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Reference values for the cross sectional area of normal tibial nerve on high-resolution ultrasonography

Kunwar Pal Singh, Sumanjeet Kaur, Vijinder Arora

Radiodiagnosis, Sgrd University of Health Sciences, India

Correspondence: Dr. Kunwar Pal Singh, Radiodiagnosis, SGRD University of Health Sciences, India; e-mail: kpsdhami@gmail.com

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Keywords
tibial nerve; cross sectional area (CSA); high-resolution ultrasonography (USG)

Abstract

Aim: The aim of the study was to establish reference values for the cross-sectional area of the tibial nerve on high-resolution ultrasonography and to investigate the relationship between the cross-sectional area of the tibial nerve and subject's age, gender, height (in cm), weight (in kg) and body mass index. **Methods:** Two hundred subjects of either gender and over 18 years of age with no history of peripheral neuropathy or trauma to the lower limb were evaluated with high-resolution ultrasonography. Mean cross-sectional areas of tibial nerves were measured at two different levels in both lower limbs, first at 1 cm below the bifurcation of the sciatic nerve into tibial and common peroneal nerves (level I) and the second at 1 cm superior and posterior to the medial malleolus (level II). **Results:** The mean cross-sectional area measured at level I (0.196 + 0.014 cm^2) was larger than the one measured at level II (0.111 ± 0.011 cm^2). A positive correlation was found between the mean cross-sectional area and height, weight, and body mass index (p <0.05). Women had smaller cross-sectional areas of the tibial nerves than men at both sites. In addition, no significant relationship was found with the age of the subjects (p >0.05). **Conclusion:** The established reference values of the cross-sectional area of the tibial nerve will aid in early diagnosis of peripheral neuropathy.

Introduction

Ultrasonography (USG) is a cost-effective imaging modality for peripheral nerve investigation[1]. Modern ultrasonography machines enable real-time, point-of-care imaging of nerves along with adjacent structures with high fidelity, without patient discomfort or radiation exposure. An important advancement in diagnostic ultrasound of peripheral nerves occurred after introduction of transducers with high frequencies (greater than 12–15 MHz)[2].

High-resolution US allows for assessing nerves over a long course within a few minutes[3]. Modern generation US scanners can illustrate subtle details of peripheral nerves[4].

The evaluation should begin from a recognized anatomic landmark proximate to the nerve. First, the nerve should be traced along its short axis and if any pathology is encountered, then the individual segment should be focused. The transducer is then turned in the long axis of the nerve for better evaluation[1]. Normal peripheral nerves comprise multiple longitudinal hypoechoic fascicular bundles giving typical sonographic appearance[5]. Fascicles along with endoneurial fluid are enclosed by the perineurium. Each fascicle is separated by collagen and they are clumped together by epineurium to form nerves. These features give nerves a specific "honeycomb" pattern[6].

The cross sectional area (CSA) variability is a beneficial parameter in inspecting peripheral nerve pathologies[7]. Motor nerves in the lower limb have larger CSA as compared to sensory nerves at same sites, and the CSA tends to be symmetrical in both limbs[8]. Sonography can easily demonstrate nerve enlargement, variation in the echogenicity of fascicles (either hypo or hyper-echogenicity), enlargement of fascicles and increased thickness of the epineurium[9]. Additionally, with the availability of power doppler imaging, it is now possible to assess vascular changes within major nerve segments[10].

