DOI: 10.7860/IJARS/2024/72966.3020

Original Article

Radiology Section

Reference Values of Shear Wave Elastography of Median and Tibial Nerve in Healthy Population: A Cross-sectional Study

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ABSTRACT

Introduction: Peripheral nerves are rarely assessed using high-resolution Ultrasonography (USG). Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) scans can be costly and occasionally inaccessible. In contrast, USG provides a dynamic, portable and cost-effective method for evaluating peripheral nerves. Shear Wave Elastography (SWE) is a relatively recent ultrasound-based technique that quantitatively measures tissue stiffness.

Aim: To determine the reference values for SWE measurements of the median and tibial nerves in healthy individuals and to explore potential associations with age, gender, height, weight and Body Mass Index (BMI) of the subjects.

Materials and Methods: The present cross-sectional study was conducted in the Radiodiagnosis and Imaging Unit, Sri Guru Ram Das Institute of Medical Sciences and Research, Sri Amritsar, Punjab, India, from October 2022 to April 2024, involved 100 subjects (45 males and 55 females). Subjects were deemed eligible for the study following evaluation by a general physician. The study was conducted over a period of one year. High-resolution real-time USG was utilised to assess the median and tibial nerves in both arms and legs bilaterally. SWE was conducted on the tibial and median nerves, and the velocities generated were subsequently evaluated to establish baseline levels for the peripheral nerves. Collected data were transformed, coded and entered into Microsoft Excel, then analysed using Statistical Package for Social Sciences (SPSS) software version 25.0 (SPSS-PC-25). Parametric data were expressed as mean±Standard Deviation (SD) or median and compared using the Mann-Whitney U test.

Results: The mean age of healthy subjects was 41.18±12.34 years, while the weight and height were 72.59±7.44 kg and 172.74±6.75 cm, respectively. The average velocities generated in healthy subjects (45 males and 55 females) using SWE were found to be 3.606±0.133 m/s and 3.632±0.173 m/s for the left and right median nerves (p-value >0.05), and 3.626±0.140 m/s and 3.623±0.138 m/s for the left and right tibial nerves (p-value >0.05), respectively. The SWE measurements obtained from the bilateral median and tibial nerves showed no significant differences in their values, indicating no significant association (p-value >0.05). No significant correlation was found between the SWE measurements and age, sex, height, weight, or BMI of the subjects (p-value >0.05).

Conclusion: The present study serves as an initial step in gathering tibial nerve stiffness values from healthy participants using SWE and exploring the factors affecting nerve stiffness.

Keywords: High-resolution ultrasound, Malleolus, Peripheral nerves, Velocities

INTRODUCTION

Peripheral nerves consist of nerve fibers responsible for transmitting signals to muscles and regulating autonomic nerve functions within the body. Assessing peripheral nerve function holds immense significance for diagnosing neuromuscular disorders and evaluating treatment effectiveness [1]. A nerve conduction study is an invasive procedure that helps assess the conductivity of an electrical impulse through the nerve and can aid in diagnosing nerve damage.

Ultrasound elastography offers a non invasive means of evaluating tissue elasticity, presenting promising avenues for diagnosing and monitoring neuromuscular and movement disorders [2]. The use of high-resolution ultrasound has gained significance by providing a non invasive approach to evaluate nerve echogenicity and stiffness, thereby improving diagnostic precision [3].

The evolution of high-resolution ultrasound technology has substantially enhanced the capability to visualise lesions with exceptional clarity and accuracy, resulting in expanded clinical utility in neuromuscular diseases. Ultrasound imaging provides valuable insights by furnishing details regarding the Cross-sectional Area (CSA), echogenicity and inner structure of nerves [4,5].

Shear Wave Elastography (SWE) is a promising technique extensively utilised across various organs, including the liver, breast and thyroid. It holds potential for quantitatively evaluating changes in tissue stiffness by measuring the velocity and propagation pattern of shear waves within the tissue of interest. However, it operates under the assumption of linear, isotropic tissue behaviour, which may not accurately reflect real tissue properties. Standard USG fails to account for phenomena such as wave refraction and reflection, which can affect the imaging of transverse wave propagation. Disparities in transverse wave velocities can be significant, resulting in notable reflective impacts. Additionally, shear wave refraction at tissue boundaries with varying velocities can exacerbate these effects [6].

