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Comparison of Ultrasonographic and Electrodiagnostic Findings Between Healthy and CTS Thais

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ABSTRACT

OBJECTIVE To compare the ultrasonography cross-sectional area (CSA) of the median nerve at the wrist (CSA-D), the wrist-to-forearm median nerve CSA ratio (WFR) and the difference (WFD) between individuals with carpal tunnel syndrome (CTS) and normal individuals in the Thai population and to explore the correlation between ultrasonography and electrodiagnosis (EDX).

METHODS A cross-sectional study was performed on a total of 112 wrists of 72 participants who were divided into two groups. Fifty-six wrists of 36 EDX-confirmed CTS patients were recruited as the CTS group and an equal number of individuals without CTS were chosen as a control group. Participants were matched for demographic data from a historical study. For both individuals with clinical CTS confirmed by EDX and the control population median nerve CSA levels at the wrist and at mid-forearm were measured by ultrasonography. A comparison was made between the parameters of the study group and those of the control group. The correlations between the CSA-D, the WFR, and the WFD and the severity of CTS evaluated by EDX were studied.

RESULTS The mean median nerve CSA-D, WFR, and WFD of the CTS patients were 14.7 ± 5.9 mm², 3.1 ± 1.4, and 9.7 ± 6.1 mm², respectively. In contrast, the mean median nerve CSA-D, WFR, and WFD of the control group were 9.6 ± 2.4 mm², 1.7 ± 0.4, and 3.8 ± 1.9 mm², respectively, indicating a statistically significant difference from the study group ($p < 0.001$). The optimal cut-point values for the median nerve CSA-D, WFR, and WFD in detecting CTS were 10.7 mm² (sensitivity 67.9%, specificity 83.9%), 1.8 (sensitivity 89.3%, specificity 71.4%), and 4.7 mm² (sensitivity 82.1%, specificity 81.8%), respectively. The median nerve CSA-D, WFR, and WFD exhibited significant moderate to strong positive correlation with the EDX grading of CTS severity.

CONCLUSIONS Ultrasonography of the median nerve CSA-D, WFR, and WFD are efficient for distinguishing CTS patients from asymptomatic controls with good sensitivity and specificity in the Thai population. WFD demonstrated superiority in the areas of sensitivity, specificity, and accuracy.

KEYWORDS carpal tunnel syndrome, median neuropathy, ultrasonography, electrodiagnosis

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. The prevalence ranges from 3.1 to 4.6 percent in the general population (1, 2). Diagnosis often relies on clinical signs, symptoms, and physical examination. Electrodiagnosis (EDX) helps in both confirming and differentiating diagnoses, e.g., cervical radiculopathy and peripheral polyneuropathy. Additionally, it can assist in the assessment of the disease severity, which consequently informs the management planning. Treatments include conservative treatment for mild to moderate degree cases and surgical procedures for severe cases. The sensitivity and specificity of the EDX for CTS are 82.0-94.0% and 65.0-97.0%, respectively, in patients with clinical symptoms. The validity relies on neurophysiological grading, various methodological issues, including variable reference standards, measurement methods, and spectrum bias in case-control studies (2, 3). Nevertheless, there are common limitations of EDX including tissue edema, patient intolerance of the evaluation procedure, and unavailability of evaluation equipment.

Currently, high-resolution ultrasound (US) serves as an effective instrument for assessing nerve anatomy and adjacent tissues. Advantages include time-saving, simplicity, and affordability. In comparison to the clinical diagnostic reference standard, the overall sensitivity of US was 86.4% and that of EDX was 91.6%. The pooled specificities for US and EDX were 79.3% and 81.9%, respectively. There were no statistically significant differences between US and EDX in terms of sensitivity, specificity, or diagnostic accuracy. In general, US and EDX have equal diagnostic accuracy for CTS diagnosis, with both having high sensitivity and intermediate specificity (4). In CTS, nerve compression can lead to a regional circulatory disruption, causing a breakdown of the blood-nerve barrier, which increases endoneurial fluid pressure, resulting in nerve swelling and further compromising local blood flow. The median nerve is frequently swollen in the proximal part of an entrapment site as a pathophysiology of CTS; hence, the nerve's cross-sectional area (CSA) is the most typical metric for diagnosis (2). The cut-point value for median nerve CSA at the distal wrist crease (CSA-D) for diagnosing CTS has previously been reported as ≥ 8.5-12 mm² (5-9). Previous researches have indicated that ethnicity, age, height, and body mass index (BMI) affect the nerve CSA. The median nerve CSA in Europeans appears to be larger than in Asians, however, there is variation in nerve CSA within the Asian population. For that reason, utilizing the same cut-point for diagnosing CTS across different nationalities may result in the nerve CSA being beyond the precise conditions range (10-12). Thus, the ratio of the median nerve CSA-D to that at the forearm (WFR) or their difference (WFD) will mitigate the influence of these factors. Several studies have reported that the diagnostic cut-point values for the WFR and the WFD in CTS are 1.4-2.4 (5, 6, 13) and 2.5-6 mm² (5, 7), respectively, indicating good sensitivity and specificity. However, in a study of the normal Thai population, the WFR of the median nerve ranged from 1.0 to 2.3, while the median nerve CSA-D measured between 5.3 and 13.3 mm² which falls within the range of the disease group (12). Measurement of only the median nerve CSA at the wrist might result in a false positive. Integrating additional US parameters may enhance the accuracy of distinguishing CTS from normal conditions. Furthermore, the measurement locations for median nerve CSA in the forearm, that is, at the pronator quadratus (PQ) (7, 8) and 10-12 cm from the wrist (5, 14), varied across the studies. The depth of tissue in the forearm in relation to the point of measurement may influence the clarity of the nerve CSA as well. According to Junck et al., the mid-forearm location significantly outperformed the distal one-third of the forearm in terms of inter-rater reliability (r = 0.81) (15).

