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ORIGINAL RESEARCH

Diagnostic Potential of High-Resolution Ultrasound of Median Nerve in Assessing the Severity of Carpal Tunnel Syndrome

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Keywords: carpal tunnel syndrome, high-resolution ultrasound, median nerve, diagnostic potential, severity assessment, nerve entrapment, cross-sectional area, nerve compression, carpal tunnel diagnosis, ultrasonographic assessment, wrist evaluation

Word count: 2,595

Abstract

Background: Carpal tunnel syndrome (CTS) is the most common peripheral compressive neuropathy diagnosed by a combination of clinical and nerve conduction studies (NCS). NCS is used to classify the severity of CTS, which forms the basis of its treatment. NCS is, however, a time-consuming, relatively expensive, and painful procedure that may not be available at all facilities. In comparison, high-resolution ultrasound (HRUS) offers several advantages — it is a painless, quick, easily accessible, and relatively inexpensive procedure. The purpose of this study is to evaluate the diagnostic potential of HRUS for grading the severity of carpal tunnel syndrome.

Methods and materials: This is a prospective descriptive study conducted at the Department of Radiology and Imaging at Nizam's Institute of Medical Sciences. It includes 42 cases of CTS that were diagnosed and classified using both clinical assessment and NCS. In this study, we measured 11 HRUS gray-scale and color Doppler parameters of the median nerve and compared them with the NCS classification of the severity of CTS.

Results: Of 42 total diagnosed cases, 27 were classified as non-severe, while 15 cases were classified as severe cases of carpal tunnel syndrome based on NCS. The cross-sectional area (CSA) of the median nerve at the inlet, outlet, wrist-forearm ratio, wrist-forearm difference, vascularity score, and flattening ratio at the outlet were statistically significant predictors of severity. The CSA at the outlet was the best predictor of the severity of CTS (AUC = 0.811). Using a cut-off of 11 mm^2, the CSA at the outlet had a sensitivity of 40% and a specificity of 94.5% for the diagnosis of severe CTS.

Conclusion: High-resolution ultrasound is a well-established modality for diagnosing carpal tunnel syndrome. HRUS parameters can also be utilized to grade the severity of CTS, which can be crucial for clinicians when selecting appropriate therapeutic interventions.

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Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral compressive neuropathy, with a high prevalence in middle-aged males and females. It significantly affects their day-to-day activities (1). CTS is typically diagnosed through a combination of clinical evaluation and nerve conduction studies (NCS). NCS is used to classify the severity of CTS, forming the basis for its treatment. Mild and moderate cases are usually managed conservatively with splinting and oral medications, while severe cases require surgical release (2). However, NCS is a time-consuming, painful, and relatively expensive procedure that may not be available in all facilities (3). In comparison, high-resolution ultrasound (HRUS) offers several advantages — it is painless, quick, readily available, and relatively cost-effective. HRUS parameters have already been established to have similar diagnostic accuracy to NCS for diagnosing CTS. However, it is unclear whether HRUS can effectively grade the severity of CTS (4-6). The purpose of this study is to evaluate the diagnostic potential of HRUS for grading the severity of carpal tunnel syndrome.

Methods and materials

Study design and patients

This is a prospective descriptive study conducted in the Department of Radiology and Imaging at Nizam's Institute of Medical Sciences in Hyderabad, India. The study was approved by the institutional ethics committee and informed consent was obtained for all patients. The study included 42 cases of CTS confirmed by nerve conduction studies. All diagnosed patients were further classified into severe (27) and non-severe (15) cases based on the nerve conduction study.

Nerve conduction study

Sierra Wave 2-channel electromyography system was used for NCSs. The NCSs were performed by experienced NCS technicians under the supervision of a neurologist. NCS tests were performed on bilateral upper extremities of all participants, with the skin temperature kept at 32°C. Severity of CTS was based on Padua classification (Figure 1) (7). All tests were performed in compliance with the guidelines set forth by the American Association of Neuromuscular and Electrodiagnostic Medicine (8):

1. Sensory nerve action potential (SNAP): Two surface cup electrodes applied to the index finger; the median nerve's action potential was antidromically recorded.

2. Sensory nerve conduction velocity (SCV): The latency of the sensory nerve action potential waveform and the distance between the recording electrodes and the stimulation point are used to calculate velocity.

3. Compound muscle action potential (CMAP): Two surface cup electrodes covering the abductor pollicis brevis were used to record the motor action potential.

