Original Article

Cross-Sectional Study of the Relationship Between Medial Plantar Nerve Conduction Studies and Severity of Diabetic Neuropathy

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Abstract

Objective: Diabetic peripheral neuropathy (DPN), a complication of diabetes, is detected only in later stages. Medial plantar nerve (MPL) can identify earlier stages of neuropathy. We evaluated the correlation of MPL sensory nerve action potentials (SNAPs) and severity of DPN measured using the Toronto Clinical Neuropathy Score (TCNS). **Methods:** In this hospital-based, cross-sectional study, we recruited diabetic subjects referred for suspected DPN. Neuropathy was graded with TCNS. Sural nerve conduction studies were performed using standard techniques. MPL studies were conducted using the modified Ponsford technique. All evaluations were performed on Nihon Kohden (model MEB 9200K). Averaged MPL SNAP was correlated with TCNS using Pearson's correlation coefficient. To estimate a correlation of 0.4 with 80% power ($P = 0.05$), we needed 46 subjects. Linear regression was conducted to adjust for age, duration, and diabetic control. Receiver operating characteristic (ROC) curve analysis was performed to obtain the cutoff for MPL SNAP values using the Youden index. **Results:** Fifty-one subjects with a mean age of 53.5 years (8.7) and mean duration of diabetes of 10.2 years (7.2) were included. MPL SNAPs were recordable in 12 patients, and the mean amplitude was 5.15 (2.9) μV. There was correlation between MPL SNAP and TCNS ($r = –0.43$, $P = 0.02$). No confounding was seen. Use of MPL SNAP resulted in diagnosis of DPN in an additional six (11.8%) patients. The ROC curve suggested that MPL SNAP cutoff of 1.05 μV had an accuracy of 67% in identifying neuropathy as defined by TCNS. **Conclusions:** MPL SNAP has a moderate correlation with clinical score and identifies more diabetic neuropathy than sural nerve.

Keywords: Sensory nerve action potential, sural nerve, Toronto Clinical Neuropathy rating Score

Introduction

Diabetic peripheral neuropathy (DPN) is an insidious, length-dependent neuropathy that involves the motor, sensory, and autonomic nerve fibers. Though there are different forms of diabetic neuropathy, the most common form is distal symmetric polyneuropathy.[1] It is believed that around one-third of diabetics have prevalent DPN and around half will develop it in their lifetime.[2] Unlike diabetic nephropathy and retinopathy where the disease is detected early, diabetic neuropathy is often diagnosed only in its pre-ulcerative stage and is an important cause of morbidity in this population.[3]

Currently, diagnosis and screening for DPN depend largely on questionnaires, neurologic examination, and monofilament testing.[4] Toronto Clinical Neuropathy Score (TCNS) is one such widely used composite scoring system that includes both symptoms and signs.[4] The maximum score of TCNS is 19, and severity is graded as 0–5: no DPN, 6–8: mild DPN, 9–11: moderate DPN, and >12: severe DPN.[4,5] This instrument has been previously used for diagnosis for DPN in India also.[6]

Nerve conduction studies continue to remain as the reference standard for diagnosis of DPN.[4] According to the Toronto DPN international consensus, one should demonstrate one symptom and/or sign with abnormality in nerve conduction studies for a diagnosis of DPN.[1,5] A stocking glove pattern of distribution is observed in typical diabetic neuropathy as it is length dependent and distal parts of a nerve are affected at first.[1] Routine nerve conduction studies evaluate sural nerve sensory conduction, though sural nerve is not the most distal nerve that can be evaluated. By the time its conduction parameters are affected, significant sensorimotor functions are already lost.[7] The medial plantar nerve (MPL) is a branch of the tibial nerve beyond the flexor retinaculum and is further distal to the sural nerve. It can be tested to elicit a sensory nerve action potential (SNAP). Recently, the normative values for MPL conduction parameters have been reported among Indian subjects.[8]

The utility of MPL for diabetic neuropathy was first suggested by Reeves *et al.*[9] in their study of 10 patients in whom

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they showed that MPL parameters improved with improved glycemic control. In a study that compared 20 patients with diabetes and controls, MPL was found to be abnormal in a larger proportion compared to sural nerve studies.[10]

In this study, we evaluate the correlation between the medial plantar SNAPs and severity of DPN measured using TCNS.