Some previous studies have utilized variable criteria and grading severity. Previous research of the relationship between the median nerve CSA and the severity grading from electrodiagnostic findings has yielded varied outcomes (7, 13, 14, 16). However, some of those studies did not use EDX to exclude cervical radiculopathy or polyneuropathy, which may also affect the nerve CSA (17).

The main objective of the present study is to compare the CSA-D of the median nerve, the WFR, and the WFD between individuals with CTS and healthy controls. The study also determined the cut-point values of the CSA-D, the WFR, and the WFD in detecting CTS and examined the correlation between these findings and disease severity classified by EDX in a Thai population.

METHODS

Study design

This cross-sectional research study with a historical control was approved by the Ethics Committee at Lerdsin Hospital, Bang Rak District, Bangkok. The certification number is LH661070. The number for Thai Clinical Trials Registry is TCTR20231108002.

Participants

The study group, CTS patients who had undergone EDX at the Physical Medicine and Rehabilitation Department of Lerdsin Hospital between April and August 2024 were invited to participate. The inclusion criteria consisted of individuals of Thai ethnicity, aged over 18, who were diagnosed with CTS based on positive electrodiagnostic findings combined with any of the following clinical features: (1) experiencing numbness or pain of the thumb, index finger, middle finger, or ring finger which worsened with specific activities and improved with rest or hand movements, (2) having sensory disturbances in the radial three-and-a-half fingers, (3) exhibiting varying degrees of thenar muscle weakness or atrophy, and (4) having positive results of the Tinel's Test and/or Modified Phalen's Test (2). The exclusion criteria were individuals with neurological conditions such as cervical radiculopathy, brachial plexopathy, median nerve damage due to trauma, or peripheral polyneuropathy, patients who had negative findings on EDX to confirm CTS, patients who had received a CTS injection within six months prior to the examination date, patients who had undergone CTS surgery, patients who exhibited anatomical variations (Martin-Gruber anastomosis, Riché-Cannieu anastomosis) as determined by electrodiagnostic testing and patients whose median nerve exhibited bifurcation by US. All participants submitted written informed consent.

The control group data was retrieved in a retrospective study that included healthy Thai individuals who exhibited no clinical numbness nor weakness in either hand and who had undergone electrodiagnostic testing to exclude peripheral neuropathy and had received ultrasonography examinations of the median nerve at the distal wrist and mid-forearm, following the same methodology as the study group. This study was conducted from March 2022 to May 2023 (LH651011). Age, weight, and BMI were used in matching the groups to ensure that the demographic characteristics of the control aligned closely with those of the study group. The sample size was determined according to previous studies (5, 13) by using the two independent means formula. The average and standard deviation (SD) of the median nerve CSA-D, WFR, and WFD were calculated. The delta of the mean median nerve CSA-D, WFR, and WFD were 6.2, 0.25, and 6.0 respectively. An alpha of 0.05 was selected. The power effect size was 0.8. A sample size of 30 individuals in each group was selected for the study. Considering an anticipated dropout rate of 20.0%, 72 individuals were included.

EDX of CTS

The median and ulnar nerve conduction studies (NCS), including sensory nerve action potential (SNAP) and compound motor action potential (CMAP), were conducted by physiatrists using Nicolet Synergy equipment (Natus Medical Inc., San Carlos, CA, USA). Needle electromyography (EMG) was performed on the patients who had no median CMAP response and to differentiate CTS from other conditions. Normal reference values were based on American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) 2020 (18).

Median CMAP: the active electrode was placed halfway between the midpoint of the distal wrist crease and the first metacarpophalangeal joint, and the stimulation sites were at the wrist (8 cm proximal to the active electrode) and the elbow (medial to the brachial artery pulse).

Ulnar CMAP: the active electrode was placed on the hypothenar eminence, and the stimulation sites were at the wrist (8 cm proximal to the active electrode) and the olecranon fossa.

Median SNAP: the active electrode was placed on the index finger, and the stimulation site was at the wrist, 14 cm proximal to the active electrode.

Ulnar SNAP: the active electrode was placed on the little finger, and the stimulation site was at the wrist, 14 cm proximal to the active electrode.

For patients who exhibited normal median SNAP and median CMAP, confirmatory electrophysiological evidence was defined as any difference ≥ 0.4 millisecond (ms) between: 1) a 8-cm orthodromic palmar median-ulnar peak latency difference;

2) a 14-cm antidromic median-ulnar sensory peak latency difference to the ring finger; 3) a 10-cm antidromic median-radial peak latency difference to the thumb; or 4) a combined summary index ≥ 0.9 ms (3). Skin temperature during the measurements was maintained at between 32 and 34 degrees Celsius.