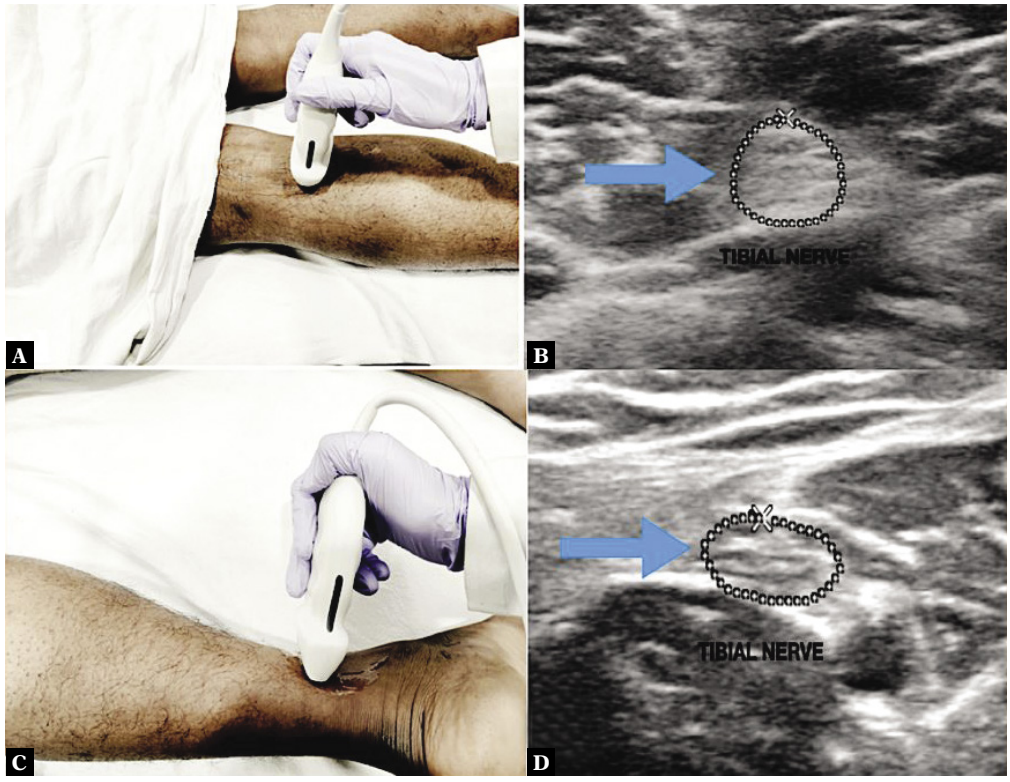

Fig. 1. A. *Subject lying in prone position, the transducer is kept perpendicular just 1 cm below the bifurcation of the sciatic nerve at the lower aspect of the popliteal fossa (corresponds to level I).* **B.** *High-resolution ultrasonography image at the same level showing normal tibial nerve (arrow).* **C.** *Transducer is kept 1 cm superior and posterior to the medial malleolus (corresponds to level II).* **D.** *High-resolution ultrasonography image at the same level showing the tibial nerve (arrow)*

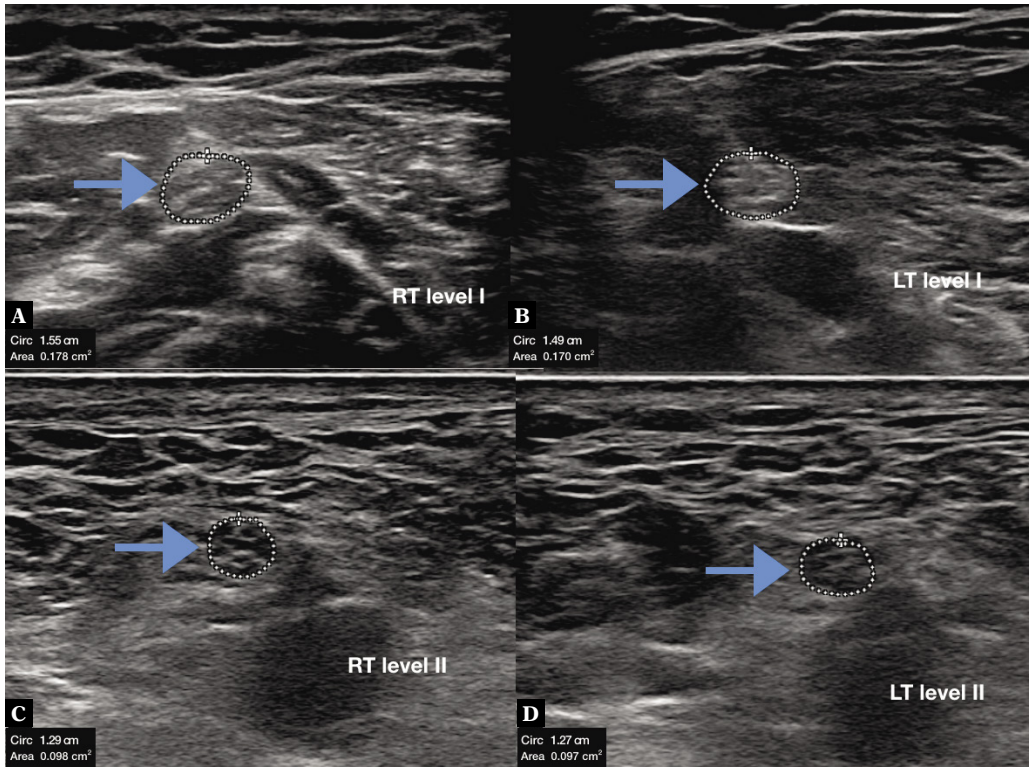

Fig. 2. *High-resolution ultrasonography of normal tibial nerve at level I (***A**, **B***) and II (***C**, **D***) in bilateral lower limb in 25 years old female weighing 46 kg, having height of 158 cm and body mass index of 19.1. Cross sectional area measured at level I was 0.178 cm² and 0.170 cm² and at level II was 0.098 cm² and 0.097 cm² in right and left lower limb, respectively (RT – right, LT – left, arrow – tibial nerve)*