4. Distal motor latency (DML): The CMAP waveform was used to calculate DML.

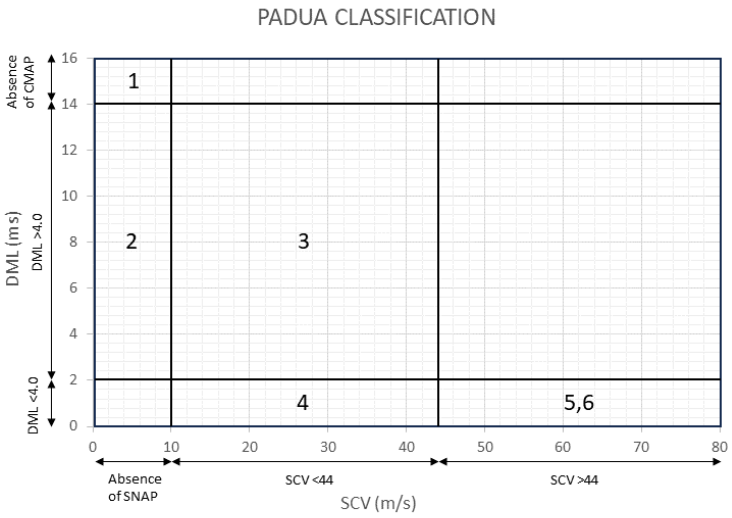

Figure 1. Electrophysiological severity classifications for CTS based on Padua classification (8).

1. Extreme CTS: absence of SNAP and CMAP.

2. Severe CTS: absence of SNAP and DML > 4.0 ms.

3. Moderate CTS: SCV < 44 m/s and DML > 4.0 ms.

4. Mild CTS: SCV < 44 m/s and DML < 4.0 ms.

5. Minimal CTS: "standard negative" hands with abnormal comparative or segmental tests.

6. Negative: normal findings on all tests.

In our study, all the cases classified as minimal, mild, and moderate CTS were grouped in the non-severe category and those classified as severe and extreme CTS were assigned to the severe category.

Ultrasound imaging

Ultrasound imaging was performed for all patients within 24 hours after the nerve conduction study. Images were obtained with a high-resolution linear array transducer (8-22 MHZ) in Esaote Mylab 9xpTM (Esaote, Genoa, Italy). Patients were seated comfortably with the forearm placed on the lap with a pillow, the elbow was flexed with forearm straight and wrist in a neutral position, and the fingers were partially flexed. Ultrasound images were obtained at three levels: forearm, carpal tunnel inlet (inlet), and carpal tunnel outlet (outlet). The median nerve was scanned in both longitudinal and transverse planes (Figures 2a-b) (9,10).

a) Grey-scale parameters

The landmark for forearm is situated between the ulna medially and the radius laterally, approximately 3 cm proximal to the wrist skin crease (Figure 3a). The landmark for inlet is between pisiform bone as the medial border and scaphoid bone as the lateral border (Figure 3b) (11). The landmark for outlet is positioned between the hook of hamate as the medial border and apex of trapezium as the lateral border (Figure 3c). The cross-sectional area (CSA) in mm2 is measured at each of the three levels along the inner border of epineurium. At the same levels, the nerve's widest mediolateral and anteroposterior diameters were measured. The maximum thickness of the flexor retinaculum is measured at the outlet (Figure 4a). The distance between the palmar apex of the flexor retinaculum and a straight line drawn between the apexes of the trapezium and hamate bone is used to quantify the palmar bowing of the flexor retinaculum at the outlet (Figure 4b) (12).

b) Derived parameters

1. **Swelling ratio:** The ratio of the nerve's area at the inlet to its area at the outlet.

2. **Flattening ratio at the forearm, inlet and outlet:** The ratio of the nerve's major axis to its minor axis, which is computed at these three locations.

3. **Wrist-forearm ratio:** The ratio of the nerve's area at the inlet and its area at the forearm.

4. **Wrist–forearm difference:** Difference between area at the forearm and area at the inlet.

Figure 2a. Median nerve is scanned in longitudinal plane.

Figure 2b. Median nerve is scanned in transverse plane.