The present study was aimed to explore SWE as a non invasive technique for assessing nerve health status. It seeks to obtain high-resolution sonographic images of healthy median and tibial nerves and establish reference SWE values. Additionally, the study intends to investigate potential associations with factors such as age, gender, height, weight and BMI in individuals.

MATERIALS AND METHODS

The present cross-sectional study was conducted in the Radiodiagnosis and Imaging Unit, Sri Guru Ram Das Institute of Medical Sciences and Research, Sri Amritsar, Punjab, India, from October 2022 to April 2024, during which 100 individuals were recruited. These individuals were deemed eligible for the study following evaluation by a general physician.

Inclusion criteria: Participants, regardless of gender, aged between 18 years and 75 years, with no history of limb trauma or peripheral neuropathy, were included in the study.

Exclusion criteria: Individuals with Peripheral Neuropathy (PN) induced by pregnancy, diabetes mellitus, trauma, hypothyroidism, or alcoholism were excluded from the study.

Study Procedure

Following written consent from each participant, comprehensive clinical histories were obtained. High-resolution USG of the median and tibial nerves was performed bilaterally, and SWE values were recorded.

Ultrasonography (USG) technique: High-resolution ultrasound and shear wave elastography were carried out on the tibial and median nerves of both the upper and lower limbs using a Logic P9 ultrasound system equipped with a high-frequency linear transducer (3-12 MHz). These examinations were conducted by experienced radiologists with over 10 years of proficiency. Three values were generated for each measurement, and the average value was used for the study.

Throughout the procedure, participants were instructed to lie in a supine position to encourage relaxation of the lower limbs and minimise ankle movement during the tibial nerve examination. For the assessment of the median nerve, the forearm was positioned supine on a pillow, with the elbow and fingers semi-flexed. Participants were instructed to maintain stillness in their fingers throughout the examination.

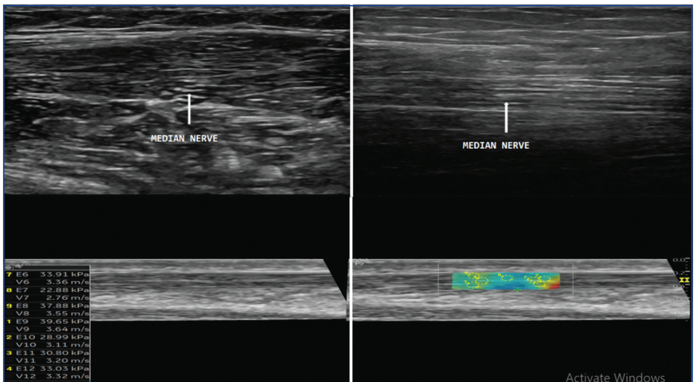
The assessment of the tibial and median nerves was conducted in the transverse orientation, with the tibial nerve located approximately 3 cm above the medial malleolus and the median nerve assessed at the midpoint of the forearm. To ensure precise measurements, the transducer was aligned perpendicular to the nerve fibers, with gentle pressure applied to avoid distortion of the nerve and erroneous measurements.

Longitudinal SWE images of the tibial and median nerves were acquired by rotating the probe 90° from the transverse position. After a brief stabilisation period to minimise motion artifacts, stable SWE images were captured.

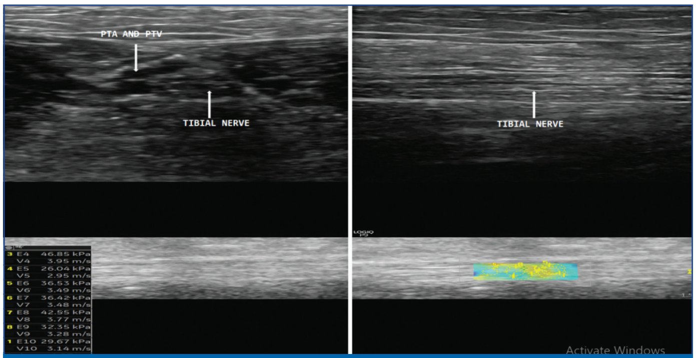
A fixed-size circular Region of Interest (ROI) was automatically positioned just inside the hyperechoic perineurium border of the nerves. Using the SWE images, the velocities of the tibial and median nerves were automatically calculated in meters per second (m/s) [Table/Fig-1-4]. The generated velocities were subsequently evaluated to establish baseline levels for the peripheral nerves.