The severity of CTS was classified into three levels according to Werner et al. as follows: (1) mild: prolonged (relative or absolute) sensory latency with normal motor study and no evidence of axonal loss; (2) moderate: abnormal median sensory latency as noted for mild CTS, and (relative or absolute) prolongation of median motor distal latency with no evidence of axonal loss. (3) severe: any of the aforementioned NCS abnormalities with evidence of axonal loss as defined by either (a) a low-amplitude or absent SNAP (b) a low-amplitude or absent thenar CMAP (c) a needle EMG with fibrillation potentials or motor unit action potential changes (large amplitude, long-duration motor unit potentials, or excessive polyphasics). Both hands were included if the patient exhibited clinical symptoms of CTS and had a positive EDX exam.

Ultrasonography

All individuals underwent ultrasonographic examination using a multifrequency linear transducer operating at 4-18 megahertz (MHz) (Konica Minolta, SONIMAGE® HS1, Tokyo, Japan) in B mode, conducted on the same day as the electrodiagnostic study by a single physician who was blinded to the CTS severity results. The participants were seated with their palms facing up, wrists in neutral position, and fingers slightly flexed. US was used to identify the median nerve. The transducer angle was set to be perpendicular to the nerve in order to get images with the smallest CSA and to avoid anisotropy effect. The Color Doppler test assessed the vascular component. The focus and depth were adjusted according to the target location. The CSA was measured at each location using the ellipsoid function to trace inside the nerve's hyperechoic border. The median nerve CSA at each site was calculated by averaging the results from three separate tests: the distal wrist crease (at the level of the pisiform bone) and the mid-forearm, which was determined at the midpoint between the distal wrist crease and the elbow (Figure 1).

Outcome measurements

The median nerve CSA at the distal wrist and the mid-forearm were recorded. The wrist-to-forearm median nerve CSA ratio (WFR) was calculated by dividing the nerve CSA at the wrist by the nerve CSA at the mid-forearm. The wrist-to-forearm difference (WFD) was calculated by subtracting the median nerve CSA at mid-forearm from the median nerve CSA at the distal wrist.

Statistical methods

Statistical analysis was performed using the PASW Statistics version 18.0 program. (SPSS Inc., Chicago, IL, USA). Continuous data was analyzed using an independent t-test and reported as mean and SD. The results for categorical data were analyzed using the Chi-square test and Fisher's exact test and are displayed as frequencies and

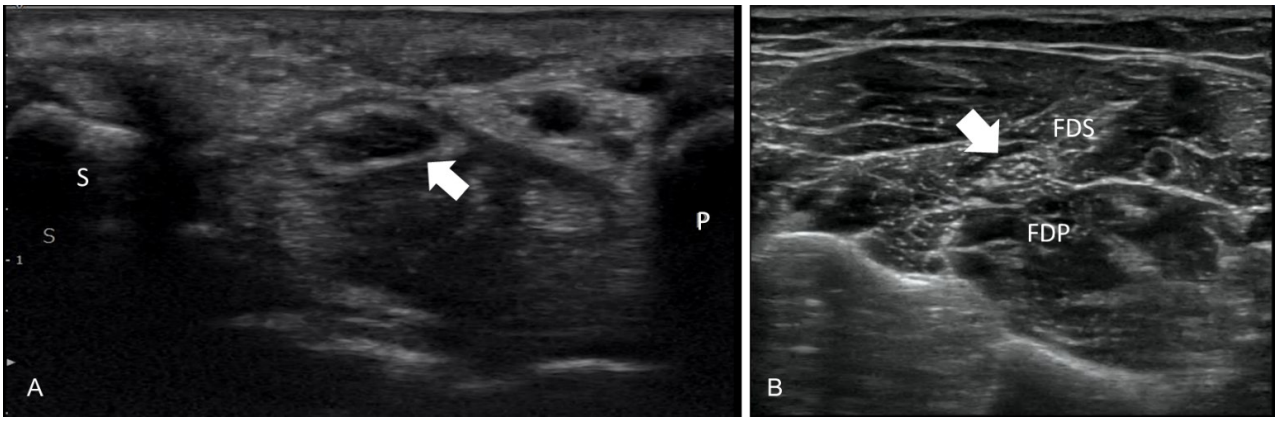

Figure 1. Ultrasonography of the nerve cross-sectional area (CSA) at each measured site. (A) median nerve at wrist, (B) median nerve at mid-forearm; FDP, flexor digitorum profundus; FDS, flexor digitorum superficialis; P, pisiform bone; S, scaphoid bone. Arrows show the median nerve.

percentages. The independent t-test was employed to compare the demographic data between the study group and the control group. One-way ANOVA with Bonferroni correction was applied to compare disease severity. The receiver operating characteristic (ROC) curve was used to evaluate the cut-point value to distinguish CTS group from the control group and for differentiating severe CTS from non-severe CTS by determining the highest accuracy. Spearman correlation coefficients (r) were utilized to assess the relationship between the severity of CTS and the median nerve CSA-D, WFR, and WFD. The relationships between the median nerve CSA-D and NCS parameters were assessed using Pearson's correlation coefficient (r). A $p < 0.05$ was considered statistically significant.

RESULTS

Of 52 participants referred for CTS evaluation, 36 participants (56 wrists) were clinically diagnosed with CTS as confirmed by EDX (Figure 2). A total of 32 females were included, representing 88.9% of the sample. The mean age, weight, height, and BMI were 53.1 ± 12.4 years, 64.7 ± 17.2 kg, 157.0 ± 7.9 cm, and 26.1 ± 5.4 kg/m^2, respectively. The demographic data did not show any statistically significant differences between the study group and the control group (Table 1).