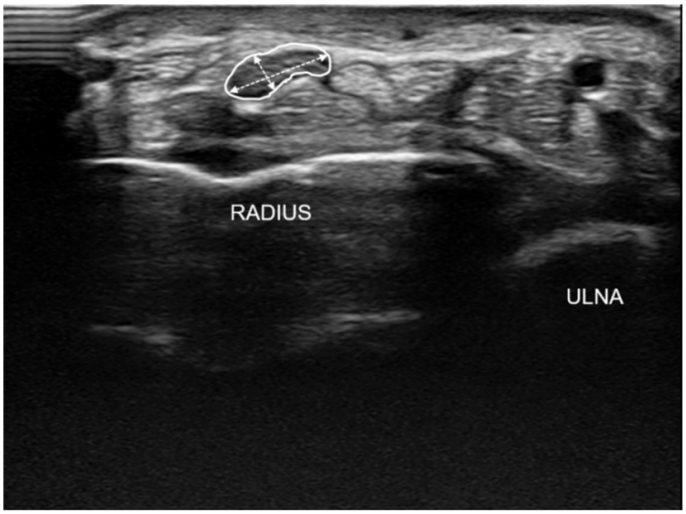

Figure 3a. Transverse view showing the measurement of cross-sectional area and anteroposterior and transverse diameter of the median nerve at forearm.

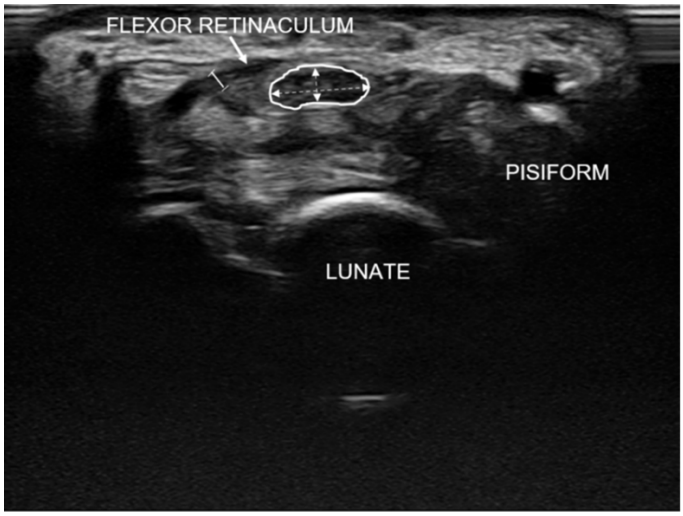

Figure 3b. Transverse view showing measurement at carpal tunnel inlet.

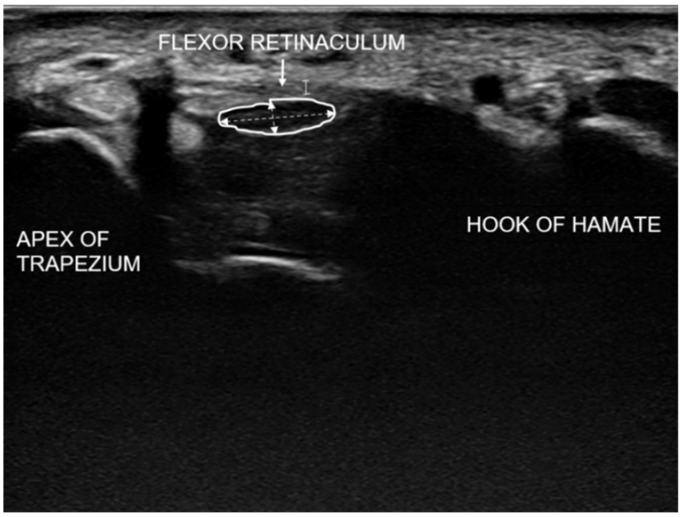

Figure 3c. Transverse view showing measurement at carpal tunnel outlet.

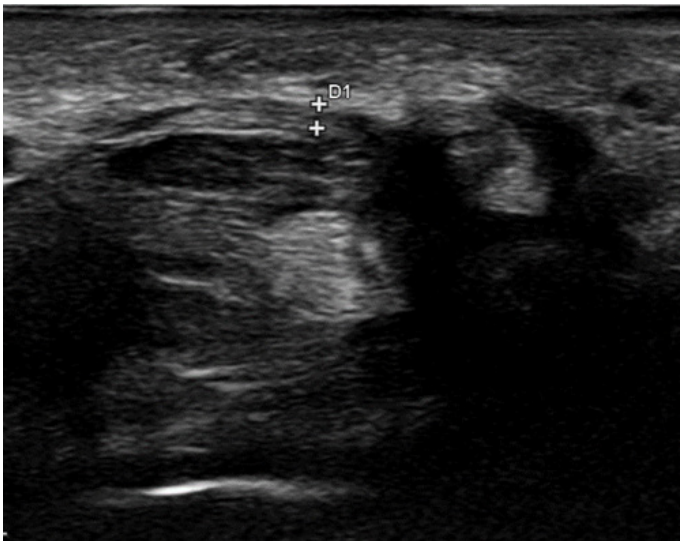

Figure 4a. Measuring maximum flexor retinaculum thickness at outlet.