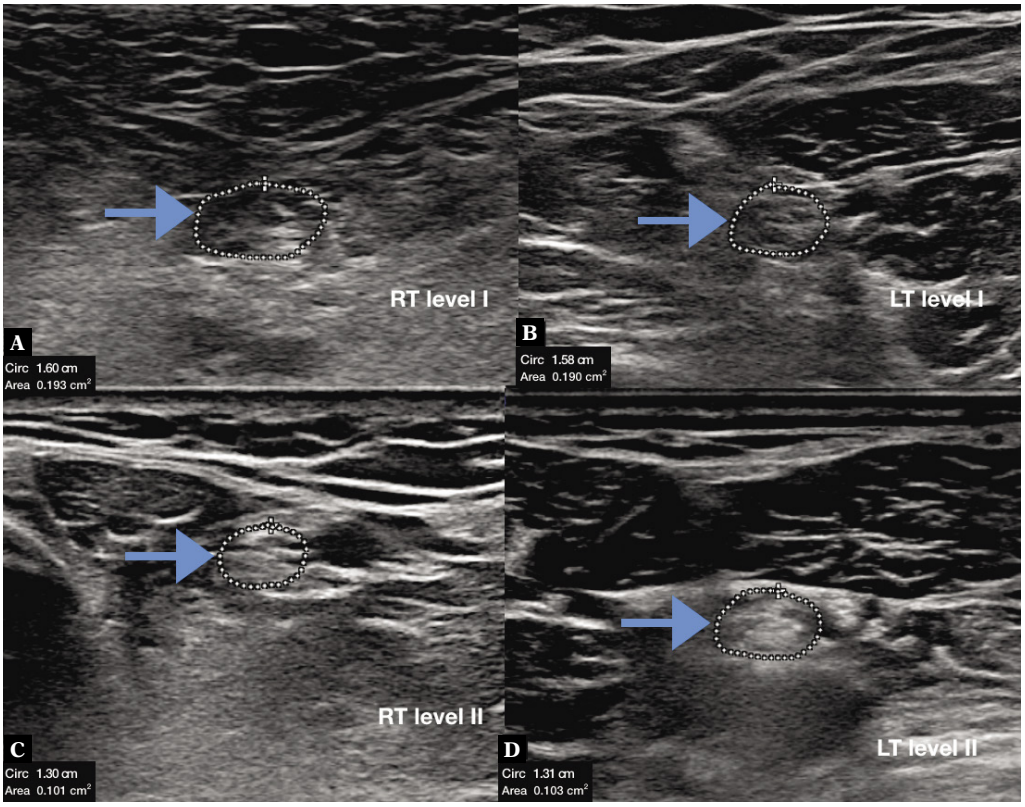

Fig. 3. *High resolution ultrasonography of normal tibial nerve at level I (***A***,* **B***) and II (images* **C***,* **D***) in left lower limb in 42 years old male weighing 63 kg, having height of 168 cm and body mass index of 22.3. Mean cross sectional area was 0.193 cm² and 0.190 cm² at level I and 0.101 cm² and 0.103 cm² at level II. (RT – right, LT – left, arrow – tibial nerve)*

