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Reference Values of Nerve Cross-sectional Area Obtained by Ultrasound in the Upper Extremity Correlated with Electrodiagnosis in Thai Adults

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ABSTRACT

OBJECTIVE To evaluate the ultrasonography cross-sectional area (CSA) reference values of nerves in the upper extremity correlated with electrodiagnosis in healthy Thai adults.

METHODS A cross-sectional study was performed. Ninety participants were recruited and their CSA at 10 sites on the median, ulnar, and radial nerves were measured bilaterally. A nerve conduction study (NCS) was conducted and the correlations between the nerve CSA and age, sex, height, weight, body mass index (BMI), and NCS parameters were studied.

RESULTS The mean CSA ranged from 5.8±1.4 to 9.5±1.5 mm^2 along the median nerve and 4.5±0.8 to 7.7±1.7 mm^2 along the ulnar nerve. The mean CSAs of the radial nerve at the elbow and spiral groove were 5.0±0.9 and 4.6±0.8 mm^2, respectively. The CSA of the median nerve at the wrist and the CSA of the radial nerve at the spiral groove were positively correlated with weight and BMI, whereas the CSA of the median nerve at the elbow was positively correlated only with weight. There was an association between CSA values and electrodiagnosis parameters as the nerve CSA increased, as the latency was prolonged, and as the amplitude decreased.

CONCLUSIONS The reference values of nerve CSA in the upper extremity at multiple sites can be helpful in the evaluation of peripheral nerve disorders in the Thai population.

KEYWORDS cross-sectional area, ultrasonography, peripheral nerves, electrodiagnosis

INTRODUCTION

High-resolution ultrasound (HRU) is an emerging technology for evaluation of the peripheral nervous system because it is a non-invasive investigation which provides real-time, high-quality images. Peripheral nerves and their surroundings can be described morphologically using HRU. The cross-sectional area (CSA) obtained by HRU provides valuable information about nerve size and potential pathological changes. It has become clear that several conditions can result in an increase in nerve CSA. These conditions include entrapment, hereditary neuropathies, acquired neuropathies, trauma, and nerve tumors (1-5). Patients with amyotrophic lateral sclerosis, however, have significantly lower median and ulnar nerve CSAs than healthy controls (6). The nerve CSA reference values and their correlation with demographics have been reported

in several studies (7-11). Hsieh et al. examined reference values for CSA of peripheral nerves in the Taiwanese population, reporting that the nerve CSAs of Taiwanese individuals were smaller than those of Caucasians. Additionally, multiple sites exhibited a positive correlation between the nerve CSA and both weight and body mass index (BMI) (11). Other studies have reported that the nerve CSA varies significantly among ethnic groups (12, 13).

Electrodiagnostic study is an important component of the evaluation of patients with suspected peripheral nerve disorders. Previous studies have shown electrodiagnostic study and ultrasound to be similar with regard to sensitivity and specificity for diagnosis of carpal tunnel syndrome (14). Bathala et al. correlated CSA reference values for the ulnar nerves with electrophysiological parameters in Asian subjects. The results showed that CSAs increased with age, and that men had larger CSAs. The correlation between distal ulnar motor latency and CSA at the wrist in that study was statistically significant (15). Another study similarly evaluated CSA reference values for median nerves and their correlation with electrophysiological parameters in Asian subjects. The results found no correlation between electrophysiological parameters and height, weight, BMI, or median nerve CSA (16).

The nerve CSAs in the upper extremity in healthy Thai adults have never been studied. The aim of this study is to evaluate the ultrasonography CSA references values of nerves in the upper extremity correlated with electrodiagnosis in healthy Thai adults.

METHODS

Study design

This cross-sectional study was conducted at Lerdsin Hospital in Bangkok, Thailand from May 2022 to May 2023. The trial protocol was approved by the Lerdsin Hospital Ethics Committee (Number LH651011) and was registered in the Thai Clinical Trials Registry (TCTR 20220204006).

Participants

Asymptomatic, healthy Thai volunteers age 19-80 years were recruited. Exclusion criteria were signs and symptoms of neurological problems, alcoholism, diabetes mellitus, chronic kidney disease, liver disease, thyroid disease, autoimmune disease, immunodeficiency disorder, malnutrition, previous surgery with metallic implants on the upper extremities, pregnancy, patients with an implanted pacemaker, and patients with abnormal nerve conduction study (NCS) results based on the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) reference values (17). All participants provided written informed consent. Age, sex, dominant hand, height,-weight, and calculated BMI were recorded for each participant.