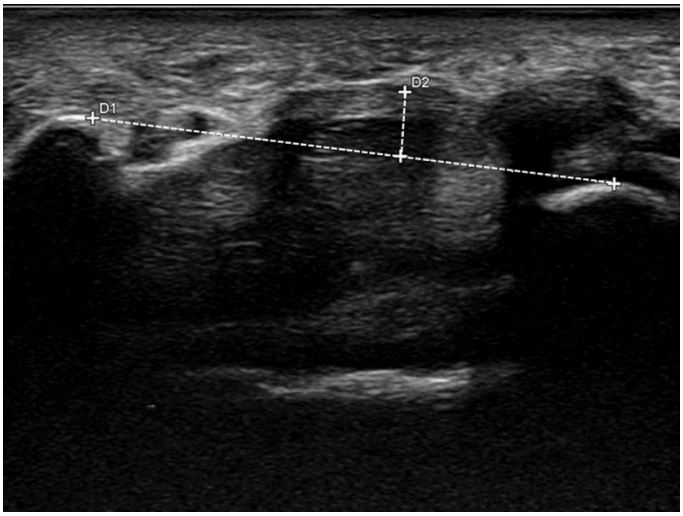

Figure 4b. Measuring palmar bowing ratio.

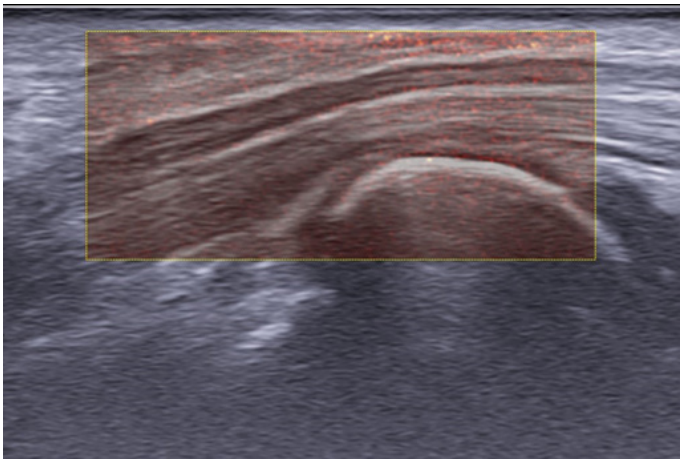

Figure 4c. Measuring vascularity score in longitudinal plane.

Table 1. Unpaired t-test values comparing non-derived and derived grey scale parameters and color Doppler parameters between the severe and the non-severe group.

PARAMETERS	SEVERITY	MEAN	SD	P VALUE
NON-DERIVED PARAMETERS				
	SEVERE	10.20	1.859	
CSA AT FOREARM (mm2)	NON-SEVERE	9.04	2.121	0.083
	SEVERE	15.80	6.062	
CSA AT INLET (mm2)	NON-SEVERE	11.04	4.090	0.004
	SEVERE	12.67	4.419	
CSA AT OUTLET (mm2)	NON-SEVERE	9.33	2.760	0.004
	SEVERE	0.9240	.23570	
FR THICKNESS(MM)	NON-SEVERE	0.7641	.28136	0.070
	SEVERE	3.0333	1.08277	
FR BOWING(MM)	NON-SEVERE	2.7870	1.03288	0.471
DERIVED PARAMETERS				
	SEVERE	1.2960	.49735	
SWELLING RATIO	NON-SEVERE	1.1969	.26888	0.404
	SEVERE	2.5737	.98158	
FLATTENING RATIO AT FOREARM	NON-SEVERE	2.4269	.75029	0.590
	SEVERE	3.4260	1.10403	
FLATTENING RATIO AT INLET	NON-SEVERE	2.9582	.76501	0.114
	SEVERE	3.0395	.55941	
FLATTENING RATIO AT OUTLET	NON-SEVERE	2.6158	.60634	0.032
	SEVERE	1.5360	.44813	
WRIST FOREARM RATIO	NON-SEVERE	1.2332	.34194	0.018
	SEVERE	5.60	5.054	
WRIST FOREARM DIFFERENCE	NON-SEVERE	2.00	3.408	0.009
COLOUR DOPPLER PARAMETERS				
	SEVERE	2.27	.799	
VASCULARITY SCORE	NON-SEVERE	1.48	1.252	0.035

c) Color doppler parameter

Hypervascularity of the median nerve is assessed by color Doppler sand power Doppler imaging in the longitudinal view. The color gain is set to the maximum level and adjusted until no noise artifacts are seen (Figure 4c).

