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Ultrasonographic measurement of median nerve and wrist skin thickness in patients with carpal tunnel syndrome: relationship with clinical, electrophysiologic and functionality

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The study aimed to investigate the relationship between the proximal and distal cross-sectional area (CSA) of the median nerve and wrist skin thickness measured by ultrasound in patients with carpal tunnel syndrome (CTS), demographics, disease characteristics, electrophysiological measurements, symptom severity, functionality, and symptom severity. 98 patients with electrophysiological diagnoses of CTS in the dominant hand were included in the study. Proximal and distal CSAs of the median nerve and wrist skin thickness were measured ultrasonographically. Demographic and disease characteristics of the patients were recorded. Patients were evaluated with the Historical-Objective scale (Hi-Ob) for clinical staging, the Functional status scale (FSS) for functional status, and the Boston symptom severity scale (BSSS) for symptom severity. Ultrasonographic findings were correlated with demographic and disease characteristics, electrophysiological findings, Hi-Ob scala, Functional status scale (FSS), and Boston symptom severity scale (BSSS). Proximal median nerve CSA median was 11.0 (7.0-14.0) mm2, distal median nerve CSA median was 10.5 (5.0-18.0) mm2, and wrist skin thickness was measured 1.10 (0.6-1.40) mm. Median nerve CSAs were positively correlated with the CTS stage and FSS, negatively correlated with the sensory nerve action potential of the median nerve (SNAP) and the compound muscle action potential of the median nerve (CMAP) ($p<0.05$). Wrist skin thickness was positively correlated with disease characteristics, including the presence of paresthesia and loss of dexterity and FSS and BSSS levels. Ultrasonographic measurements in CTS are associated with functionality rather than demographics. Especially the increase in wrist skin thickness leads to an increase in symptom severity.

Keywords : Carpal tunnel syndrome, cross-sectional nerve area, neuromuscular ultrasound.

INTRODUCTION

Carpal tunnel syndrome is the most common peripheral neuropathy[1]. Clinical findings result from mechanical compression of the median nerve at the wrist. Depending on the compression level, pain, numbness, and loss of sensation may be observed in the distribution area of the median nerve. As the level and duration of compression increase, atrophy of the thenar muscles and motor deficits occur[2]. The prevalence of CTS is 5.8% in women and 0.6% in men[3].

CTS is diagnosed with a detailed anamnesis, clinical examination and electrophysiological studies. Electrophysiological studies support the diagnosis of CTS and determine the severity of the disease. The sensitivity of electrophysiological tests ranges from 49% to 86%, and the false-negative rate ranges from 16% to 36%[4,5]. Since electrophysiologic studies can be invasive, time-consuming and expensive, ultrasonography has increased in recent years to facilitate the diagnosis of CTS. Ultrasonography (sensitivity: 77.6%; specificity: 86.8%) is recommended for both diagnostic and etiologic information (bifid median artery, tenosynovitis, ganglion cyst, etc.)[6,7].

In studies performed with ultrasound to diagnose CTS, CSA measurements were often measured at the level of the median nerve at the tunnel inlet[8-10]. The CSA of the median nerve at the carpal tunnel inlet has high sensitivity and specificity[9-11]. Studies have shown that the CSA of the median nerve is higher in patients with carpal tunnel syndrome compared to healthy individuals. There are different studies on the cut-off value of median nerve CSA in diagnosing CTS. In these studies, the cut-off value for the CSA measured before entering the carpal tunnel of the median nerve varies between 6.5 and 15 mm^2 [12-15].

Although there are studies stating that the median nerve CSA measurement is electrophysiologically correlated with the severity of the disease, there are studies stating the opposite[9-12,16,17].

In this study, we evaluated the relationship between the proximal and distal CSA of the median nerve and wrist skin thickness measured by ultrasonography with patient demographic and disease characteristics, electrophysiologic findings, symptom severity and functionality in patients diagnosed with CTS.

MATERIAL AND METHODS

The study included 98 patients referred to the electrophysiology laboratory between January 2020 and January 2022 and diagnosed with CTS in the dominant hand.

The study was approved by the local ethical committee and all subjects signed written informed consent prior to the study. Helsinki's declaration was respected in all steps.

Patients aged 18-65 years with symptoms of CTS in the dominant hand (such as hand numbness, weakness, and pain) underwent electrophysiologic studies in the EMG laboratory by the same practitioner and were diagnosed with CTS were included.