Sample size

The sample size estimation was based on a study by Tan et al. (13). The sample size was determined using the estimation of an infinite population mean formula. We assumed $\alpha = 0.05$ and a margin of error of 0.06, and represented the mean CSA and the standard deviation (SD) of the median, ulnar, and radial nerves of each site. The maximum calculated sample size (radial nerve) of 80 participants was used. With an estimated drop-out rate of 10%, the target sample size was 88 participants. We attempted to recruit an equal number of males and females with 30 in each of three age groups: 18 to 30 years, 31 to 50 years, and 51-80 years. The final sample size was 90 participants.

Intervention

Electrodiagnosis studies

Two experienced, board-certified physiatrists performed a standardized NCS on each subject using a standard electrodiagnostic machine (Nicolet Synergy, Natus Medical Inc., San Carlos, California, USA) in accordance with AANEM recommendations (17). Motor and sensory NCS of bilateral upper and lower extremities was performed to screen for peripheral neuropathies, including median compound motor action potential (CMAP), median sensory nerve action potential (SNAP), ulnar CMAP, ulnar SNAP, sural SNAP, tibial CMAP, and fibular CMAP. Throughout the procedure skin temperature was maintained at between 32 and 34 degrees Celsius. NCS parameters of the median and

ulnar nerves were used to evaluate correlations with the CSA.

Median CMAP: the active electrode was placed on the abductor pollicis brevis motor point, and the stimulation sites were at the wrist (8 cm proximal to the active electrode) and the elbow (medial to the brachial 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.

Tibial CMAP: the active electrode was placed on the medial foot, and the stimulation sites were at the ankle (posterior to the medial malleolus and 8 cm proximal to the active electrode) and mid-popliteal fossa.

The fibular CMAP: the active electrode was placed on the midpoint of the extensor digitorum brevis, and the stimulation sites were at the ankle (lateral to the tibialis anterior tendon, 8 cm proximal to the active electrode) and below fibular head.

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.

Sural SNAP: the active electrode was placed posterior to the lateral malleolus, and the stimulation site was at the calf, 14 cm proximal to the active electrode.

Ultrasound examinations

All ultrasound examinations were conducted bilaterally by a single board-certified physiatrist with 6 years of experience in musculoskeletal ultrasound using 4- to 18- megahertz (MHz) linear array transducers (SONIMAGE HS1, Konica Minolta Inc., Tokyo, Japan) in B mode. The transducer was positioned perpendicular to the nerve to obtain the minimal cross-sectional image. Using the ultrasound machine's elliptical function, the CSA was measured at the inner border of the nerve's hyperechoic rim from the distal to the proximal arm. The color Doppler was used to distinguish between nerves and blood vessels. Based on the distance between the skin and the target area, the focus and depth were adjusted as necessary. The CSA was measured three times for each site for intra-rater reliability, and the average value was used for analysis. The inter-rater reliability evaluation was performed one week after the participant's first visit by a board-certified physiatrist with 1 year of experience in neuromuscular ultrasound who was blinded from the results. Thirty participants were chosen randomly. The average value of the three measurements was analyzed. Both investigators underwent specialized training for this investigation prior to commencing data collection. Anatomical landmarks or clinically significant points were used to select the measured sites of each nerve (Figure 1).

Median nerve: Participants were supine with 45 degrees shoulder abduction and the forearm supinated. Four locations along the median nerve were assessed: (1) wrist (proximal margin of the flexor retinaculum), (2) mid-forearm (halfway between the distal wrist crease and the elbow crease where the nerve is located between the flexor digitorum superficialis and flexor digitorum profundus muscles), (3) elbow (antecubital fossa), and (4) mid-humerus (halfway between the elbow crease and the axilla).

Ulnar nerve: Participants were supine with 45 degrees of shoulder abduction and external rotation, with the forearm supinated and the elbow flexed to 90 degrees. Four locations along the ulnar nerve were assessed: (1) wrist (between the pisiform bone and the ulnar artery at the distal wrist crease), (2) forearm (2 cm distal to the tip of the medial epicondyle), (3) elbow (the tip of medial epicondyle), and (4) mid-humerus (halfway between the elbow crease and the axilla).

Radial nerve: Participants were supine with the forearm pronated and the elbow fully extended. Two locations of the radial nerve were assessed: (1) elbow (antecubital fossa at elbow crease, where the nerve is located between the brachialis and brachioradialis muscles) and (2) spiral groove at mid-humerus.