Hypervascularity was evaluated by scores based on El Miedany, et al.'s study (13):

Score 0: No color flow signal

Score 1: One single vessel within the nerve

Score 2: 2 or 3 single or 2 confluent vessels

Score 3: More than 3 single or more than 2 confluent vessels

Statistical analysis

Clinical history including age, sex, and side of disease were recorded. All data were entered into a Microsoft Excel sheet (Microsoft Corporation, Redmond, WA, USA) and analyses were performed using Medcalc. The CSA and ratios were expressed in means and standard deviation. An unpaired t-test was used to compare the severe and non-severe groups. ROC curves were used to determine the cutoff values, sensitivity, specificity, and best predictor. A p-value < 0.05 was considered statistically significant.

Results

Of the total 42 diagnosed cases, 27 (64%) were categorized as non-severe and 15 (36%) were categorized as severe cases of carpal tunnel syndrome. The mean age of those with severe disease was 56 years (range: 50-65 years), while those with non-severe disease had a mean age of 46 years (range: 33-62 years). Among these patients, 29 (69.1%) were female, 10 (34 %) of whom had severe disease, and 13 (30.9%) were male, 5 (38.4%) of whom had severe disease. An unpaired t-test (Table 1) was used to compare the grey scale and color Doppler values in severe (Figures 5a-c) and non-severe (Figures 6a-c) groups. The CSA at inlet (mean: severe – 15.80±6.062, non-severe – 11.04±4.090, P-value: 0.004) and outlet (mean: severe – 12.67±4.419, non-severe – 9.33±2.760, P-value: 0.004), the flattening ratio at outlet (mean: severe – 3.034±0.56, non-severe – -2.616±0.606, P-value: 0.032), wrist to forearm ratio (mean: severe – 1.53±0.44, non-severe – 1.23±0.34, P-value: 0.018), wrist to forearm difference (mean: severe – 5.6±5, non-severe – -2±3.4, P-value: 0.009) and vascularity score (mean: severe – 2.27±0.8, non-severe – 1.48±1.2, P-value: 0.035) showed statistically significant difference between the two groups.

ROC curve analysis (Table 2) was used to assess diagnostic ability of each parameter. Among the grey-scale and Doppler parameters, CSA at outlet had the largest AUC (AUC=0.759) (Figure 7a), and among the derived parameters, wrist-forearm difference had the largest AUC (AUC = 0.811) (Figure 7b). Both had 95% confidence intervals, making these parameters the best predictors of severity.

Using Youden's Index, the optimal cutoff for CSA at outlet was determined to be 11 mm2. At this cutoff, CSA had a specificity of 94.5% and a sensitivity of 40%. The optimal cutoff for wrist-forearm difference was 5 mm2, with a specificity and sensitivity of 92.5% and 40%, respectively, for diagnosis of severe CTS.

Discussion

While counselling patients about treatment, the severity of CTS has significant implications. Non-severe CTS is typically treated with conservative therapies such as splinting, perineural corticosteroid injections and oral medications, while severe CTS often necessitates surgical release. Therefore, obtaining an objective measurement of severity adds value to the clinical examination. Conventionally, the preferred test for classification has always been the NCS, with a substantial body of literature supporting its usage (11,12,15). However, due to its invasive nature, patient discomfort, extended duration, and limited availability, there is a need for an alternative diagnostic test to address these limitations. Given its affordability, high efficiency, ready availability, and comparable diagnostic accuracy to NCS, HRUS has garnered increased attention in recent times. Additionally, HRUS provides an objective visualization of the nerve, excluding other physical causes of nerve compression.

Mohammadi et al. (11) measured the CSA of the median nerve at the carpal tunnel inlet and outlet in 164 wrists with NCS-confirmed CTS. The authors found that the difference in median nerve CSA between mild, moderate, and severe CTS was not statistically significant. However, the results in our study differ from this study, as we found a statistically significant correlation between severity and CSA at inlet, outlet, and flattening ratio at outlet.

In a separate study of 90 wrists, Mohammadi et al. (16) found a significant correlation between median nerve hypervascularization and the severity of CTS for moderate and severe disease. Our study also showed that the vascularity score has a statistically significant correlation between the severe and non-severe groups. However, it is not the best predictor, as the area under the curve is not sufficiently large.