Methods

This was a hospital-based, cross-sectional study conducted between April and August 2023. Ethics approval was obtained. We recruited all consecutive diabetic subjects who had been referred to the electrodiagnostic lab for suspicion of diabetic neuropathy, after obtaining their written informed consent. We excluded pregnant women, those with established diabetic neuropathy, those with other risk factors for neuropathy (like chronic kidney disease), and subjects in whom nerve conduction studies in the lower limb might be difficult, like those with ulcers or edema. A previous study by Altun *et al*.[11] found a negative correlation between MPL amplitude and neuropathy symptoms score ($r = -0.36$, $P = 0.023$). Assuming a similar coefficient of 0.4 with an alpha of 0.05 and 80% power, it was estimated that 46 subjects would be required. After obtaining consent from the patients, their demographic details, duration of diabetes, last blood sugar values, last known glycated hemoglobin levels, other comorbidities, and current drug list were noted.

TCNS was performed using standard methodology and scored between 0 and 19, with higher scores indicating more severe neuropathy. Sural nerve on both sides was evaluated using the standard procedure, with stimulation proximal to the lateral malleolus. MPL on both sides was studied using the modified Ponsford technique [Supplement A]. If despite two attempts the nerve could not be stimulated, we classified it as not recordable and recorded the value as zero for amplitude. The MPL SNAPs and sural SNAPs obtained bilaterally were averaged, and this was correlated with TCNS scores using Pearson's correlation coefficient. For further analysis, we used only amplitudes, as latency and velocity estimation of these small amplitude potentials was more likely to be error prone. Comparison of sural SNAP and MPL SNAP for prediction of TCNS scores was done using multiple linear regression analysis, with age, duration of diabetes, and last available fasting blood sugar levels as the covariates. We plotted a receiver operating characteristic (ROC) curve for averaged MPL SNAPs for a diagnosis of neuropathy by TCNS using the nonparametric Delong method. We used the Youden index to define the optimum cutoff value. All statistical tests were carried out on STATA ver. 14.2 (StataCorp LLC, College Station, TX, USA) at a significance level of 0.05.

Results

We evaluated 51 diabetic patients who had been referred to the electrodiagnostic lab for nerve conduction studies with suspicion of diabetic neuropathy. The demographic characteristics of this group are presented in Table 1. The most common comorbidity seen was hypertension in 18 (35.3%) patients. The results of nerve conduction studies are presented in Table 2. Bilateral MPL could not be stimulated in 37 (72.5%) patients, and in an additional two individuals, the left MPL alone was not stimulable. Bilateral sural nerves were not stimulable in 17 (33.3%) patients, while in one individual, the right sural nerve alone and in another individual, the left sural nerve alone could not be stimulated. Sural SNAP abnormalities were seen in 31 (60.8%) patients. Using an age-appropriate cutoff for MPL amplitude (2.9 μV),[8] MPL SNAP abnormalities were seen in 42 (82.3%) patients. Only five (9.8%) patients had normal TCNS scores and normal nerve conduction studies. The proportion with abnormal sural nerve and MPL studies in each grade of severity by TCNS

Table 1: Baseline characteristics of patients

Parameter	Number of participants	Value
Age in years	51	53.5 (8.7)
Women	51	17 (33.3%)
Duration of diabetes in years	51	10.2 (7.2)
Fasting blood sugar in mg/dL	43	155.6 (96.6)
Postprandial blood sugar in mg/dL	38	247.9 (102.1)
HbA1c in %	25	8.1 (1.7)
Total TCNS[a]	51	6 (5)
Severity of neuropathy based on TCNS		
No neuropathy (0–5)		20 (39.2%)
Mild neuropathy (6–8)		18 (35.3%)
Moderate neuropathy (9–11)		8 (15.7%)
Severe neuropathy (≥12)		5 (9.8%)
Any comorbidity	51	19 (37.2%)