Outcome measurements

The nerve CSA of each measured site was recorded. The wrist-to-forearm median nerve CSA ratio (WFR) was calculated by dividing the median nerve CSA at the wrist by the median

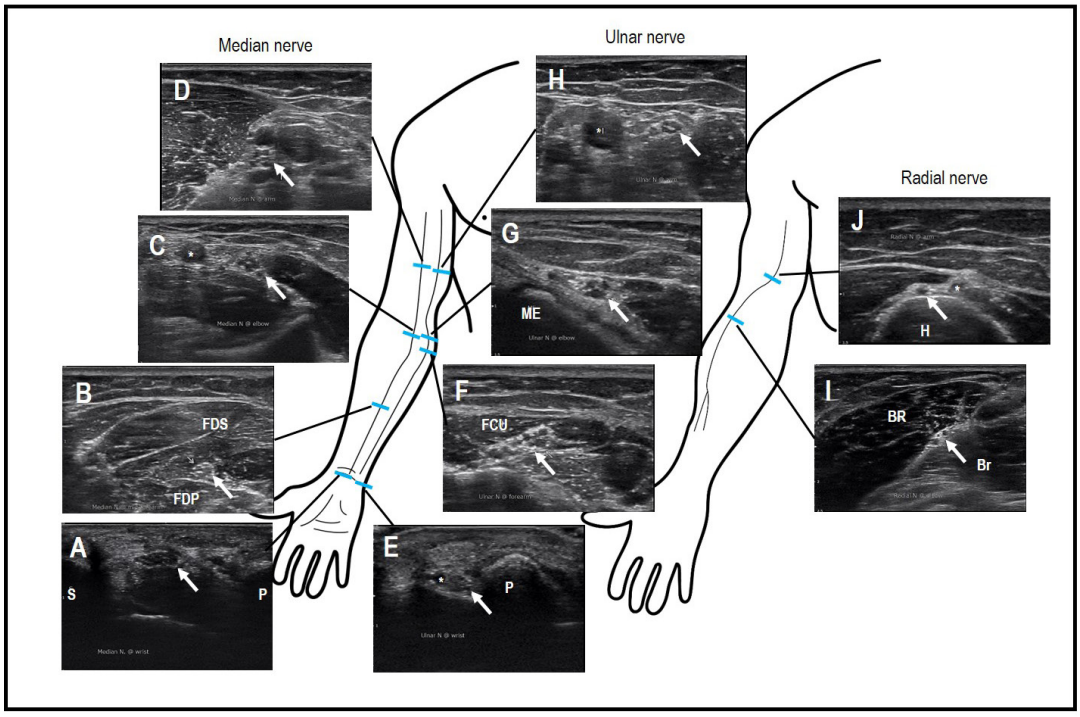

Figure 1. Ultrasonography of the nerve cross-sectional area (CSA) at each measured site. (A) median nerve at wrist, (B) median nerve at mid-forearm, (C) median nerve at elbow, (D) median nerve at mid-humerus, (E) ulnar nerve at wrist, (F) ulnar nerve at forearm, (G) ulnar nerve at elbow, (H) ulnar nerve at mid-humerus, (I) radial nerve at elbow, (J) radial nerve at spiral groove. Br - brachialis; BR - brachioradialis; FCU - flexor carpi ulnaris; FDP - flexor digitorum profundus; FDS - flexor digitorum superficialis; H - humerus bone; ME - medial epicondyle; P - pisiform bone; S - scaphoid bone. Arrows show the CSA of the nerves. The vessels are indicated by an asterisk (*).

nerve CSA at the mid-forearm. The NCS parameters were recorded, including SNAP latency, SNAP amplitude, CMAP distal latency, CMAP distal amplitude, CMAP distal area under the curve, CMAP proximal latency, CMAP proximal amplitude, CMAP proximal area under the curve, and nerve conduction velocity (NCV) of the median and ulnar nerves.

Statistical methods

Continuous data are presented as mean and SD and categorical data are presented as frequencies and percentages. The reference range for the nerve CSA was determined as the mean± 2SD. The upper limit reference values for the side-to-side difference were calculated by determining the mean of the absolute difference between the measurements on the right and left sides of each site plus 2SD. The Pearson's correlation coefficient (r) was used to determine the correlation between the nerve CSA and age, weight, height, BMI, and NCS parameters. Male and female nerve CSAs were compared using the unpaired t-test. The paired t-test was used to compare differences of the nerve CSA between two sides, while one-way ANOVA was used to compare differences among age groups. Statistical significance was set at a p-value of less than 0.05. The data were analyzed using the PASW Statistics version 18.0 program (SPSS Inc., Chicago, IL., USA).