Nkrumah et al. (17) measured CSA at the inlet for 274 hands in NCS-diagnosed and classified CTS cases and compared the measurements with functional severity score, sensory severity score and CTS-6 scores from the clinical examination. The authors found that CSA at the inlet was the best predictor, with a CSA cut-off of 12 mm^2 having a specificity of 81.2% and sensitivity of 33.3%. In contrast to

Table 2.ROC analysis of non-derived, derived grey scale parameters and color Doppler parameters.

PARAMETERS	AREA UNDER THE CURVE	P VALUE
NON-DERIVED PARAMETERS		
CSA AT FOREARM (mm2)	.669	.072
CSA AT INLET (mm2)	.749	.002
CSA AT OUTLET (mm2)	.811	.001
FR THICKNESS(MM)	.696	.037
FR BOWING(MM)	.588	.351
DERIVED PARAMETERS		
SWELLING RATIO	.477	.803
FLATTENING RATIO AT FOREARM	.553	.572
FLATTENING RATIO AT INLET	.627	.176
FLATTENING RATIO AT OUTLET	.715	.022
WRIST FOREARM RATIO	.731	.014
WRIST FOREARM DIFFERENCE	.759	.006
COLOUR DOPPLER PARAMETERS		
VASCULARITY SCORE	.677	.061

their findings, our study identified CSA at the outlet and wrist-forearm difference as superior predictors with higher specificity.

In recent research, artificial intelligence technology has been employed to assess the morphological characteristics of the median nerve on ultrasound, facilitating the classification of severity of carpal tunnel syndrome cases.

In a 2024 study conducted by Ando et al. (18), a dataset comprised of 600 randomly selected median nerve images underwent analysis using convolutional neural networks (CNNs). Two convolutional neural networks (CNNs) architectures, U-Net and SegNet, were employed to assess the HRUS morphological features of median nerve. The CNNs accurately estimated ultrasound parameters, including the cross-sectional area, circumference, and diameter — which, when compared with manual annotation estimations, showed a robust agreement, with 95% limits of agreement.

In another retrospective study led by Lyu et al. (19), 237 wrists with CTS were categorized into mild, moderate, and severe cases based on clinical symptoms. The cases were then randomly allocated into a training set and a test set.

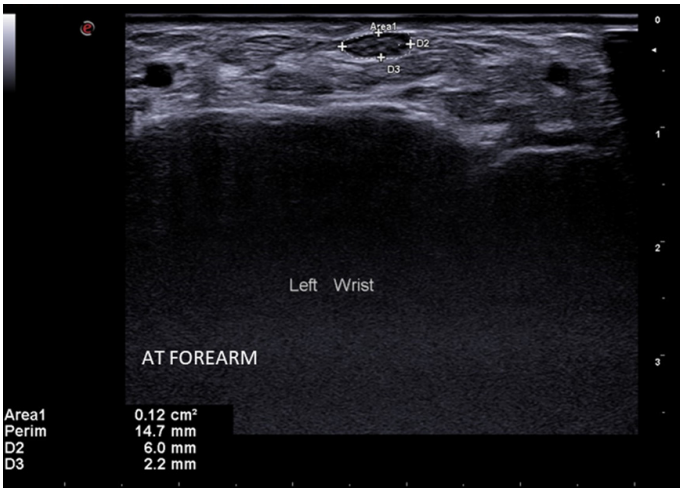

Figure 5a. A 69-year-old female patient diagnosed as severe CTS by NCS has a CSA at forearm of 12mm^2.

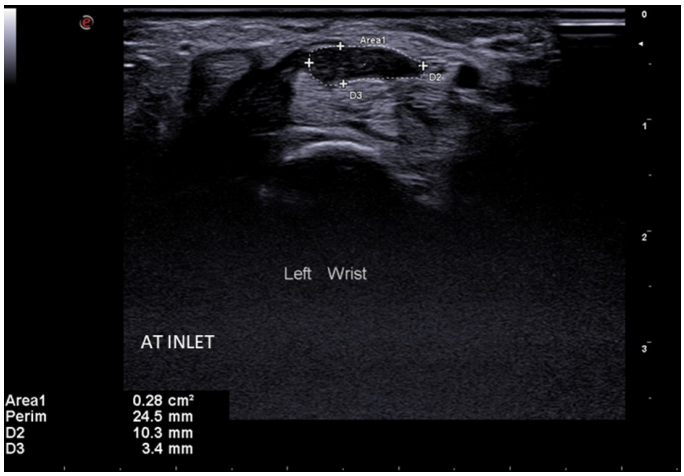

Figure 5b. CSA at inlet measured at 28 mm^2.