Patients under the age of 18 years and over the age of 65 years with non-dominant hand involvement, patients with known inflammatory, autoimmune, endocrine/metabolic and severe renal disease, patients with central nervous system disease and/or cervical disc disease and/or polyneuropathy, patients with a history of previous hand trauma and/or surgery, patients with severe degenerative osteoarthritis of the hands, anatomical variation, ganglion cyst, tenosynovitis and/or tendinitis in the hand, patients with a history of pregnancy and lactation were excluded.

Age, gender, occupation, height, weight, and comorbidities were recorded. Body mass index was calculated with height and weight measurements.

Patients' symptoms (pain, paresthesia, weakness, and loss of dexterity), symptom duration (months), and clinical stage were recorded. The clinical stage was scored between 0-5 points according to the modified criteria of the Italian study group using the historical-objective scale (Hi-Ob scale) consisting of 5 stages according to the patient's symptoms and findings. It includes grade-1 = nocturnal paresthesias only; grade-2 = nocturnal and diurnal paresthesias; grade-3 = sensory deficit; grade-4 = hypotrophy or motor deficit of the thenar muscles innervated by the median nerve; grade-5 = plegia of the thenar muscles innervated by the median nerve. Low scores (1-2 points) indicated mild CTS and high scores (3-5 points) indicated severe CTS[18].

To maintain homogeneity in the study, we included median nerve studies performed by the same practitioner using a Medelec Synergy 10-channel ENMG (Oxford, U.K.) device, evaluated according to the protocol defined by Oh et al.[19].

Median nerve peak sensory conduction velocity and sensory nerve action potential (SNAP) were recorded from the second finger, distal motor latency, combined muscle action potential (CMAP) and median nerve motor conduction velocity recorded from the abductor pollicis brevis muscle were recorded.

Ultrasonografic measurements were performed in arm extension, forearm supination, wrist in neutral position, palm facing upwards on a pillow and sitting position. Real-time imaging of cross-sectional areas (CSAs) were performed by an ultrasound device (GE Logiq P5, General electric, Korea) and 9-12 MHz linear array transducer, by an experienced PMR specialist. The transducer was placed on the line and special care was taken to avoid excessive pressure. The examination started with visualization of the median nerve in the transverse plane at the wrist level. The proximal median nerve area was measured at the level of the scaphoid and pisiform bones (carpal tunnel inlet) and distal median nerve CSA was measured at the level of the trapezium and hamate bones (carpal tunnel outlet)[20]. In the same position, skin thickness, including epidermis and dermis, was measured at the level of the proximal median nerve area measurement, just above the median nerve. All measurements and evaluations were performed on the same day. Ultrasonographic measurements were correlated with demographic and disease characteristics, electrophysiologic evaluation findings, functionality and symptom severity.

Data were analyzed using the SPSS for Windows 22.0 package program. Descriptive statistics 1were presented as mean±standard deviation or median (minimum-maximum) for continuous variables and number of observations and (%) for nominal and categorical variables. The Kolmogorov-Smirnov test was used to evaluate whether continuous variables conformed to normal distribution. The relationship between ultrasonographic measurements and evaluation parameters was analyzed by Spearman's rho correlation test. Results were considered statistically significant for $p<0.05$.

RESULTS

The mean age of the 98 patients included in the study was 57.89±9.17 years, and all patients were female and BMI was 30.12 ±5.07 kg/cm^2. The most common symptom of the patients was pain (n=98, 100%), and the majority of the patients were severe CTS patients in clinical staging (n=73, 74.5 %). Demographic and disease characteristics of the patients are presented in Table I and electrophysiologic and ultrasonographic measurements are presented in Table II.

Electrophysiologically, mild CTS was determined in 25 (25.5%), moderate in 55 (56.1%) and severe in 18 (18.4%) patients. Proximal median nerve CSA median was 11.0 (7.0-14.0) mm^2, distal median nerve CSA median was 10.5 (5.0-18.0) mm^2, and wrist skin thickness was 1.10 (0.6-1.40) mm.

The results of the correlation analysis of ultrasonographic measurements (proximal and distal median nerve CSA and wrist skin thickness) with demographic and disease characteristics, electrophysiologic measurements, functionality and symptom severity findings are presented in Tables III and IV.

Between all three measurements, wrist skin thickness was positively correlated with both proximal and distal median nerve CSA (r:0.301, p=0.023, r:0.258, p=0.022, respectively). The proximal area was also positively correlated with the distal area (r:0.591, p=0.001).

Demographic characteristics and ultrasonographic measurements were not correlated. Proximal and distal median nerve CSAs were positively correlated with CTS stage (r=0.346, p=0.001 and r=0.278, p=0.024, respectively) and negatively correlated with median nerve SNAP (r=-0.275, p=0.033 and r=-0.388, p=0.002, respectively) and CMAP (r=-0.251, p=0.010 and r=-0.271, p=0.028).