HbA1c = Glycated hemoglobin, TCNS = Toronto Clinical Neuropathy Score. [a]Values given as median (interquartile range); all other values given as mean (standard deviation) or *n* (%)

Table 2: Results of the nerve conduction studies of sural and medial plantar nerves

	Number recorded (of 51)	Value mean (SD)
Right medial plantar nerve		
Latency in milliseconds	12	2.97 (0.43)
Amplitude in microvolts		5.23 (3.07)
Conduction velocity in M/s		50.68 (7.07)
Left medial plantar nerve		
Latency in milliseconds	11	2.86 (0.56)
Amplitude in microvolts		6.09 (2.38)
Conduction velocity in M/s		54.17 (9.18)
Right sural nerve		
Latency in milliseconds	33	3.34 (2.67)
Amplitude in microvolts		10.15 (8.99)
Conduction velocity in M/s		46.9 (15.2)
Left sural nerve		
Latency in milliseconds	33	2.93 (0.36)
Amplitude in microvolts		8.74 (4.82)
Conduction velocity in M/s		46.8 (9.9)

SD = Standard deviation

is shown in Figure 1. Based on the Toronto DPN consensus statement, DPN by TCNS and sural nerve abnormalities was seen in 21 (41.2%) patients, and all of them had abnormal MPL SNAP. Combination of TCNS with MPL SNAP abnormalities identified an additional 32 (62.7%) patients with DPN.

The amplitude and conduction velocities of both nerves showed a negative correlation with increasing severity of neuropathy as evidenced by higher TCNS scores [Table 3, Figure 2]. TCNS has three components – the symptom score, the sensory exam score, and the reflex score. We evaluated the correlation of MPL SNAP with each of these subscores and found significant correlation only with the sensory exam score (r = –0.43, P = 0.02). Linear regression of TCNS using amplitudes of MPL, sural SNAP amplitudes, age, duration of diabetes, and fasting blood sugar (as a proxy for glycemic control) with backward elimination yielded the simplest model with only the amplitude of MPL being significantly associated, suggesting no confounding by these factors. MPL SNAPs accounted for of 8% of the variability (R^2 = 0.084) in TCNS, with a regression coefficient of –0.3 (–0.77 to –0.02, P = 0.039).

The area under the ROC curve of average MPL SNAP for neuropathy by TCNS was 0.6 (95% confidence interval = 0.44–0.72), suggesting moderate accuracy [Figure 3]. Using Youden index, a cutoff point of MPL SNAP amplitude of 1.05 µV was obtained with 66.7% correct classification rate [Table 4].

Discussion

Among subjects with suspected DPN, we were able to identify 21% more DPN using a combination of MPL SNAP abnormalities and clinical scores compared to clinical score and sural nerve abnormalities. The area under the ROC curve for MPL amplitude to identify those with clinical neuropathy by TCNS was suggestive of moderate accuracy, and the optimum cutoff point was 1.05 µV.

Kong *et al*.[12] identified 63,779 electrodiagnostic encounters for evaluation of diabetic neuropathy. They reported that in this group, 52.6% had abnormal sural and peroneal studies while 19.3% had normal studies of both nerves. They concluded that electrodiagnostic studies provided confirmatory evidence in 71.9% of this group. We also found a similar proportion of abnormal studies in both nerves (31, 60.8%) and normal studies (9, 17.6%), accounting for 78.4% having confirmatory evidence for the presence or absence of neuropathy, despite suspicion by the treating physician. When we used stricter diagnostic criteria for DPN as recommended by the Toronto DPN international consensus, we found a greater prevalence of DPN on using MPL SNAP abnormalities rather than sural abnormalities, with no extra case being missed. This definition resulted in an overall prevalence of DPN in our group of 32 (62.7%). This is higher than what has been reported,[13,14] but there is some evidence to suggest that the incidence of neuropathy may be higher in India due to possible associated nutritional deficiencies.[2]