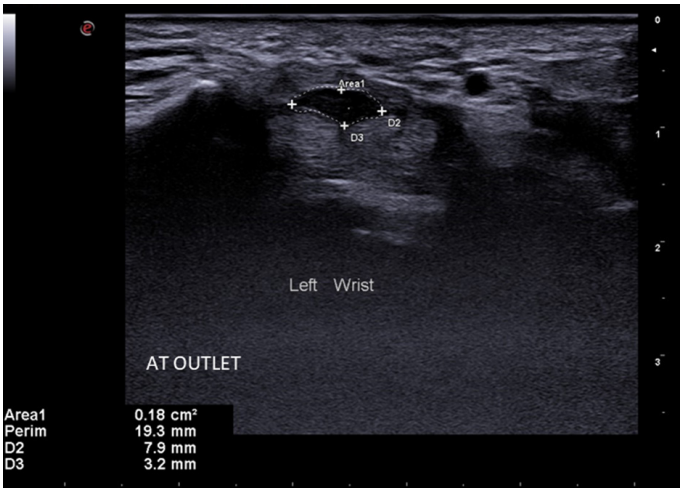

Figure 5c. CSA at outlet measured at 18 mm2 and a wrist forearm difference of 16 mm^2.

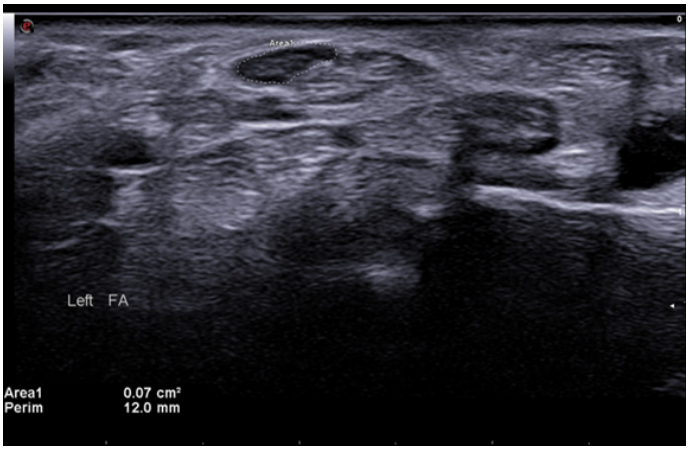

Figure 6a. 41-year-old female diagnosed as non-severe CTS by NCS has CSA at forearm measured at 7 mm^2.

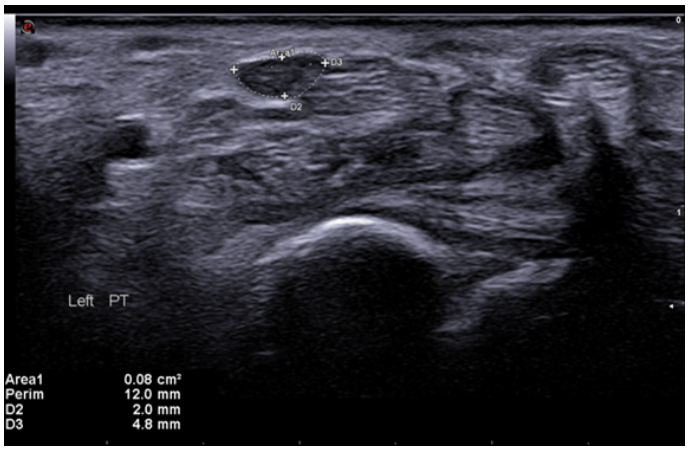

Figure 6b. CSA at inlet measured at 8 mm^2.

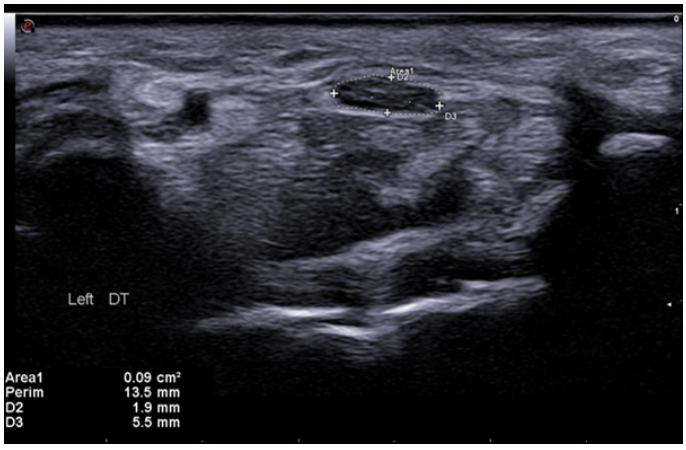

Figure 6c. CSA at outlet measured at 9 mm^2, with wrist forearm difference of 1 mm^2.

