 supporting the idea that tibial nerve expansion is a repeatable morphological marker in DPN.

Over 60% of the limbs in our group showed increased echogenicity, indicating structural nerve change. This result is similar to that of Tawfik et al.14 who found that 58% of DPN patients had increased echogenicity, which they attributed to intraneural fibrosis and microvascular impairment. The idea that persistent hyperglycaemia causes structural remodeling of peripheral nerves is supported by Liu et al.'s15 description of echogenic alterations that correlate with metabolic severity.

Almost half of our patients had loss of the typical honeycomb (fascicular) pattern. Recent ultrasonographic studies have also reported this architectural disturbance. According to a 2021 study by Sharma et al.16 fascicular distortion was shown to be significantly correlated with neuropathy severity scores in 47% of DPN cases. These results are consistent with our findings that the course of disease is correlated with structural disorganization.

Importantly, the present study demonstrated a moderate positive correlation between CSA and clinical severity (mTCNS), along with a negative correlation between CSA and electrophysiological parameters. This structural–functional association has been supported by multiple contemporary studies. Singh et al.12 found a significant negative correlation between CSA and CMAP amplitude (r ≈ –0.40), closely mirroring our results. Additionally, Kerasnoudis et al.11 showed that larger nerve CSA was associated with reduced conduction velocity, reinforcing the concept that morphological enlargement reflects axonal dysfunction.

Patients with increased echogenicity and loss of fascicular pattern exhibited significantly higher mTCNS scores (p < 0.001). These findings are consistent with the study by Breiner et al.17, who demonstrated that ultrasound-detected structural abnormalities strongly correlate with clinical neuropathy scales. Furthermore, hyperechoic foci and rim, though less common, were associated with higher mTCNS scores in our study (p = 0.02). Similar focal echogenic abnormalities were described by Padua et al.18, who suggested that such changes may represent advanced fibrotic remodeling in severe neuropathy.

The diagnostic performance of CSA in our study was notable, with an AUC of 0.82 at a cut-off value of 17.1 mm^2 (Sensitivity 81%, Specificity 74%). These results are comparable to those of Liu et al.15(AUC 0.80) and Sharma et al.16 (AUC 0.78–0.84), supporting the reliability of tibial nerve CSA as a diagnostic parameter. Riazi et al.10 reported a cut-off around 16.5 mm^2 for detecting DPN. Kerasnoudis et al.11 observed abnormal CSA values typically exceeding 17 mm^2 in moderate-to-severe neuropathy. Singh et al.12 (2021) identified a diagnostic threshold of approximately 16.8 mm^2. Liu et al.15 (2022) reported optimal cut-offs ranging between 16.0–17.5 mm^2 depending on severity stratification. Sharma et al.16 (2023) demonstrated a cut-off of 16.8 mm^2 with sensitivity around 78–82%. Minor variations in cut-off values across studies may be attributed to ethnic differences, probe frequency, and measurement level.

Multivariate logistic regression analysis demonstrated that CSA was an independent predictor of DPN (OR ≈ 1.28 per mm^2 increase), even after adjusting for age and duration of diabetes. This finding aligns with recent multivariate analyses by Won et al.19, who reported nerve CSA as an independent risk factor after controlling for metabolic variables. Our finding that duration of diabetes was also a significant predictor (p = 0.01) is consistent with established epidemiological evidence that prolonged hyperglycaemia accelerates neuropathic damage.3 Interestingly, age did not remain significant after adjustment, suggesting that neuropathic structural changes are more strongly influenced by metabolic exposure than chronological aging.

Overall, the present study reinforces the growing evidence that HRUS is not merely a supplementary imaging tool but a clinically meaningful modality capable of reflecting structural severity, functional impairment, and diagnostic probability in DPN. The integration of CSA measurement with clinical scoring and electrophysiological evaluation provides a comprehensive assessment framework for diabetic neuropathy.

CONCLUSION

The present study demonstrates that high-resolution ultrasonography is a valuable adjunctive modality in the evaluation of diabetic peripheral neuropathy. Tibial nerve cross-sectional area (CSA) was significantly increased in patients with long-standing diabetes and showed a meaningful association with clinical severity as assessed by mTCNS, as well as with electrophysiological dysfunction. Structural abnormalities such as increased echogenicity and loss of the normal fascicular (honeycomb) pattern were strongly correlated with higher neuropathy severity scores, supporting the concept that morphological nerve changes parallel functional deterioration.

The diagnostic performance of CSA was found to be good, with an optimal cut-off value of 17.1 mm^2 demonstrating satisfactory sensitivity and specificity. Importantly, multivariate analysis confirmed CSA as an independent predictor of diabetic peripheral neuropathy, even after adjusting for age and duration of diabetes. These findings underscore the potential of ultrasonographic nerve assessment as a non-invasive, reproducible, and clinically meaningful tool for early detection and severity stratification of DPN.

Incorporating ultrasonography alongside clinical scoring and nerve conduction studies may enhance comprehensive neuropathy assessment. Further longitudinal studies are warranted to determine its prognostic value and utility in monitoring disease progression.

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