When defining diabetic neuropathy as a TCNS score >5, we found that MPL amplitude had a moderate accuracy in identifying neuropathy as indicated by AUC. Galiero *et al*.[15] reported a similar accuracy of MPL amplitude for the detection of clinically identified neuropathy. They reported a cutoff point of 4.55 µV for those under 60 years of age and 2.65 µV for those >60 years of age. We were unable to perform such stratified analysis because of small numbers, but we found a smaller amplitude of 1.05 µV to have an accuracy of 66.7% with a similar specificity of 87.1% but a much lower sensitivity (35%) for diagnosis of diabetic neuropathy. This cutoff point is lower than the age-adjusted lower limit of normal value suggested by Sharma *et al*.[8]

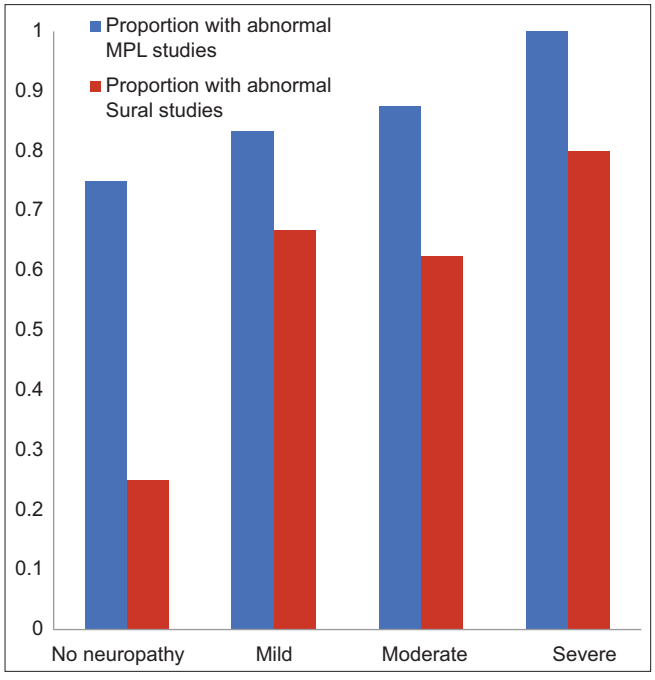

Figure 1: Proportion with abnormal sural and MPL SNAP by severity of neuropathy based on TCNS. TCNS = Toronto Clinical Neuropathy Score

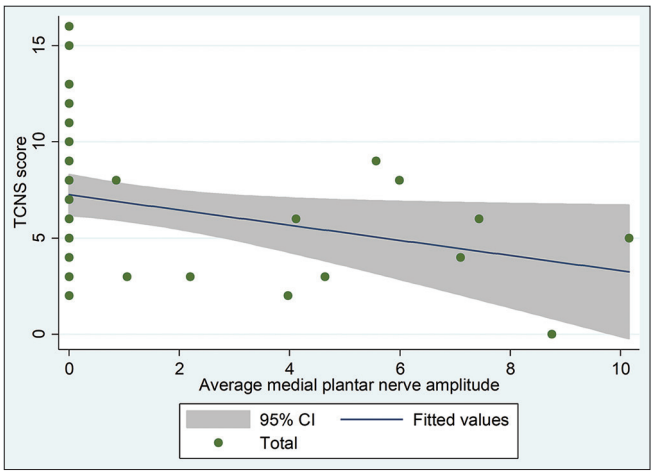

Figure 2: Correlation between average medial plantar nerve SNAP and TCNS scores. SNAP = sensory nerve action potential, TCNS = Toronto Clinical Neuropathy Score