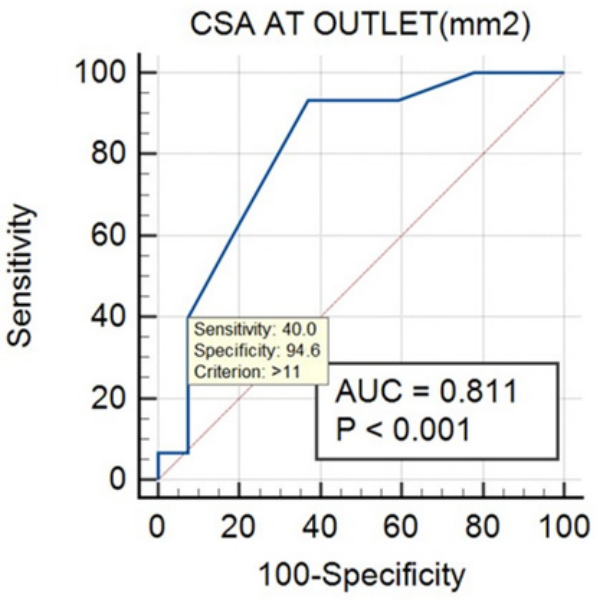

Figure 7a. ROC curve of CSA at outlet.

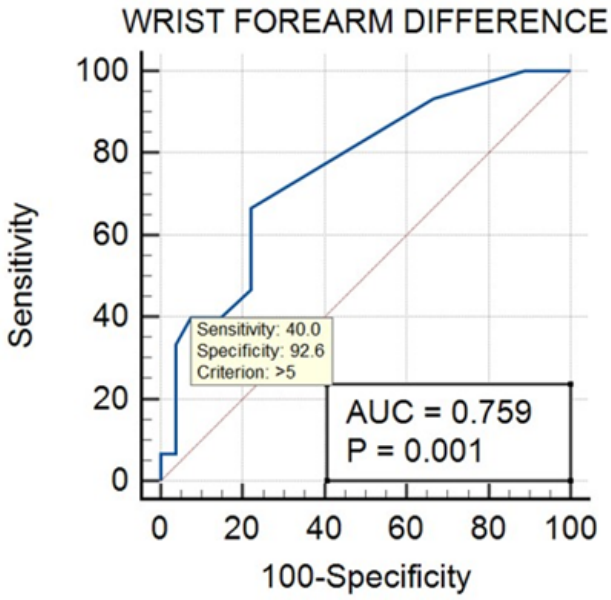

Figure 7b. ROC curve of wrist forearm difference of CSA.

The study employed ultrasound measurements of the median nerve cross-sectional area at the entrance of the carpal tunnel and utilized a recursive feature elimination (RFE) method to identify discriminative radiomic features. The radiomics model achieved 100% accuracy in classifying severity in the training set, while in the testing set, it accurately classified 76.39% of participants. Although it should be noted that diagnostic efficacy of this model does fall short of neuroelectrophysiology and multiple combined ultrasound parameters.

The findings of the aforementioned studies emphasize the promising potential of artificial intelligence-based models as effective tools for analyzing ultrasound images of the median nerve, and their ability to offer a quick and reliable alternative to manual measurement of parameters.

Our data indicate that a CSA at the outlet exceeding 11 mm^2 and a wrist-forearm difference exceeding 5 mm^2 are the best predictors of severe changes in CTS, with high specificity and moderate sensitivity. The high specificity is of clinical significance, as it aids in minimizing false positive cases of severe CTS and ensures that patients with non-severe CTS are not subjected to unnecessary surgical interventions.

The limitations of our study include a small sample size comprising only 42 wrists, moderate sensitivity of our proposed values, and absence of a control group comprised of individuals without symptoms of carpal tunnel syndrome. This may result in an increased number of false-negative cases. Therefore, we recommend that in patients classified as non-severe, physicians should exercise caution and complement HRUS findings with clinical judgment for a more comprehensive assessment.

Conclusion

High-resolution ultrasound is already a well-established modality for the diagnosis of carpal tunnel syndrome. Given its affordability, patient comfort and high availability, we propose that HRUS be used as an alternative to NCS for predicting the severity of CTS.

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