A significant difference was observed in the median nerve CSA-D, measuring 14.7 ± 5.9 mm^2 in the study group compared to 9.6 ± 2.4 mm^2 in the control group. The median nerve CSA-D (mm^2) for mild, moderate, and severe degrees was measured at 11.1 ± 2.5, 14.0 ± 4.6, and 21.4 ± 5.6, respectively, with statistically significant differences observed both between the mild to severe group and between the moderate to severe group. A notable difference in the median nerve CSA (mm^2) at the mid-forearm was seen between the study (5.0 ± 1.0) and control (5.8 ± 2.0) groups. However, there was no significant difference across the severity categories (Table 2).

The WFR of the median nerve for the study and control groups was 3.1 ± 1.4 and 1.7 ± 0.4, respectively, a statistically significant difference The groups classified as mild, moderate, and severe had mean values of 2.3 ± 0.7, 2.9 ± 1.2, and 4.6 ± 1.2, respectively. A statistically significant difference was observed between the mild and severe groups and between the moderate and severe groups (Table 2).

The WFD of the median nerve for the study group was 9.7 ± 6.1 mm^2, while for the control group it was 3.8 ± 1.9 mm^2, a statistically significant difference. The subgroups mild, moderate, and

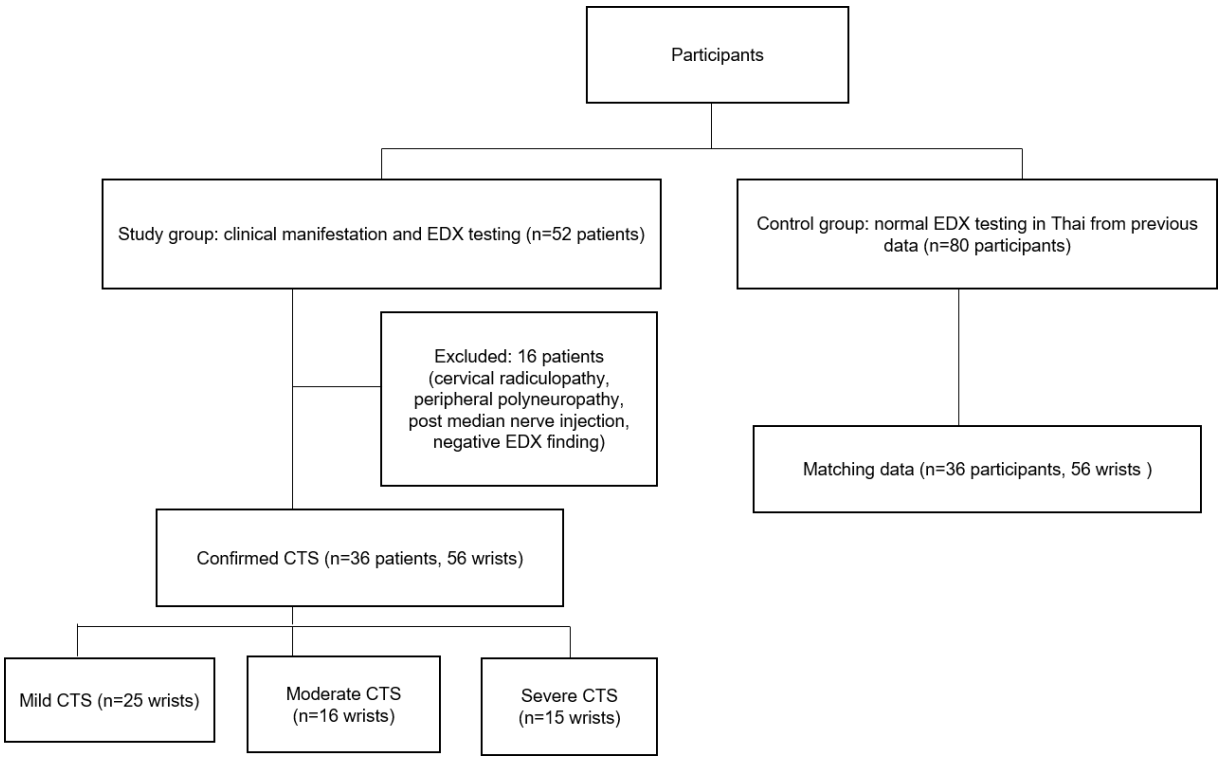

Figure 2. Flow chart of participants; EDX, electrodiagnosis; n, number; CTS, carpal tunnel syndrome

Table 1. Characteristics of patients (n = 36 individuals) with carpal tunnel syndrome and the control group (n = 36 individuals)