RESULTS

A total of 90 healthy participants, 30 each in the groups 18-30 years, 31-50 years, and 51-80 years, with an equal number of males and females in each group were recruited for the study. The mean age was 41.4±14.5 years (range 19-72 years). The mean weight, height, and BMI were 64.1±13.8 kg, 163.2±8.5 cm, and 25±4.3 kg/m^2, respectively. Of the participants, 95.6% were right-handed (Table 1).

The nerve CSAs were obtained bilaterally. There was no significant difference in the CSA between the right and left sides, with the exception of the median nerve at the wrist (right: 9.4±2.1 vs. left 9.1±2.0 mm^2, p = 0.03). A bifid median nerve at the wrist was observed in 8

Table 1. Demographic data of the participants

Parameters[a]	Total (n=90) (SD) [range]	Male (n=45) (SD) [range]	Female (n=45) (SD) [range]
Age (yr)	41.4 (14.5) [19-72]	40.6 (14.4) [19-72]	42.2 (14.8) [23-70]
Weight (kg)	64.1 (13.8) [42-100]	69.4 (12.5) [45-100]	58.9 (13.1) [42-90]
Height (cm)	163.2 (8.5) [144-189]	169.2 (6.4) [157-189]	157.3 (5.8) [144-168]
BMI (kg/m^2)	25.0 (4.3) [15.2-34.1]	24.2 (4.1) [15.2-33.9]	23.7(4.5) [17.5-34.1]

[a]Mean (SD)
BMI, body mass index; kg, kilogram; cm, centimeter; m, meter; n, number; SD, standard deviation

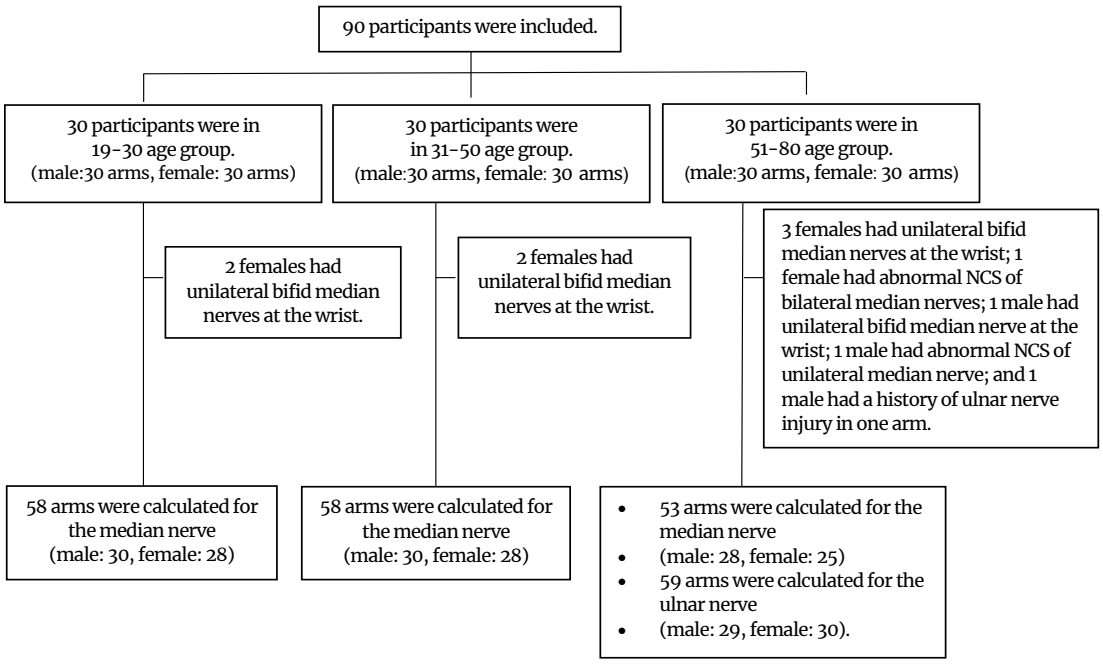

Figure 2. Participant flow chart

arms, and 3 arms had abnormal median NCS based on the AANEM reference values, so we included the CSA values of the median nerve in only 169 arms. The ulnar nerve was excluded in 1 arm because of a history of ulnar nerve injury, so 179 arms were used to calculate the CSA value of the ulnar nerve (Figure 2). During elbow flexion greater than 90°, ulnar nerve dislocation was observed in 16 of 169 arms (9.5%). The mean CSA and reference range for each measured site, the mean WFR, as well as the side-to-side difference upper limit, are shown in Table 2.