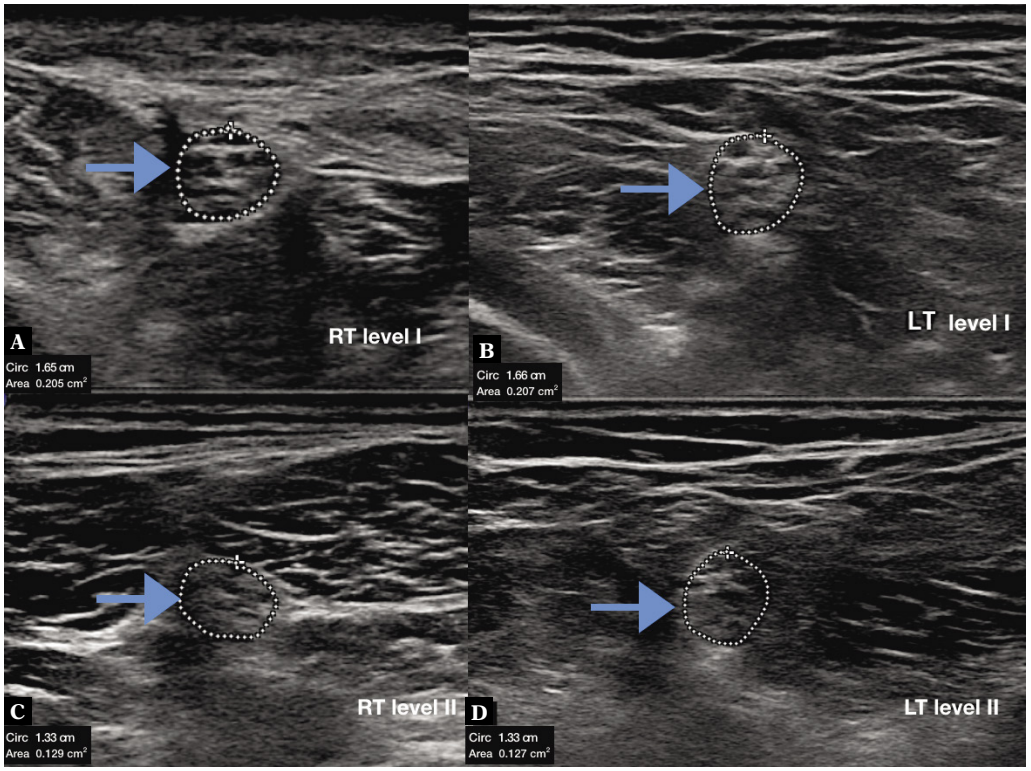

Fig. 4. *High resolution ultrasonography of normal tibial nerve at level I (***A***,* **B***) and II (***C***,* **D***) in bilateral lower limb in 61 years old male weighing 79 kg, having height of 177 cm and body mass index of 25.3. Cross sectional area was 0.205 cm² and 0.207 cm² at level I and 0.129 cm² and 0.127 cm² at level II in right and left lower limb respectively. (RT – right, LT – left, arrow – tibial nerve)*

Tab. 1. *Mean cross-sectional area (CSA) of the tibial nerve at two levels*

Levels	Cross-sectional area (cm²)	
	Mean	Standard deviation
Level I	0.196	0.014
Level II	0.111	0.011
p-value	0.001	

both clinical and electrodiagnostic assessment is needed, but the magnitude of injury cannot be well determined in the first six months due to the limitations of these approaches[12]. High-resolution US of peripheral nerves may become the tool of choice in the diagnosis of diabetic peripheral neuropathy[3].

Tab. 2. *Mean cross-sectional area (CSA) of both tibial nerves at levels I and II and their correlation with weight*

Weight (kg)	No. of cases	Level I mean CSA (cm²)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
≤60 (Group I)	64	0.18116	0.005671	*r* = 0.908 *p* = 0.001	0.18110	0.005591	*r* = 0.909 *p* = 0.001
61–70 (Group II)	60	0.19412	0.004268		0.19459	0.004425	
>70 (Group III)	76	0.21193	0.007021		0.21213	0.007113	
		Level II mean CSA (cm²)					
Weight (kg)	No. of cases	Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
≤60 (Group I)	64	0.09794	0.005812	*r* = 0.918 *p* = 0.001	0.09870	0.006217	*r* = 0.903 *p* = 0.001
61–70 (Group II)	70	0.11092	0.003175		0.11145	0.003194	
>70 (Group III)	76	0.12405	0.004734		0.12369	0.005031	

Tab. 3. *Mean cross sectional area (CSA) of both tibial nerves at levels I and II and their correlation with height*

Height (cm)	No. of cases	Lower limb level I mean CSA (cm²)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
≤165 (Group I)	74	0.18330	0.008366	*r* = 0.857 *p* = 0.001	0.18339	0.008204	*r* = 0.850 *p* = 0.001
166–175 (Group II)	63	0.19641	0.005966		0.19691	0.006370	
0 >175 (Group III)	63	0.21285	0.007225		0.21288	0.007830	
Height (cm)	No. of cases	Lower limb level II mean CSA (cm²)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
≤165 (Group I)	74	0.10005	0.007583	*r* = 0.855 *p* = 0.001	0.10083	0.007720	*r* = 0.834 *p* = 0.001
166–175 (Group II)	63	0.11266	0.004997		0.11306	0.005514	
>175 (Group III)	63	0.12459	0.005458		0.12413	0.005470	

Tab. 4. *Mean cross sectional area (CSA) of both tibial nerves at levels I and II and their correlation with body mass index (BMI)*

Body mass index	No. of cases	Lower limb level I mean CSA (cm²)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
19.5–22.5 (Group I)	84	0.18540	0.009219	*r* = 0.768 *p* = 0.001	0.18553	0.009138	*r* = 0.767 *p* = 0.001
22.6–24.5 (Group II)	80	0.20050	0.008742		0.20073	0.009125	
>24.5 (Group III)	36	0.21485	0.009913		0.21516	0.009689	
Body mass index	No. of cases	Lower limb level II mean CSA (cm²)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
19.5–22.5 (Group I)	84	0.10228	0.008917	*r* = 0.735 *p* = 0.001	0.10293	0.008621	*r* = 0.730 *p* = 0.001
22.6–24.5 (Group II)	80	0.11561	0.007212		0.11558	0.007218	
>24.5 (Group III)	36	0.12531	0.007759		0.12532	0.007666	