Parameters	CTS (n = 36) Mean (SD), (min, max)	Control (n = 36) Mean (SD), (min, max)	*p*-value
Sex[a] n (%)			
Male: female	4 (11.1):32 (88.9)	10 (27.8):26 (72.2)	0.074
Age (years)[b]			
All	53.1 (12.4), (22, 79)	52.5 (12.6), (23, 72)	0.822
Male	59.0 (11.4), (46, 73)	56.3 (8.7), (41, 72)	0.639
Female	52.4 (12.5), (22, 79)	51.0 (13.7), (23, 70)	0.684
Weight (kg)[b]			
All	64.7 (17.2), (44, 110)	61.8 (13.0), (42, 90)	0.424
Male	78.0 (16.5), (65, 101)	69.1 (11.0), (51, 85)	0.255
Female	63.1 (16.8), (44, 110)	59.0 (12.8), (42, 90)	0.318
Height (cm)[b]			
All	157.0 (7.9), (143, 174)	158.7 (7.7), (144, 175)	0.361
Male	169.0 (5.0), (163, 174)	166.4 (5.5), (158, 175)	0.432
Female	155.5 (6.9), (143, 170)	155.7 (6.3), (11, 168)	0.899
Body mass index (kg/m^2)[b]			
All	26.1 (5.4), (18.7, 38.5)	24.4 (3.9), (18.2, 34.1)	0.144
Male	27.3 (5.4), (21.5, 34.1)	24.8 (2.8), (20.4, 29.0)	0.274
Female	25.9 (5.4), (18.7, 38.5)	24.2 (4.3), (18.2, 34.1)	0.215
Underlying disease[a] n (%)			
None	33 (91.6)	36 (100.0)	
Diabetic mellitus	2 (5.6)	-	
Hypothyroidism	1 (2.8)	-	
Duration of symptoms[b] (month) median (range)	9.5 (1, 156)	-	
Severity[a] (56 wrists) n (%)			
Mild	25 (44.6)	-	
Moderate	16 (28.6)	-	
Severe	15 (26.8)	-	

[a]Chi-square test, [b]Independent t-test
CTS, carpal tunnel syndrome; SD, standard deviation; min, minimum; max, maximum; kg, kilogram; cm, centrimeter; mm^2, square millimeter

Table 2. Ultrasonographic findings of the median nerve in relation to the electrophysiological classification of carpal tunnel syndrome severity

Ultrasonographic findings	Electrophysiological classification of CTS severity (n=56 wrists): mean (SD) (min, max)				Control (n=56 wrists)	*p*-value[b]	*p*-value[a]
	All[a]	Mild	Moderate	Severe			
CSA at wrist (mm^2)	14.7 (5.9) (8.3, 32.3)	11.1 (2.5) (8.3, 20.3)	14.0 (4.6) (8.7, 24.3)	21.4 (5.6) (12.3, 32.3)	9.6 (2.4) (6.0, 17.7)	<0.001*+	<0.001#
CSA at MF (mm^2)	5.0 (1.0) (3.0, 7.7)	5.1 (1.1) (3.0, 7.7)	5.2 (0.9) (4.0, 7.0)	4.8 (0.7) (3.7, 6.0)	5.8 (2.0) (3.0, 15.7)	0.468	0.008#
WFR	3.1 (1.4) (1.4, 7.0)	2.3 (0.7) (1.4, 4.1)	2.9 (1.2) (1.6, 6.0)	4.6 (1.2) (2.6, 7.0)	1.7 (0.4) (1.1, 3.1)	<0.001*+	<0.001#
WFD (mm^2)	9.7 (6.1) (3.0, 26.3)	6.0 (2.7) (3.0, 15.3)	8.9 (4.9) (4.0, 20.0)	16.6 (5.4) (8.0, 26.3)	3.8 (1.9) (0.7, 10.7)	<0.001*+	<0.001#

[a]*p*-value compared between the study (all) and the control groups by Independent t-test, [b]*p*-value compared among the severity groups by One-Way ANOVA with Bonferroni correction, *statistical significance between mild and severe degree, +statistical significance between moderate and severe degree, #statistical significance between the study and the control groups ($p < 0.05$), CTS, carpal tunnel syndrome; SD, standard deviation; min, minimum; max, maximum; CSA, cross-sectional area; mm^2, square millimeter; MF, mid-forearm; WFR, wrist-to-forearm ratio; WFD, wrist-to-forearm difference

Table 3. Sensitivity and specificity of ultrasonographic nerve assessment in determining carpal tunnel syndrome and identifying severe carpal tunnel syndrome from non-severe patients

Ultrasonographic findings	Cut-point	Sensitivity %	Specificity %	Accuracy %
CSA at wrist (mm^2)				
CTS from control	10.7	67.9	83.9	75.9
Severe from non-severe	14.5	86.7	90.2	89.3
WFR				
CTS from control	1.8	89.3	71.4	80.4
Severe from non-severe	3.1	86.7	85.4	85.7
WFD (mm^2)				
CTS from control	4.7	82.1	81.8	82.0
Severe from non-severe	11.0	86.7	90.2	89.3

CSA, cross-sectional area; mm^2, square millimeter; CTS, carpal tunnel syndrome; WFR, wrist-to-forearm ratio; WFD, wrist-to-forearm difference

severe degrees exhibited a WFD of 6.0 ± 2.7 mm^2, 8.9 ± 4.9 mm^2, and 16.6 ± 5.4 mm^2, respectively. A statistically significant difference was found between the mild and severe groups and between the moderate and severe groups (Table 2).

In comparison of the mild and moderate CTS subgroups, no statistically significant difference was observed in the median nerve CSA-D, the CSA at the mid-forearm, the WFR, and the WFD.