STATISTICAL ANALYSIS

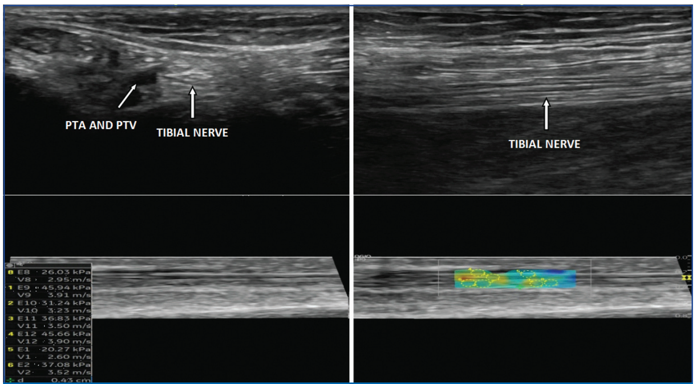
The collected data were transformed, coded and entered into Microsoft Excel, then analysed using SPSS-PC-25. Parametric data were expressed as mean±SD and compared using the Mann-Whitney U test.



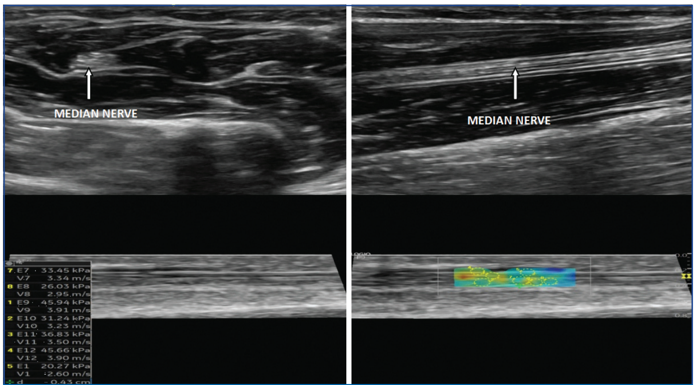
[Table/Fig-1]: A 31-year-old healthy subject weighing 76 kgs, having a height of 179 cm with a Body Mass Index (BMI) of 23.7 was evaluated after matching. Median nerve of right upper limb (white arrows) was observed in cross-sectional plane at mid-point of forearm. The probe was switched 90 degrees to obtain longitudinal section. The stiffness (m/s) was generated three times with average value being taken as 3.45 m/s.



[Table/Fig-2]: A 52-year-old healthy subject weighing 78 kgs, having a height of 168 cm with a Body Mass Index (BMI) of 27.6 was evaluated after matching. Tibial nerve of left lower limb (marked by the arrows) was observed 3 cm above medial malleolus in in cross-sectional plane. It was lying along Percutaneous Transluminal Angioplasty (PTA) and Planning Target Volume (PTV) in cross-section. The probe was rotated 90 degrees to find longitudinal section. The stiffness (m/s) was generated three times with average value being taken as 3.68 m/s.



[Table/Fig-3]: A 27-year-old healthy subject weighing 78 kgs, having a height of 177 cm with a Body Mass Index (BMI) of 24.9 was evaluated after matching. Tibial nerve of right lower limb (marked by the arrows) was observed 3 cm above medial malleolus in cross-sectional plane. It was lying along PTA and PTV in cross section. The probe was rotated 90 degrees to find longitudinal section. The stiffness (m/s) was generated three times with average value being taken as 3.41 m/s.



[Table/Fig-4]: A 61-year-old healthy subject weighing 68 kgs, having a height of 172 cm with a Body Mass Index (BMI) of 22.9 was evaluated after matching. Median nerve of left upper limb (white arrows) was observed in cross-sectional plane at mid-point of forearm. The probe was switched 90 degrees to obtain longitudinal section. The stiffness (m/s) was generated three times with average value being taken as 3.52 m/s.

RESULTS

The study included 100 healthy subjects, comprising 45 males and 55 females. The mean age of the healthy subjects was 41.18±12.34 years, while the mean weight and height were 72.59±7.44 kg and 172.74±6.75 cm, respectively. The mean BMI was found to be 25.3±0.1 kg/m^2.