Therefore, US helps in early detection of neuropathy and its causes, such as traumatic, inflammatory, infective, neoplastic and compressive pathologies, which previously required resource-intensive nerve conduction studies[1,11]. In the case of traumatic peripheral nerve injuries,

Materials and methods

The study included 200 subjects. Individuals >18 years of age, with no history of peripheral neuropathy or trauma to the lower limb, who were referred to the Department

Tab. 5. *Mean cross-sectional area (CSA) of both tibial nerves at levels I and II and their correlation with age*

Age group (years)	No. of cases	Level I mean CSA (cm^2)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
18–30 (Group I)	43	0.19494	0.014106	$r = 0.254$ $p = 0.081$	0.19424	0.012472	$r = 0.244$ $p = 0.092$
31–50 (Group II)	81	0.19514	0.012935		0.19545	0.013611	
>50 (Group III)	76	0.20116	0.015516		0.20119	0.015043	
Age group (years)	No. of cases	Level II mean CSA (cm^2)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
18–30 (Group I)	43	0.10932	0.009898	$r = 0.229$ $p = 0.060$	0.10941	0.010568	$r = 0.244$ $p = 0.073$
31–50 (Group II)	81	0.11035	0.011360		0.11061	0.011258	
>50 (Group III)	76	0.11220	0.012728		0.11256	0.011637	

Tab. 6. *Mean cross-sectional area (CSA) of both tibial nerves at levels I and II and their correlation with gender*

Gender	No. of cases	Level I mean CSA (cm^2)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
Male	101	0.20538	0.012126	$r = -0.615$ $p = 0.001$	0.20585	0.011966	$r = -0.630$ $p = 0.001$
Female	99	0.18793	0.010277		0.18785	0.010261	
Gender	No. of cases	Level II mean CSA (cm^2)					
		Right		*p*-value	Left		*p*-value
		Mean	SD		Mean	SD	
Male	101	0.11924	0.008997	$r = -0.637$ $p = 0.001$	0.11903	0.009269	$r = -0.614$ $p = 0.001$
Female	99	0.10412	0.009390		0.10487	0.009054	

of Radiodiagnosis in our institute for other medical or surgical conditions, were included in the study. There were 101 males (50.5% of the sample size) and 99 females (49.5%). All patients with peripheral neuropathy or with history of pain, weakness, numbness, tingling or burning sensation in the lower limb, due to one or more of trauma involving lower extremity and/or lumbar plexus injury, hypothyroidism, diabetes mellitus, pregnancy, alcohol, or drugs were excluded from the study.

After obtaining informed written consent from each subject, thorough clinical history was recorded and high-resolution US of the tibial nerve was performed in both lower limbs.

Sonography technique

The high-resolution US was performed using Philips Affinity 50 with a linear transducer having frequency of 5–18 Mhz. Sonography gel was applied liberally in order to avoid missing the nerve while tracing its course.

US position

Depth, gain, and dynamic range were adjusted in order to attain finest demarcation between the nerves and the neighbouring soft tissue structures. The images were obtained with the subject lying in prone position. The transducer was positioned perpendicular while acquiring tibial nerve CSA. Pressure of the transducer on the skin surface was kept minimum to avoid deformation of the underlying soft tissue structures. Some of the studies have showed the practice of standard imaging as well as write-zoom magnification methods for CSA measurement. In this study, we used standard imaging method.

Cross-sectional area of the tibial nerve was measured at the following locations: level I was located at 1 cm below the bifurcation of the sciatic nerve into the tibial and the common peroneal nerves and level II was located at 1 cm superior and posterior to medial malleolus (measured on ultrasound screen) (Fig. 1). At each specified site, the cross-sectional area of the tibial nerve was taken by continuous tracing of the nerve just inside its peripheral hyperechoic rim. CSA was measured three times at the same level with the transducer repositioned to calculate the mean value (Fig. 2, Fig. 3, Fig. 4).

Statistical analysis

Age, gender, height, weight and body mass index obtained from each subject were documented and correlation coefficients were obtained by correlating the aforementioned parameters with CSA of the tibial nerve at both levels.