ROC curves were used to determine the optimal US cut-point values to distinguish CTS group from the control group. The median nerve CSA-D, WFR, and WFD had areas under the curve (AUC) of 0.830 (95% confidence interval [CI]; 0.756, 0.905), 0.867 (95%CI; 0.801, 0.934), and 0.882 (95%CI; 0.822, 0.943), respectively. All the AUCs showed high values. The median nerve CSA-D has an optimum cut-point value of 10.7 mm^2, with a sensitivity of 67.9% and specificity of 83.9%. The WFR, with a cut-point value of 1.8, has a sensitivity of 89.3% and a specificity of 71.4%. The WFD's cut-point was determined to be 4.7 mm^2, with 82.1% sensitivity and 81.8% specificity (Table 3, Figure 3).

In differentiating severe from non-severe CTS, the AUCs for the CSA-D, WFR, and WFD in severe CTS were 0.932 (95%CI; 0.868, 0.996), 0.920 (95%CI; 0.847, 0.994), and 0.928 (95%CI; 0.861, 0.994), respectively. An optimal cut-point value for median nerve CSA-D was determined to be 14.5 mm^2, with a sensitivity of 86.7% and a specificity of 90.2%. The cut-point value of the WFR was established at 3.1, demonstrating a sensitivity of 86.7% and a specificity of 85.4%. The cut-point value of the WFD was determined to be 11.0 mm^2, with a sensitivity of 86.7% and a specificity of 90.2% (Table 3, Figure 4).

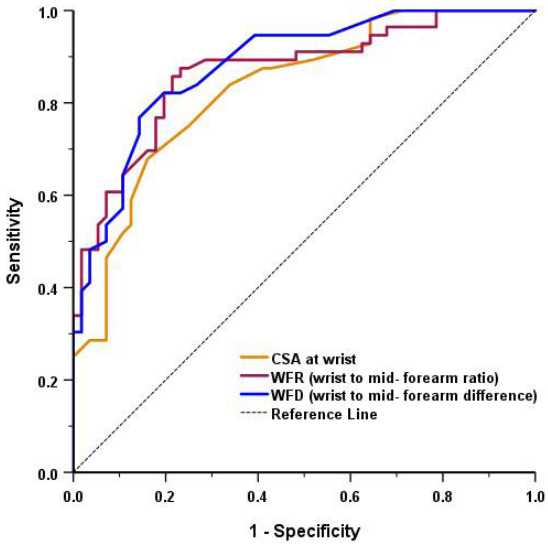

Figure 3. Receiver operating characteristic (ROC) curves with area under the curve of median nerve cross-sectional area (CSA) at the wrist, WFR (wrist-to-forearm ratio), and WFD (wrist-to-forearm difference) for diagnosing carpal tunnel syndrome

All median nerve CSA-D, WFR, and WFD values showed moderate to strong, positive and statistically significant correlation with disease severity (Table 4). A statistically significant moderate positive correlation was observed between the median nerve CSA-D and both the median SNAP latency and the median CMAP latency. The median nerve CSA-D showed a notable weak negative correlation with the amplitude of median SNAP and a moderate negative correlation with the amplitude of median CMAP. Additionally, there was a weak negative correlation with the median nerve conduction velocity (NCV) measured from the forearm to the wrist segment (Table 5).

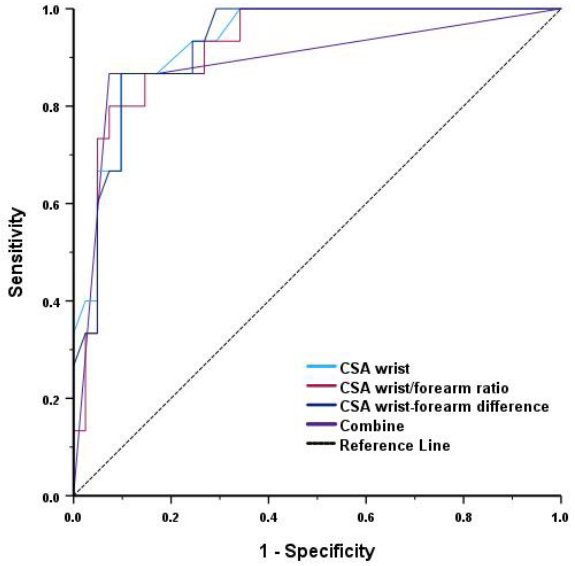

Figure 4. Receiver operating characteristic (ROC) curves with area under the curve of median nerve cross-sectional area (CSA) at the wrist, WFR (wrist-to-forearm ratio), and WFD (wrist-to-forearm difference) to assess severity of carpal tunnel syndrome

DISCUSSION

The results of this study indicate that the median nerve CSA-D, the WFR, and the WFD exhibit a substantial increase in CTS participants when compared to normal participants in Thailand. Additionally, the median nerve CSA-D, the WFR, and the WFD in CTS demonstrate a statistically significant moderate to strong positive correlation with disease severity as determined by the EDX.