In a study from Japan evaluating glycemic fluctuations in diabetic neuropathy, the authors found 13 of 40 patients (32.5%) had a sural nerve abnormality while 27 patients (67.5%) had an MPL abnormality.[16] Similarly, we had a higher incidence of abnormal MPL SNAP (60.8% sural vs. 82.3% MPL), and this appeared to increase with increased severity of neuropathy. Other authors have also reported finding increased frequency of abnormal MPL CNAPs in individuals with mixed small and large fiber neuropathy.[17] This suggests that MPL can identify diabetic neuropathy at an earlier state. This relationship is further corroborated by the moderate negative correlation we were able to demonstrate between MPL CNAP and TCNS score. Altun *et al.*[11] similarly wanted to evaluate the relationship between MPL CNAP and neuropathy symptoms score and neuropathy disability score. They reported a similar negative correlation between MPL CNAP and neuropathy symptoms score (P = 0.0001, r = –0.64). But unlike them, we found significant correlation with the sensory test scores. Other studies have also found such a negative correlation with diabetic neuropathy symptoms scores (r = –0.215, P = 0.03)[18]

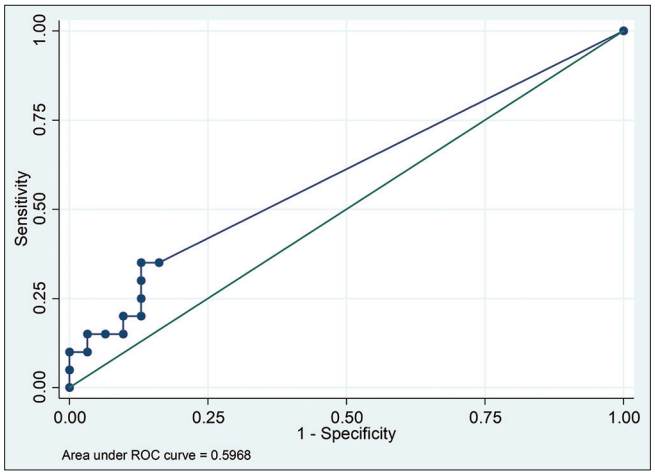

Figure 3: ROC curve of average medial plantar nerve SNAP and neuropathy as diagnosed by TCNS. ROC = Receiver operating characteristic, SNAP = sensory nerve action potential, TCNS = Toronto Clinical Neuropathy Score

We were adequately powered to estimate the correlation between the clinical score (TCNS) and MPL SNAP, and we included a fairly homogenous population with less-severe neuropathy and very little comorbidity. We did not look specifically for tarsal tunnel syndrome; however, motor nerve conduction studies across the tarsal tunnel of the tibial nerve, a highly sensitive measure of the tarsal tunnel,[19] were abnormal in only three subjects. Our study is limited by its cross-sectional design as we are unable to decide if this increased diagnosis of DPN will mean better clinical outcomes.

Conclusion

MPL SNAPs are correlated with clinical diabetic neuropathy scoring systems and can identify more patients with neuropathy

Table 3: Correlation of nerve conduction parameters with TCNS scores

Parameter	Value[a]	Correlation coefficient with TCNS score (*P*)
Average MPL latency in milliseconds	2.66 (0.59)	+0.10 (0.75)
Average MPL amplitude in microvolts	5.15 (2.9)	-0.29 (0.04)
Average MPL conduction velocity in M/s	47.9 (14.4)	-0.32 (0.02)
Average sural latency in milliseconds	3.04 (1.36)	+0.04 (0.79)
Average sural amplitude in microvolts	9.17 (6.42)	-0.26 (0.07)
Average sural conduction velocity in M/s	45.52 (13.57)	-0.22 (0.1)

MPL = Medial plantar nerve, TCNS = Toronto Clinical Neuropathy Score. [a]All values presented as mean (standard deviation)