Table 3 shows the mean CSA values at each site and WFR for the different age groups (18-30 years, 31-50 years, and 51-80 years) and sex. The CSA at most sites was significantly larger in the older age groups except for the two measured sites of the radial nerve (Table 3). There were no significant differences in CSA between males and females except for the median nerve at the elbow, where males tended to have a larger CSA than females (Table 3). The correlation between age, weight, height, and BMI with the nerve CSA at each site and WFR is shown in Table 4. Except for the radial nerve at the spiral groove, the CSA at most sites increased significantly with age. The CSA of the median nerve at the wrist and that of the radial nerve at the spiral groove were positively correlated with weight and BMI, whereas the CSA of the median nerve at the elbow was positively correlated only with weight. The WFR was not significantly correlated with age, sex, weight, or height, but it was significantly correlated with BMI (Table 4).

We found a moderate correlation between CSA values and electrodiagnosis parameters between the median nerve CSA at the wrist and median SNAP latency, median SNAP amplitude, and median CMAP distal latency, and

Table 2. Nerve CSA (mm^2) reference values, WFR reference values, and side-to-side difference upper limit (mm^2)

Nerve	Sites (n)	Mean	SD	Min, Max	Reference range	Side-to-side difference upper limit
Median	Wrist (169)	9.2	2.0	6, 17	5.3-13.1	2.3
	Mid-forearm (169)	5.8	1.4	3.7, 15.2	3.0-8.5	1.8
	Elbow (169)	9.3	1.8	5.2, 15.5	5.8-12.9	3.3
	Mid-humerus (169)	9.5	1.5	6.0, 14.8	6.6-12.4	2.6
	WFR (169)	1.6	0.3	0.9, 2.7	1.0-2.3	0.7
Ulnar	Wrist (179)	4.5	0.8	3.0, 7.5	2.8-6.2	1.5
	Forearm (179)	7.2	1.4	4.5, 11.2	4.4-9.9	2.4
	Elbow (179)	7.7	1.7	5.2, 13.8	4.3-11.1	2.6
	Mid-humerus (179)	6.5	1.2	4.0, 10.3	4.2-8.9	2.7
Radial	Elbow (180)	5.0	0.9	3.5, 9.8	3.2-6.7	1.5
	Spiral groove (180)	4.6	0.8	3.2, 6.7	3.0-6.2	1.6

CSA, cross-sectional area; mm^2, square millimeter; WFR, wrist-to-forearm median nerve cross-sectional area ratio; n, number; SD, standard deviation; Min, minimum; Max, maximum
The reference range was determined as the mean±2SD. The side-to-side difference upper limit is the mean plus 2SD for the absolute value of the side-to-side difference in each site.

Table 3. The nerve CSA (mm^2) classified by age group and sex and its correlation

Nerve	Site	Age[a]				Sex[b]		
		18-30	31-50	51-80	*p*-value	Male	Female	*p*-value
		Mean (SD)	Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)	
Median	Wrist	8.6 (1.7)	8.5 (1.4)	10.5 (2.2)	< 0.001*	9.4 (1.8)	8.9 (2.1)	0.215
	Mid-forearm	5.4 (0.7)	5.6 (1.0)	6.3 (2.0)	0.032*	5.8 (0.9)	5.7 (1.8)	0.845
	Elbow	8.8 (1.7)	9.3 (1.4)	10.0 (2.0)	0.034*	10.1 (1.5)	8.5 (1.7)	< 0.001*
	Mid-humerus	9.0 (1.3)	9.5 (1.3)	10.0 (1.6)	0.020*	9.8 (1.3)	9.2 (1.6)	0.053
	WFR	1.6 (0.3)	1.6 (0.3)	1.7 (0.3)	0.130	1.7 (0.3)	1.6 (0.3)	0.545
Ulnar	Wrist	4.3 (0.8)	4.4 (0.8)	4.9 (0.8)	0.013*	4.6 (0.9)	4.4 (0.8)	0.127
	Forearm	6.6 (1.2)	7.0 (1.3)	7.9 (1.3)	< 0.001*	7.4 (1.3)	6.9 (1.4)	0.064
	Elbow	7.1 (1.2)	7.3 (1.4)	8.6 (2.0)	< 0.001*	8.0 (1.6)	7.4 (1.8)	0.088
	Mid-humerus	5.9 (0.8)	6.6 (1.2)	7.2 (1.2)	< 0.001*	6.7 (1.0)	6.3 (1.3)	0.119
Radial	Elbow	4.8 (0.5)	5.0 (0.8)	5.2 (1.1)	0.186	5.0 (0.7)	4.9 (1.0)	0.533
	Spiral groove	4.5 (0.7)	4.6 (0.6)	4.7 (1.0)	0.592	4.7 (0.8)	4.4 (0.8)	0.070