The median nerve CSA-D (mm^2) of the study group (14.7 ± 5.9) was comparable to that of several studies which reported results ranging from 14.0 to 15.0 (6, 19, 20), however, Xu's (16.1 ± 0.8) (8) and Elnady's (18.4 ± 5.4) (7) studies reported larger averages. In contrast, the median nerve CSA-D in Billakota's study (12.6) (9), and El-Najjar's study (12.5 ± 3.4)(16) were smaller than our finding. The median nerve CSA-D (mm^2) in our control group (9.6 ± 2.4) is consistent with the findings of Phongamwong's study (9.4 ± 2.1) conducted in Thailand (21), while it differed slightly from previous studies (Hunderfund [8.6 ± 2.9], Webb [10.0 ± 2.3], Ratasvuori [7.0]) (5, 19, 20). Differences in demographic factors, including age in years (ours [52.5 ± 12.6], Webb [39.2 ± 14.2], Hunderfund [56 ± 16]) and ethnicity may influence the nerve CSA. Additionally, the different finger positions in different laboratories may also affect the nerve CSA. For example, some studies assessed the nerve CSA in finger flexion position (14, 22), while others evaluated it in finger extension position (20, 23). The measuring method used, which includes the trace and ellipsoid functions, may also have had an impact on the findings. Therefore, the nerve CSAs could differ between studies.

Table 4. Correlation between the median nerve CSA at wrist, wrist-to-forearm ratio (WFR), wrist-to-forearm difference (WFD) and severity of carpal tunnel syndrome

Parameters	Correlation coefficients[a]	*p*-value
CSA at wrist (mm^2)	0.678	<0.001*
WFR	0.713	<0.001*
WFD (mm^2)	0.743	<0.001*

[a]Spearman rank correlation coefficients, *statistically significant ($p < 0.05$)
CSA, cross-sectional area; mm^2, square millimeter; WFR, wrist-to-forearm ratio; WFD, wrist-to-forearm difference

Table 5. Correlation between ultrasound cross sectional area at wrist and electrodiagnostic parameters in carpal tunnel syndrome patients

Electrodiagnostic parameters of CTS	Correlation coefficient[a]	*p*-value
Latency SNAP	0.483	<0.001*
Amplitude SNAP	-0.358	0.012*
Latency CMAP	0.631	<0.001*
Amplitude CMAP	-0.479	<0.001*
NCV	-0.368	0.007*

[a]Pearson's correlation coefficient (r); *statistically significant ($p < 0.05$)
CTS, carpal tunnel syndrome; SNAP, sensory nerve action potential; CMAP, compound motor action potential; NCV, nerve conduction velocity (from wrist to forearm segment)

The average median nerve CSA-D (mm^2) in CTS severity grading by EDX in our study revealed values of 11.1 ± 2.5 for mild degree, 14.0 ± 4.6 for moderate degree, and 21.4 ± 5.6 for severe degree. Our results correspond with one previous study (12.0 ± 3.0 for mild, 15.0 ± 3.0 for moderate, 19.0 ± 6.0 for severe) (14) which applied the same CTS clinical and EDX criteria for diagnosis as ours. However, two other studies which used different criteria reported different findings (9-11 for mild, 11-13 for moderate, 12-15 for severe) (22, 24). Additionally, in the present study the median nerve CSA-D, WFR, and WFD exhibited statistically significant increases as the severity of CTS progressed according to the EDX grading. That correlation was comparable to those of the previous studies (6, 14, 16, 21, 25). However, one study reported no significant change in the

relationship between the median nerve CSA-D and the EDX severity grading (22), while others showed a weak correlation (5, 14). The discrepancy might arise from the classification of CTS severity grade, which was not consistent among the studies. A mild or moderate degree CTS involves mainly demyelination whereas a severe degree involves the axon. Patients with advanced degree CTS had greater CSA and more pronounced clinical manifestations compared to those with only demyelination (25, 26).

Because demographic factors can affect the nerve CSAs, the WFR and the WFD of the median nerve were the most suitable parameters to use as internal controls for detecting CTS. Moreover, direct measurement of the median nerve CSA at the wrist may not provide the most effective ultrasonographic criterion for diagnosis in CTS, especially for patients with other underlying pathologies, e.g., a patient with demyelinating hereditary sensorimotor neuropathy may have generalized enlargement of all nerves (27).

The WFR in CTS in our study group was 3.1 ± 1.4, which was statistically significantly different from the control group (1.7 ± 0.4). This outcome is comparable to those of earlier studies that measured the median nerve CSA at 12 cm proximal to the wrist or at mid-forearm level (Mhoon [2.3 ± 0.67], Hunderfund [3.1 ± 1.5]) (5, 6). However, in studies where the measurement was taken at the pronator quadratus (PQ) muscle, the ratio was 1.6 ± 0.1 (8, 23), which is lower than that of our control group. In CTS, the median nerve has a slight enlargement, reaching approximately 4 cm proximally from the wrist (28). Therefore, the WFR, calculated from the distal wrist and divided by the distal third of the forearm, would be reduced. Moreover, the intra- and inter-rater reliability rates were highest for visuals obtained at the wrist, with inter-rater reliability being fairly high at the mid-forearm and lowest at the PQ level (15). The median nerve CSA at the mid-forearm measurement appears to be more appropriate. While there are few studies on the median nerve WFD, our group found a significant difference ($p < 0.001$) compared to the control group. The value of our result is slightly lower than that in an earlier study (5).

In the present study, the WFR and the WFD (mm^2) cut-point values for CTS and non-CTS were 1.8 and 4.7. Our study's WFR was higher than Mhoon's study at 1.4 (6) and lower than Hunderfund's study at 2.4 (5). The sensitivity in Mhoon's study was high (97.0%) (6), similar to ours (89.3%), while it was medium in the Hunderfund's study (67.0%) (5). The median nerve WFR cut-points in our study were acceptable. Comparing the three values in our study, the cut-point value of the WFR and the WFD showed excellent sensitivity and accuracy (>80.0%), while the sensitivity (67.9%) and the accuracy (75.9%) of the median nerve CSA-D cut-point value were lower. The WFD also showed greater specificity (81.8%) compared to the WFR (71.4%). The WFD demonstrated superiority over the other methods for CTS screening, consistent with the findings of a previous study (5). Calculating the WFD may also be simpler than calculating the WFR. However, the CSA of nerves can differ among ethnic groups. The WFD values from our study may be applicable only to Thais but not to other ethnicities.