Table 4: Results of ROC analysis

Cutoff point in microvolts	Sensitivity (%)	Specificity (%)	Correctly classified (%)	LR+	LR-
(≥0)	100.00	0.00	39.22	1	
(≥0.85)	35.00	83.87	64.71	2.17	0.775
(≥1.05)	35.00	87.10	66.67	2.7125	0.7463
(≥2.195)	30.00	87.10	64.71	2.325	0.8037
(≥3.97)	25.00	87.10	62.75	1.9375	0.8611
(≥4.115)	20.00	87.10	60.78	1.55	0.9185
(≥4.64)	20.00	90.32	62.75	2.0667	0.8857
(≥5.565)	15.00	90.32	60.78	1.55	0.9411
(≥5.99)	15.00	93.55	62.75	2.325	0.9086
(≥7.1)	15.00	96.77	64.71	4.65	0.8783
(≥7.435)	10.00	96.77	62.75	3.1	0.93
(≥8.75)	10.00	100.00	64.71		0.9
(≥10.15)	5.00	100.00	62.75		0.95
(>10.15)	0.00	100.00	60.78		1

LR+ = Positive likelihood ratio, LR− = Negative likelihood ratio, ROC = Receiver operating characteristic

than sural nerve studies. More long-term studies are needed to evaluate the ability of this early diagnosis to change clinical outcomes.

Acknowledgement

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Ethics

Institute ethics board approval was obtained (JIP/IEC-OS/165/2023). All participants provided written informed consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Supplement A

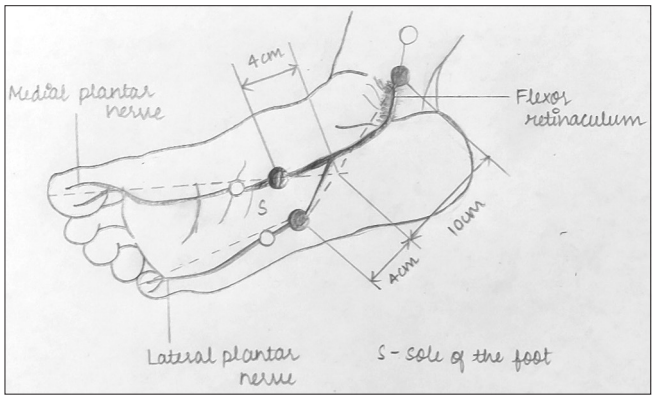

Figure A1: Diagram of modified Ponsford technique used for MPL nerve conduction studies. MPL = medial plantar nerve

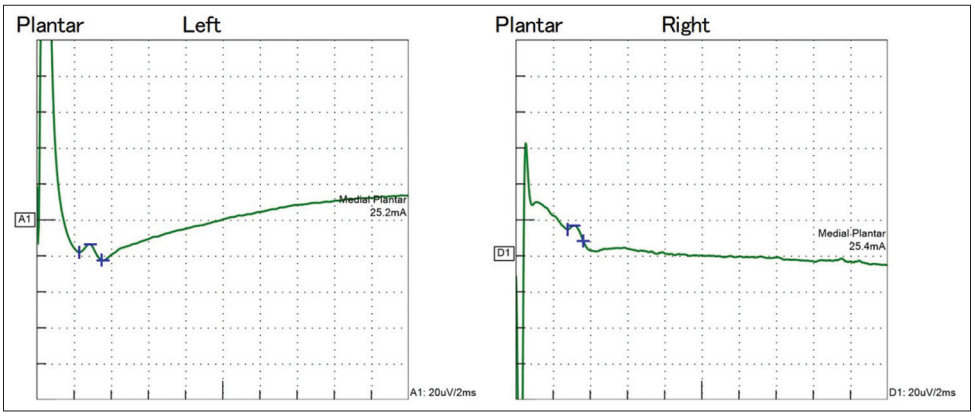

Figure A2: Tracing of medial plantar nerve SNAP. SNAP = sensory nerve action potential