[a]One-way ANOVA test, [b]Unpaired t-test, *statistically significant ($p < 0.05$)
CSA, cross-sectional area; mm^2, square millimeter; SD, standard deviation; WFR, wrist-to-forearm median nerve cross-sectional area ratio

between the median nerve CSA at the elbow and median CMAP proximal latency. As the nerve size increased, the latency was prolonged, and the amplitude decreased (Table 5). There was a weak correlation between the ulnar nerve CSA at the wrist and ulnar SNAP amplitude and ulnar CMAP distal amplitude, as well as between the ulnar nerve CSA at the elbow and ulnar CMAP proximal latency, ulnar CMAP proximal amplitude, and ulnar CMAP proximal area under the curve (Table 6). There was a significant correlation between the median nerve CSA at the wrist and the median NCV. As the CSA increased, the NCV slowed (Table 7). The intra-rater reliability was moderate to excellent (intraclass correlation coefficient (ICC) = 0.735-0.945), as was the inter-rater reliability (ICC = 0.735-0.984).

DISCUSSION

This is the first study to report reference values for the CSA of upper extremity nerves at multiple sites in healthy Thai adults. The CSA values observed in our study are comparable to those reported in studies of other Asian populations (7, 9, 18). In our study, we found the CSA of median nerve at wrist (9.2±2.0 mm^2), median nerve at elbow (9.3±1.8 mm^2), median nerve at mid-humerus (9.5±1.5 mm^2), ulnar

Table 4. Correlation between the nerve CSA and age, weight, height, and BMI

Nerve	Site	Correlation coefficient (*p*-value)[a]			
		Age	Weight	Height	BMI
Median	Wrist	0.461 (< 0.001*)	0.240 (0.024*)	-0.066 (0.539)	0.226 (0.033*)
	Mid-forearm	0.310 (0.003*)	0.034 (0.755)	-0.003 (0.981)	-0.008 (0.939)
	Elbow	0.307 (0.003*)	0.281 (0.008*)	0.008 (0.942)	0.157 (0.141)
	Mid-humerus	0.317 (0.002*)	0.138 (0.196)	-0.112 (0.297)	0.125 (0.242)
	WFR	1.183 (0.086)	0.205 (0.054)	-0.092 (0.390)	0.265 (0.012*)
Ulnar	Wrist	0.312 (0.003*)	0.145 (0.173)	-0.017 (0.876)	0.098 (0.359)
	Forearm	0.431 (< 0.001*)	0.200 (0.058)	-0.030 (0.776)	0.138 (0.194)
	Elbow	0.435 (< 0.001*)	0.129 (0.227)	-0.070 (0.514)	0.088 (0.407)
	Mid-humerus	0.398 (< 0.001*)	0.178 (0.094)	-0.082 (0.440)	0.167 (0.116)
Radial	Elbow	0.264 (0.012*)	0.172 (0.105)	-0.071 (0.509)	0.142 (0.182)
	Spiral groove	0.150 (0.158)	0.289 (0.006*)	-0.112 (0.295)	0.226 (0.032*)

[a]Pearson's correlation coefficient (r); *statistically significant ($p < 0.05$)
CSA, cross-sectional area; BMI, body mass index; WFR, wrist-to-forearm median nerve cross-sectional area ratio

Table 5. Correlation between the median nerve CSA and NCS parameters

	CSA of median nerve at wrist[a]		CSA of median nerve at elbow[a]	
	r	*p*-value	r	*p*-value
Median SNAP lat	0.534	<0.001*	-	-
Median SNAP amp	-0.486	<0.001*	-	-
Median CMAP D lat	0.459	<0.001*	-	-
Median CMAP D amp	-0.170	0.112	-	-
Median CMAP D area	-0.067	0.533	-	-
Median CMAP P lat	-	-	0.384	< 0.001*
Median CMAP P amp	-	-	-0.110	0.307
Median CMAP P area	-	-	-0.044	0.685

[a]Pearson's correlation coefficient (r); *statistically significant ($p < 0.05$)
CSA, cross-sectional area; NCS, nerve conduction study; SNAP, sensory nerve action potential; CMAP, compound motor action potential; lat, latency; amp, amplitude; D, distal; P, proximal

Table 6. Correlation between the ulnar nerve CSA and NCS parameters

	CSA of the ulnar nerve at wrist[a]		CSA of the ulnar nerve at elbow[a]	
	r	*p*-value	r	*p*-value
Ulnar SNAP lat	-0.027	0.798	-	-
Ulnar SNAP amp	-0.308	0.003*	-	-
Ulnar CMAP D lat	0.067	0.531	-	-
Ulnar CMAP D amp	-0.240	0.023*	-	-
Ulnar CMAP D area	-0.140	0.187	-	-
Ulnar CMAP P lat	-	-	0.275	0.009*
Ulnar CMAP P amp	-	-	-0.292	0.009*
Ulnar CMAP P area	-	-	-0.223	0.035*