The sole ultrasonographic parameter to detect CTS demonstrated poor to intermediate sensitivity (47.0-70.0%), but the combination of two sonographic measurements, i.e., proximal CSA combined with volar bulging, yielded greater sensitivity (>90.0%) while maintaining the same specificity found in a previous study (29). Using multiple parameters for detection may enhance the screening process; however, because both the WFR and the WFD exhibited comparable good sensitivity (>80.0%) and accuracy (>80.0%), using both the WFR and the WFD may not result in better outcomes.

The median nerve CSA-D (mm^2) cut-point value for distinguishing CTS from non-CTS in this investigation was 10.7. That median nerve CSA-D cut-point value resembles previous studies (5, 7, 20). However, the mean CSA-D of the median nerve and the WFR in normal Thai individuals over 50 years of age were 10.5 mm^2, and 1.7, respectively (12). Ultrasonography should be used with caution when detecting CTS in the elderly (age > 50). In this study, the control group's WFR was 1.7, near to the CTS cut-point of 1.8. If the ratio is not clearly over the threshold limit, we recommend clinical diagnosis with EDX confirmation.

We analyzed the cut-point value to separate severe from non-severe cases because the median nerve CSA-D, WFR, and WFD significantly corre-

lated with the severity of EDX in our study. The cut-point values for detecting the median nerve CSA-D, the WFR, and the WFD in severe CTS in this study were 14.5 mm^2, 3.1, and 11.0 mm^2, respectively, demonstrating high sensitivity and specificity of more than 85.0%. These findings are consistent with Abrishamchi's study (CSA-D 15 mm^2, WFR 3), but that study had lower sensitivity and specificity (64.8-70.9%) than ours (14). Furthermore, research that used the median nerve CSA-D to distinguish CTS with moderate to severe degrees from none to mild degrees found 14.0 as a cut-point value, similar to ours, with high specificity (91.4%) but with low sensitivity (42.3%) (21). Although the median nerve CSA-D cut-point value appeared to be insufficient for screening across trials, it demonstrated great specificity in identifying patients with severe CTS.

CTS is generally diagnosed using clinical data and physical examination. The EDX is regarded as the reference standard for diagnosing and grading the severity of the disease, with sensitivities of 82.0-94.0% and specificities of 65.0-97.0% (2, 30). Surgery is the recommended treatment for severe cases. The cut-point values of the median nerve CSA measurements are essential for identifying severe CTS in locations where EDX equipment is not available and for patients who will not tolerate EDX investigation. Additionally, the US is painless, inexpensive, less time consuming, has no contraindications, and is easy to assess. It also enables observation of anatomical variation and nerve morphology which is also beneficial for treatment planning. According to a recent study, imaging is a supplemental tool to the basic clinical and EDX assessments of CTS, even if the combination of a typical clinical history and EDX results provides the most accurate diagnosis of this condition. Patients with unilateral CTS affecting the non-dominant hand, typical syndromes with negative electrophysiological findings, and atypical upper limb sensory syndromes are recommended to undergo ultrasonography (30). However, a standard protocol for scanning, including the positioning of the forearm and hand, the measurement site, and the tracing method, should be established.

Limitations

Our research has many limitations. Firstly, the absence of blinding the ultrasonographer to the diagnosis may have led to selection bias and may have affected the outcomes of the ultrasonography. Secondly, our control group did not coincide temporally with that of the study group. Third, there was an absence of inter-rater reliability evaluation. A recent study using ultrasonography scanning, however, did reveal good to excellent inter-rater reliability for median nerve assessment, suggesting that high-resolution ultrasonography is a reliable technique for evaluating the nerve CSA (12, 21). Forth, the study was conducted within the Thai ethnic group, so the cut-point values for identifying CTS are applicable only to that specific group. We utilized clinical criteria and EDX to diagnose CTS in accordance with AANEM guidelines; however, the ultrasound outcomes might have varied if other criteria had been employed in other laboratories. Fifth, when a patient has a CTS, the EDX may provide a false negative result, a situation which was not considered in this research. The cut-point values were not applicable to CTS patients who were diagnosed based on only their clinical presentation. Future research should improve the methodology, involve a larger prospective population, categorize participants into three severity groups for CTS, and should also include CTS patients with negative EDX findings.

CONCLUSIONS

Median nerve ultrasonography parameters are useful for identifying CTS in a healthy Thai population. The findings demonstrate that the WFR and the WFD, which are not dependent on demographic factors, are appropriate additional variables for detecting CTS with positive EDX. Cut-points of all three measures demonstrated good sensitivity and moderate to high specificity. The ultrasonography parameters were also able to distinguish severe from mild to moderate degrees. A significant moderate to strong positive correlation was found between the median nerve CSA-D, WFR, and WFD and the CTS severity by EDX. The diagnostic recommendations are primarily based on clinical and physical examinations, with ultrasound serving as a complementary method.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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