The SPSS 19.5 software was used for data analysis. *P* value of less than 0.05 was considered statistically significant. Independent sample *t*-test was used to evaluate and interpret the data. Correlation of the mean CSA of the tibial nerve with subject's age, gender, height, weight and body

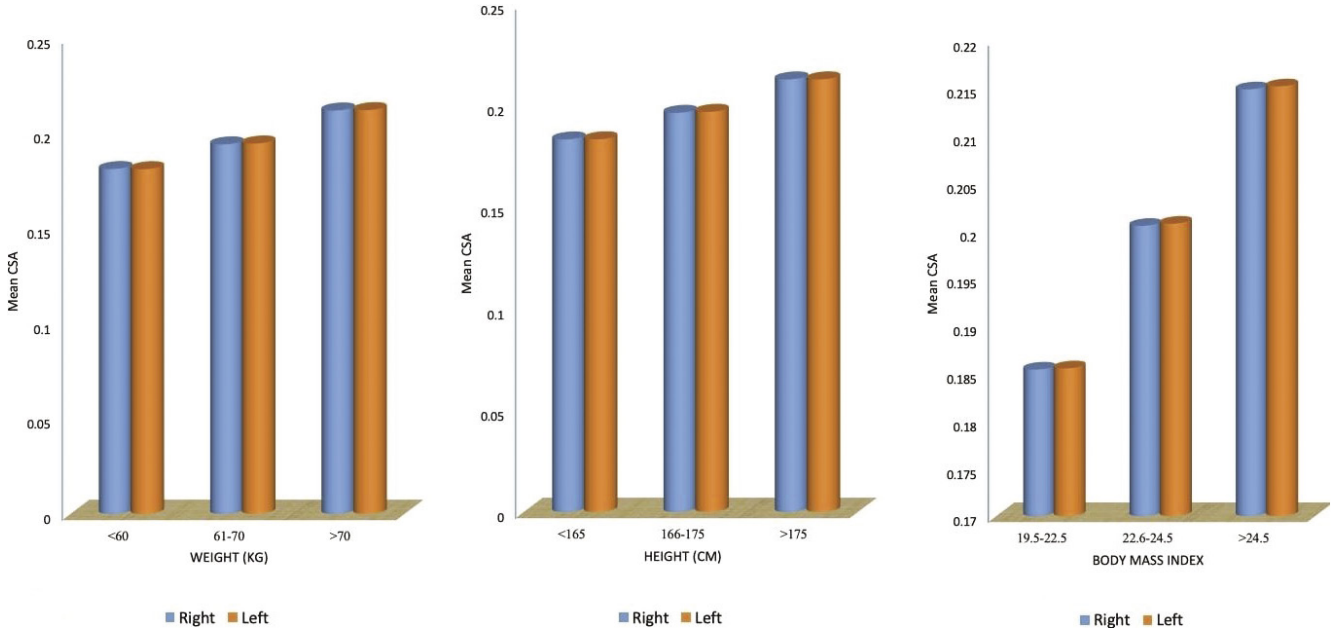

Fig. 5. *Graph representation of positive correlation of mean cross sectional area (CSA) of both tibial nerves with weight (***A***), height (***B***) and BMI (***C***)*

mass index (BMI) was established using Pearson's correlation analysis('r' value).

Results

The mean CSA of normal tibial nerves was 0.195 cm^2 in the right lower limb and 0.196 cm^2 in the left lower limb at level I and 0.110 cm^2 in the right lower limb and 0.111 cm^2 in the left lower limb at level II. The mean CSA of the tibial nerve in 200 subjects was 0.196 + 0.014 cm^2 at level I and 0.111+ 0.011 cm^2 at level II (Tab. 1). There was a noteworthy difference between the areas at these two levels with a *p*-value of 0.001 (Tab. 1). Mean CSA at two levels in both lower limbs exhibited a positive correlation ($p < 0.05$) with height (Tab. 2), weight (Tab. 3) and body mass index (Tab. 4). Females had relatively smaller CSA than males at two measuring sites (Tab. 5). However, no correlation was noted between the CSA and the age of the subjects ($p > 0.05$) (Tab. 6).

Discussion

The tibial nerve is formed by the ventral divisions of anterior primary rami of L4, L5, S1, S2,S3. The nerve continues its course inferiorly after bifurcation and passes directly down the midline of the popliteal fossa, where it enters the leg[13]. At the ankle, the tibial nerve travels posterior to the medial malleolus along with the posterior tibial artery and veins[6]. It runs posterior to these blood vessels, and anterior to the flexor hallucis longus. Beneath to the flexor retinaculum, the nerve bifurcates into end branches: medial plantar and lateral plantar nerves[14].

Bedewi *et al*. conducted a case-control study to determine the CSA of the peripheral nerves of the lower limb in order to establish some reference values. CSA values were obtained for the tibial nerve, common peroneal nerve and sural nerve. Normal reference values for the tibial nerve were 19 $mm^2 \pm 6.9$ at the popliteal fossa and 12.7 $mm^2 \pm 4.5$ at the level of the medial malleolus. The study revealed a positive correlation between the cross sectional area value and weight, BMI, and age of subjects. No significant relationship was observed between the cross sectional area and height or gender[15]. In order to evaluate focal lesions, such as entrapment syndromes and inflammatory polyneuropathies, Fisse *et al*. performed a systematic review and a meta-analysis of published CSA reference values for lower extremity nerves. They calculated the mean cross sectional area of the tibial nerve at popliteal fossa and at malleolus, which was 25.9 mm^2 and 10.0 mm^2, respectively[16]. Similarly, the mean CSA values for the tibial nerve obtained in the present study were0.196 $\pm$ 0.014 cm^2 at level I and 0.111 $\pm$ 0.011 cm^2 at level II.