[a]Pearson's correlation coefficient (r); *statistically significant ($p < 0.05$)
CSA, cross-sectional area; NCS, nerve conduction study; SNAP, sensory nerve action potential; CMAP, compound motor action potential; lat, latency; amp, amplitude; D, distal; P, proximal

Table 7. Correlation between the CSA and NCV of the median and ulnar nerves

CSA	NCV of the median nerve[a]		NCV of the ulnar nerve[a]	
	r	*p*-value	r	*p*-value
Median nerve at wrist	-0.319	0.002*	-	-
Median nerve at mid-forearm	-0.058	0.589	-	-
Median nerve at elbow	-0.158	0.139	-	-
Ulnar nerve at wrist	-	-	-0.159	0.136
Ulnar nerve at forearm	-	-	-0.135	0.206
Ulnar nerve at elbow	-	-	-0.181	0.088

[a]Pearson's correlation coefficient (r); *statistically significant ($p < 0.05$)
CSA, cross-sectional area; NCV, nerve conduction velocity

nerve at elbow (7.7±1.7 mm^2), and ulnar nerve at mid-humerus (6.5±1.2 mm^2) were close to the values reported by Bae et al. (9.33±1.55 mm^2, 8.96±2.41 mm^2, 9.34±2.38 mm^2, 7.31±1.69 mm^2, and 6.37±1.56 mm^2 respectively) (9). Although the CSA values of the radial nerve in our study were smaller than those obtained by Bae et al. (elbow, 7.26±1.7 mm^2; spiral groove, 6.81±1.75 mm^2), they are comparable to those reported by Hsieh et al. (elbow, 4±1.4 mm^2; spiral groove, 5.1±1.6 mm^2) (11). Despite the similarities, the CSA values obtained in our study are greater than some previously published values for Asian participants (8, 13, 15, 16). These findings support a previous study conducted by Tan et al., which showed that nerve CSA was significantly different among Asian ethnic groups (13). In our study, the median nerve CSA at the wrist (9.2±2.0 mm^2) was larger than in a previous study that assessed the mean CSA of the median nerve at the wrist in healthy Thai adults (6.83±0.98 mm^2) (19). This difference might be due to the fact that our study included more participants (90 vs 44) and a wider age range (19-72 vs 30-57 years) than the Wanitwattanarumlug study. A number of studies have investigated the cut-off value of the CSA of the median nerve at the wrist for diagnosing carpal tunnel syndrome (CTS). Reported values range from 9 to 14 mm^2 (20). In contrast to our finding that the median nerve CSA at the wrist was 9.2±2.0 mm^2, a previous study found that using a cut-off value of 9 mm^2 provided high sensitivity and specificity in diagnosing CTS in the Thai population (21). This might be due to the use of different cut-off values for diagnosing CTS. Another possible reason is that the participants in the previous study did not include individuals older than 60 years (30-53 years in the control group and 32-59 years in the CTS group). A future study should investigate the cut-off value of each age group separately.

Demographic variables, including sex, age, height, weight, and BMI, were found to correlate with nerve CSA. In a number of previous studies, male nerve CSA was significantly greater than female nerve CSA (8, 9, 15, 16). In our study, males had a significantly larger CSA than females at only one of the ten sites (the median nerve at the elbow). This trend was also observed at the other measured sites, but without statistical significance. Previous studies have reported a positive correlation between nerve CSA and age (8, 15, 16, 22). In our study, we found a similar correlation: older participants had a significantly larger CSA than younger participants at most measured sites. In this study, weight was found to have a significant positive correlation with nerve CSA at 3 of 10 sites, while a positive correlation with BMI was found at only 2 sites. These results are consistent with previous research findings reporting that weight and BMI are correlated with nerve CSA (7, 9, 11, 13). In contrast, height had a very weak negative correlation with nerve CSA which was not statistically significant. These findings were similar to those of Niu et al., Tan et al., and Qrimli et al., which found that height had no significant correlation with nerve CSA (8, 13, 23). Based on these results, weight and BMI should be considered while assessing the nerve CSA for patients who are either overweight or underweight. The correlation between WFR and demographic factors in previous studies has shown varied results. Bae et al. reported that WFR was correlated with sex differences (9),