No significant associations were found between the SWE measurements, and age, sex, height, weight and BMI of the subjects (p-value >0.05), as stated in [Table/Fig-5-9]. The average velocities generated in healthy subjects (45 males and 55 females) using SWE were found to be 3.606±0.133 m/s and 3.632±0.173 m/s for the left and right median nerves (p-value >0.05) and 3.626±0.140 m/s and 3.623±0.138 m/s for the left and right tibial nerves (p-value >0.05), respectively [Table/Fig-10].

Gender	n	Average Shear Wave Velocity (SWV) bilateral median nerve	p-value (Wilcoxon test)	Average Shear Wave Velocity (SWV) bilateral tibial nerve	p-value
Male	45	3.621	0.371	3.628	0.378
Female	55	3.616		3.620	
Total (N)	100	3.619		3.625	

[Table/Fig-5]: Study population stratified on the basis of gender with average of bilateral median and tibial shear wave measurements.
Mann-Whitney U test was used

Age (years)	n	Average Shear Wave Velocity (SWV) bilateral median nerve	p-value	Average Shear Wave Velocity (SWV) bilateral tibial nerve	p-value
18-29	20	3.626	0.215	3.625	0.202
30-54	53	3.616		3.623	
≥55	27	3.620		3.619	

[Table/Fig-6]: Study population stratified on the basis of age with average of bilateral median and tibial shear wave measurements.
Mann-Whitney U test was used

Weight (kg)	n	Average Shear Wave Velocity (SWV) bilateral median nerve	p-value	Average Shear Wave Velocity (SWV) bilateral tibial nerve	p-value
≤69	30	3.622	0.115	3.626	0.211
70-79	47	3.617		3.620	
≥80	23	3.620		3.622	

[Table/Fig-7]: Study population stratified on the basis of weight with average of bilateral median and tibial shear wave measurements.
Mann-Whitney U test was used

Height (cm)	n	Average Shear Wave Velocity (SWV) bilateral median nerve	p-value	Average Shear Wave Velocity (SWV) bilateral tibial nerve	p-value
≤159	11	3.624	0.271	3.690	0.109
160-169	34	3.618		3.611	
≥170	55	3.617		3.64	

[Table/Fig-8]: Study population stratified on the basis of height with average of bilateral median and tibial shear wave measurements.
Mann-whitney U test was used

BMI (kg/m^2)	n	Average Shear Wave Velocity (SWV) bilateral median nerve	p-value	Average Shear Wave Velocity (SWV) bilateral tibial nerve	p-value
≤22.9	23	3.620	0.216	3.624	0.157
23-25.9	34	3.621		3.628	
≥26	43	3.617		3.618	

[Table/Fig-9]: Study population stratified on the basis of BMI with average of bilateral median and tibial shear wave measurements.
Mann-whitney U test was used

Variable	Left median nerve	Right median nerve	p-value
Shear Wave Elastography (SWE) value (M/S)	3.606±0.133	3.632±0.173	0.281
Variable	Left tibial nerve	Right tibial nerve	p-value
Shear Wave Elastography (SWE) value (M/S)	3.626±0.140	3.623±0.138	0.112

[Table/Fig-10]: Shear Wave Elastography (SWE) values of left and right median nerves.
Mann-Whitney U test was used

DISCUSSION

A typical peripheral nerve appears as several hypoechoic longitudinal fascicles separated by discontinuous echogenic bands that correspond to the epineurium on USG [7-10].

Pathological abnormalities, such as nerve hypertrophy and altered echopatterns, can be detected using ultrasound [11]. Ultrasound can reveal the specific position, anatomical path and extent of the nerve, in addition to providing information on its morphology [12].

In their investigation, Tang X et al., found that SWE measurements of peripheral nerves in healthy individuals were influenced by various factors, including different measurement sites, nerve types and genders. However, no associations were found between SWE measurements and factors such as age, BMI, nerve thickness, or CSA [1]. In the present study, the authors also observed no correlation between SWE measurements and factors such as age and BMI. However, unlike the findings of Tang X et al., the current research did not uncover any correlation between SWE measurements and gender.

Greening J and Dilley A found that shear wave elastography is a valuable means of investigating nerve biomechanics in both healthy individuals and patients. Nevertheless, it is crucial to consider factors such as limb position, age and the impact of nerve tension on neural architecture during the assessment process [13].