Qrimli *et al*. conducted a study in 100 healthy volunteers. Median, ulnar, fibular, tibial, sural and superficial fibular nerves were evaluated at predetermined sites with high-resolution US. Positive correlation was observed between the nerve CSA and the age of the subjects. However, there was no significant relationship between gender or BMI and the cross sectional area of the nerve.

The CSA tends to be bilaterally symmetrical in both lower limbs[8]. Another study was conducted by Kerasnoudis *et al*. The CSA reference values for peripheral nerves acquired in their study showed a positive correlation with age, weight and sex. However, no obvious correlation was seen with patients' height[7].

In our study, the CSA of the tibial nerve showed a positive correlation with patients' height and weight. No significant relationship was established with the age of the subjects. Cross-sectional area was towards higher side in men than

Tab. 7. *Tabulated list of studies as mentioned in literature along with references*

Sr No.	Study performed by	Result
1	**Bedewi *et al.*** did a case control study for determining the CSA of lower limb peripheral nerves to establish some reference values. CSA values were obtained for tibial nerve, common peroneal nerve and sural nerve[15].	Normal reference value for the tibial nerve was 19 mm^2 ± 6.9 at the popliteal fossa and 12.7 mm^2 ± 4.5 at the level of the medial malleolus. The study revealed a positive correlation between CSA and weight, BMI, and age of subjects. No significant relationship was observed between CSA and height or gender.
2.	**Fisse *et al.*** performed a systematic review and a meta-analysis of published CSA reference values for lower extremity nerves[16].	They calculated the mean CSA of the tibial nerve at popliteal fossa and at malleolus, which was 25.9 mm^2 and 10.0 mm^2, respectively.
3.	**Qrimli *et al.*** conducted a study in 100 healthy volunteers. Median, ulnar, fibular, tibial, sural and superficial fibular nerves were studied at predetermined sites with high-resolution US[8].	Positive correlation was observed between the CSA of nerve and age of the subjects. However, gender and BMI had no significant relationship with the cross sectional area of nerve. CSA tends to be bilaterally symmetrical in both lower limbs.
4.	Study conducted by **Kerasnoudis *et al.***[7]	CSA reference values for peripheral nerves acquired in their study, showed a positive correlation with age, weight and sex of the subjects. However, no obvious correlation was seen with height.
5.	**Singh *et al.*** performed study on radial nerve[17].	Strong correlation between the CSA of the radial nerve and height, weight, BMI was seen with no statistically significant correlation with age. Males had higher CSA values for the radial nerve than females.
6.	**Singh *et al.*** performed study on the sciatic nerve[18].	Reference CSA values for the sciatic nerve were also studied by Singh *et al*. and the values were correlated statistically with the demographic parameters. They concluded that a positive correlation of the mean cross-sectional area was established with height, weight, and body mass index. Women had smaller cross-sectional areas of the normal sciatic nerves than men at both measuring sites. No significant relationship was established with the age of the subjects.
7.	In a study by **Chen *et al.*** on sciatic nerve[5].	CSA of sciatic nerves was measured with high resolution US in 200 subjects. The results showed that females had smaller CSA of sciatic nerves than males at the two different sites (p <0.05).
8.	**Kowalska *et al.*** performed a study on median, ulnar, common peroneal, digital, cutaneous nerve in the deltoid area, mental and posterior interosseous nerve in patients referred for ultrasound due to clinical suspicion of traumatic peripheral neuropathies[14].	US findings were consistent with the clinical and surgical verification in almost 100 % of cases.
9.	**Singh *et al.*** performed a study on thetibial nerve in diabetic patients having diabetic peripheral neuropathy[19].	The mean CSA along with maximum thickness of nerve fascicles of the tibial nerve in patients with diabetic peripheral neuropathy was significantly on higher side as compared with controls. Statistically significant correlation was also found with the Toronto Clinical Neuropathy Score (p <0.001).
10.	Study conducted by **Riazi *et al.*** in diabetic patients on peripheral nerve[20].	Mean CSA of the posterior tibial nerve above the medial malleolus was considerably larger in the diabetic sensorineural polyneuropathy subjects compared with controls.
11.	**Singh *et al.*** performed a study in diabetic patients with clinically diagnosed diabetic polyneuropathy and healthy adult volunteers[3].	The mean CSA of the medial, ulnar, common peroneal and posterior tibial nerves was measured in the two groups at identical sites. CSA was significantly higher in diabetic patients as compared to healthy volunteers.
12.	**Afsal *et al.*** performed a study in five patients with diabetic peripheral neuropathy[21].	Diffuse thickening of peripheral nerves along with higher mean CSA of the median nerve and the ulnar nerve was found in patients with diabetic peripheral neuropathy when compared to controls.
13.	Study by **Lee *et al.*** on peripheral nerves[22].	Concluded that ultrasonography plays a vital role in diagnosing a lesion and its location accurately in the 13 cases who were the subjects of their study. In 7 (58%) out of 12 cases, ultrasonography contributed to establishing the correct diagnosis when other imaging and electrophysiological studies were inconclusive or inadequate.