whereas Won et al. found no correlation between WFR and any demographic variables (7). Sugimoto et al. studied the CSA ratio of the median nerve between the distal wrist crease and the distal forearm and found the ratio was correlated with gender, age, height, and wrist circumference (18). In our study, we found that WFR is significantly correlated with BMI. The cut-off values of WFR for the diagnosis of CTS varied, ranging from 1.34 to 2.4, although a WFR of 1.3 and 1.4 showed a high sensitivity (20). Based on the finding of our study that the mean WFR in healthy Thai adults is 1.6±0.3, future studies should investigate the cut-off values of WFR for the diagnosis of CTS in the Thai population. There was no statistically significant difference in the CSA observed between the right and left sides at most measured sites, which is comparable to several previous studies (13, 15, 24). This finding suggests that the side-to-side difference could be used to detect unilateral nerve pathology.

There was a correlation between the CSA values and electrodiagnosis parameters as the nerve CSA increased, as the latency was prolonged, as the amplitude decreased, and as the area under the curve decreased, which is similar to a study by Bathala et al. which found that the ulnar nerve CSA at the wrist had a positive correlation with distal motor latency across the wrist (15). The CMAP amplitude indicates the number of responding motor nerve fibers, and the SNAP amplitude indicates the number of depolarized sensory axons (25). The area under the curve is an alternative way to estimate the quantity of depolarized muscle fibers and axons (26). Previous research has reported that the tibial nerve's histology exhibits a larger CSA as the nerve fascicle increases (27). This is contrary to our finding that in a healthy population as the CSA increases, the NCS amplitude decreases suggesting that the morphology of a nerve may not always correspond with its physiological properties (i.e., the number of nerve fascicles may not represent the number of functioning axons). The nerve CSA in a normal population could demonstrate an inverse relationship with the NCS amplitude. Nerve CSA should be considered for use in the interpretation of nerve pathology because several focal neuropathy conditions can also result in an increase in nerve CSA as well as a decrease in NCS amplitude (4, 5, 28). Although the correlations between the median and the ulnar nerve CSAs and the NCS parameters were not significant for all parameters in this study, the correlations were in the same direction for almost all parameters. The results of this study provide information for future studies use in further investigation of the correlation between the nerve CSA and the NCS parameters as a primary outcome. A study with a larger sample size might show greater statistical significance. A significant correlation was observed between the median nerve CSA at the wrist and the median NCV. As the CSA increased, the NCV slowed, which could be due to the nerve being slightly thicker at the entrapment site (8, 12, 16). Even routine activities like using a computer keyboard and mouse put the wrist in a posture that increases carpal tunnel pressure, compromising blood flow to nerves and putting users at risk for median nerve damage (29). There is a possibility of the existence of some degree of asymptomatic nerve damage with the NCS still showing normal values as the median nerve at the wrist tends to be larger and have a slower NCV.

Limitation

Our study has several limitations. First, we used elliptical function to measure the nerve CSA, which might not have included some nerve fascicles, especially nerves that have an irregular circumference. Second, the more proximal parts, such as the median and ulnar nerves at the axilla, were not studied. A future study should include the more proximal part of the nerves. Third, although the sample size of 90 participants was sufficient to evaluate the primary outcome, i.e., the nerve CSA, this sample size might not be large enough to evaluate the secondary outcomes (correlation between the nerve CSA and the NCS parameters) and the correlation between the nerve CSA and demographic data. Future studies investigating the correlation between the nerve CSA and the NCS parameters and the correlation between the nerve CSA and subgroup demographic data as a primary outcome are suggested. Fourth,

repeat reliability was not performed in this study. In future studies, repeat reliability of the same rater should be accomplished to help assure the accuracy of the results. Lastly, to investigate deeper structures, e.g., in an extremely obese participant, results would be more accurate using high-frequency ultrasound (24-70 MHz). There were also some positive aspects to this study. First, NCS of all extremities was performed to ensure that the participants did not have peripheral nerve disorders. Second, a single experienced physician was responsible for all ultrasonography. Finally, there was moderate to excellent inter-rater reliability in our study, which indicates that the measures had good accuracy.

CONCLUSIONS

Our study was the first investigation of reference values of the nerve CSA obtained by ultrasound in the upper extremities at multiple sites in healthy Thai adults. The mean CSA of the median nerve at the wrist was 9.2±2.0 mm^2, and the mean CSA of the ulnar nerve at the elbow was 7.7±1.7 mm^2. This should be helpful in the evaluation of peripheral nerve disorders in the Thai population. There was an association between the CSA values and electrodiagnosis parameters as the nerve CSA increased, the latency was prolonged, and the amplitude decreased.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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