Bedewi MA et al., found that in the short axis, the average shear elastic modulus of the tibial nerve was 23.3 kPa, while in the long axis, it was 26.1 kPa. Additionally, there was no observed correlation between the elastic modulus of the tibial nerve and its CSA, regardless of the axis. Furthermore, factors such as age, height, weight and BMI did not exhibit any correlation with the tibial nerve's elastic modulus in either the short or long axes [14]. Likewise, the present investigation revealed no noteworthy correlation between the SWE values of the tibial and medial nerves and the age, height, weight, or BMI of the subjects.

Shang S et al., found that SWE measurements of the tibial nerve revealed no significant differences between legs, genders, or various age groups. Interestingly, higher stiffness values of the tibial nerve were observed in participants with lower body mass [15]. Upon closely examining the present study, the authors found no substantial correlation between the SWE measurements of the tibial and medial nerves and factors such as age, height, weight, or BMI among the subjects.

Neto T et al., concluded that, although reliability metrics were highly favourable, reported Shear Wave Velocity (SWV) values varied significantly across studies for the tibial nerve, ranging from 2.3-9.1 m/s. Factors such as the proximity of measurements to joint regions, limb postures that induce axial stretching of nerves, and the alignment of the transducer with nerve fiber orientation were identified as contributors to increased SWV. These observations imply region-specific mechanical properties of nerves, non linear elastic behaviour and pronounced mechanical anisotropy [16].

Aslan M et al., found that patients diagnosed with type 1 diabetes mellitus exhibited greater stiffness in both the median nerve and posterior tibial nerve compared to healthy volunteers. There were no significant differences observed in terms of sex, age and BMI among the groups [17].

Wei M and Ye X found that the stiffness values of the tibial nerve were significantly higher in the overall patient group, as well as, in patients with Diabetic Peripheral Neuropathy (DPN) and those without DPN, compared to the control group (p-value <0.05). A cut-off value of p-SWE for evaluating DPN was determined to be 2.60 m/s. At this threshold, the sensitivity was 63.33%, and the specificity was 92.50% [18].

In a study conducted by He Y et al., individuals diagnosed with DPN demonstrated increased rigidity in both the median and tibial nerves when compared to healthy volunteers and diabetic patients without

DPN (p-value <0.001). Upon bilateral analysis, no notable disparity in nerve stiffness between the left and right median nerves and tibial nerves was observed in DPN patients (p-value <0.05). Additionally, there was no significant discrepancy in stiffness between the median nerve and tibial nerve on each side in patients with DPN [19].

Jiang W et al., found that patients with DPN and clinically diagnosed DPN exhibited significantly increased stiffness in the tibial nerve, as indicated by mean (E_{Mean}), minimum (E_{Min}), and maximum (E_{Max}) shear elasticity indices, compared to those without DPN and control subjects (p-value <0.05). The Area Under the Curve (AUC) for SWE measurements of E_{Mean}, E_{Min}, and E_{Max} was 0.846, 0.867, and 0.821, respectively [20].

Conventional ultrasound is a common tool for diagnosing peripheral nerve disorders, effectively illustrating the echotexture of peripheral nerves. The integration of SWE assessment provides significant value, aiding in the diagnosis and evaluation of disease progression.

Limitation(s)

Despite all the advantages that SWE offers, it remains a technique that heavily relies on the operator's skill and entails a steep learning curve. Because SWE focuses on specific areas of peripheral nerves, it may easily overlook any pathology that extends beyond the scanning site.

CONCLUSION(S)

The present study serves as an initial step in gathering tibial nerve stiffness values from healthy participants using SWE and exploring the factors that affect nerve stiffness. The authors' next objective is to develop a scoring system for ultrasound-based neuropathy assessment that incorporates both morphological and elastic characteristics. The authors will assess its diagnostic efficacy in patients with PN. The authors anticipate that such an ultrasound-based scoring system will enhance standardisation and clinical adoption of ultrasound for neuropathy diagnosis, assisting physicians in the timely and accurate detection of PN.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]

- Plagiarism X-checker: May 19, 2024
- Manual Googling: Aug 14, 2024
- iThenticate Software: Aug 16, 2024 (18%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **May 18, 2024**
Date of Peer Review: **Jul 01, 2024**
Date of Acceptance: **Aug 19, 2024**
Date of Publishing: **Nov 01, 2024**