in women. Also, cross-sectional area measures turned out to be symmetrical in both limbs. In our study, one supplementary parameter, i.e. BMI, is integrated. Just like the other parameters, such as height and weight, BMI also exhibited a positive correlation with the cross-sectional area.

Similar results were observed by Singh *et al*. A strong correlation between the CSA of the radial nerve and height, weight, and BMI was seen, with no statistically significant correlation with age. Males had higher CSA values of the radial nerve than females[17]. Reference values for the cross-sectional area of the sciatic nerve were also investigated by Singh *et al*., and the values were statistically correlated with demographic parameters. The authors concluded that a positive correlation of the mean cross-sectional area was established with height, weight, and body mass index. Women had smaller cross-sectional areas of the normal sciatic nerves than men at both measuring sites. No significant relationship was established with the age of the

subjects[18]. In a study by Chen *et al*., sciatic nerve CSA was measured with high-resolution US in 200 subjects. The results showed that females had smaller CSA of sciatic nerves than males at the two different sites ($p < 0.05$)[5].

Kowalska *et al*. performed a study in 47 patients referred for ultrasound due to clinical suspicion of traumatic peripheral neuropathies. Median, ulnar, common peroneal, digital, cutaneous nerve in the deltoid area, mental and posterior interosseous nerve were studied. The ultrasound findings were consistent with the clinical and surgical verification in almost 100% of cases[14].

Singh *et al*. performed a study in75 patients with clinically diagnosed type 2 diabetes mellitus with diabetic peripheral neuropathy. The mean CSA along with maximum thickness of nerve fascicles of the tibial nerve in patients with diabetic peripheral neuropathy was significantly on the higher side as compared with the control group. Statistically significant correlation was also found with the Toronto Clinical Neuropathy Score ($p < 0.001$)[19]. Riazi *et al*. also found that the mean CSA of the posterior tibial nerve above the medial malleolus was considerably larger in diabetic sensorineural polyneuropathy subjects compared with controls in their study[20].

Similar results were obtained by Singh *et al*., who conducted their study in37 adult diabetic patients with clinically diagnosed diabetic polyneuropathy and 45 healthy adult volunteers. The mean CSA of the medial, ulnar, common peroneal and posterior tibial nerves was measured in the two groups at identical sites. CSA was significantly higher in the diabetic patients as compared to healthy volunteers[3].

Afsal *et al*. performed a study in five patients with diabetic peripheral neuropathy. Diffuse thickening of peripheral nerves along with higher mean CSA of median nerve and ulnar nerve was found in patients with diabetic peripheral neuropathy when compared to controls[21].

Lee *et al*. stated that ultrasonography plays a vital role in diagnosing a lesion and its location accurately in 13 cases who were the subjects of their study. In 7 (58%) out of 12 cases, ultrasonography contributed to establishing the correct diagnosis when other imaging and electrophysiological studies were inconclusive or inadequate[22].

In the present study, high-resolution US provided normal CSA reference values, which helps reach early diagnosis of tibial nerve pathologies. The reference values in the present study were similar to the above mentioned studies (Tab. 7). Therefore, any deviation from the reference mean cross sectional area certainly indicates nerve pathology, such as neuropathy or compression syndromes. This allows for early diagnosis especially in patients with diabetic neuropathy.

The fact that the CSA of the tibial nerve was measured at two sites only and the sample population was restricted to one demographical strata is a limitation of the present study.

Conclusions

The mean cross-sectional area of the tibial nerve in our study was 0.196 + 0.111 cm^2 at level I and 0.014 + 0.011 cm^2 at level II. There is a significant correlation of the cross sectional area of normal tibial nerve with height, weight and body mass index of the subjects. Males had higher cross sectional area of normal tibial nerve than females. There is no significant correlation of cross sectional area of normal tibial nerve with the age of the subjects.

Conflict of interest

The 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.

Author contributions

Original concept of study: KPS. Writing of manuscript: KPS, SK. Analysis and interpretation of data: KPS, SK, VA. Final acceptation of manuscript: KPS. Collection, recording and/or compilation of data: KPS, SK. Critical review of manuscript: KPS.

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