In term of symptoms, functionality and symptom severity, proximal and distal median nerve CSAs and wrist skin thickness were positively correlated with FSS (r=0.415, p=0.001, r=0.364, p=0.003 and r=0.481, p=0.001, respectively). In addition, wrist skin thickness was positively correlated with the

Table I. — Demographic and disease characteristics of the patients.

	n=98
Gender n(%) Woman Male	 98 (100) 0
Age (years) mean±SD	57.89±9.17
Dominant-affected hand n(%) Right Left	 93 (94.9) 5 (5.1)
Occupation n(%) Housewife White-collar Blue-collar	 89 (90.8) 5 (5.1) 4 (4.1)
Presence of additional comorbidity n(%)	75 (76.5)
BMI (kg/cm^2) mean±SD	30.12 ±5.07
Semptomlar n(%) Pain Paresthesia Weakness Loss of fine dexterity	 98 (100) 84 (85.7) 79 (80.6) 65 (66.3)
Symptom duration (months) median (min-max)	24.0 (12.0-72.0)
CTS Clinical stage (1-5) 1 2 3 4 5	 7 (7.1) 18 (18.4) 45 (45.9) 28 (28.6) 0
FSS (8-40) mean±SD	20.55±6.85
BSSS (11-55) mean±SD	28.52±8.44
BMI: Body mass index, FSS: Functional status scale, BSSS: Boston symptom severity scale	

Table II. — Electrophysiologic and ultrasonographic evaluation findings.

	n=98 median (min-max)
Median nerve sensory amplitude (μV)	22.80 (0.0-67.20)
Median nerve sensory conduction velocity (meters/sec)	31.50 (0.0-37.50)
Median nerve motor amplitude (mV)	6.30 (1.60-14.60)
Median nerve distal motor latency (millisecond)	4.18 (2.95-8.0)
Median nerve motor conduction velocity (meters/sec)	54.50 (40.0-62.0)
Proximal median nerve area (mm^2)	11.0 (7.0-14.0)
Distal median nerve area (mm^2)	10.5 (5.0-18.0)
Wrist skin thickness (mm)	1.10 (0.60-1.40)
Min-max: minimum-maximum	

Table III. — Correlation analysis results of ultrasonographic measurements with demographic, clinical stage and electrophysiological findings.

	Age r/p	BMI r/p	Right-hand dominance r/p	Being a housewife r/p	Having comor-bidity r/p	Clinical stage r/p	Median nerve SNAP r/p	Median nerve sensory conduction velocity r/p	Median nerve CMAP r/p	Median nerve DML r/p	Median nerve motor conduction velocity r/p
Proximal median nerve area	0.091/ 0.375	0.107/ 0.297	0.087/ 0.393	0.163/ 0.108	0.187/ 0.165	0.361/ 0.001	-0.233/ 0.021	0.167/ 0.113	-0.237/ 0.011	0.145/ 0.063	0.022/ 0.832
Distal median nerve area	0.262/ 0.073	-0.138/ 0.269	0.102/ 0.394	0.117/ 0.351	0.155/ 0.128	0.305/ 0.021	-0.388/ 0.002	0.118/ 0.341	-0.274/ 0.025	0.052/ 0.895	-0.211 / 0.085
Wrist skin thickness	0.188/ 0.097	-0.170/ 0.094	0.094/ 0.357	0.059/ 0.561	0.035 / 0.730	0.079/ 0.637	0.180/ 0.087	0.087/ 0.411	0.045/ 0.584	0.048/ 0.631	-0.165/ 0.318
r: correlation coefficient, BMI: body mass index, DML: distal motor latency SNAP: sensory nerve action potential, CMAP: combined muscle action potential.											

Table IV. — Correlation analysis results of ultrasonographic measurements and symptoms, functionality and symptom severity.

	Pain r/p	Paresthesia r/p	Weakness r/p	Loss of dexterity r/p	Symptom duration r/p	FSS r/p	BSSS r/p
Proximal median nerve area	0.095/0.354	0.071/ 0.582	0.059/ 0.564	0.118/ 0.263	0.087/ 0.392	0.415/0.001	0.116/ 0.102
Distal median nerve area	0.109/0.382	0.196/ 0.115	0.076/ 0.512	0.128/ 0.317	0.158/ 0.211	0.364/ 0.003	0.211/ 0.125
Wrist skin thickness	-0.048/0.640	0.351/ 0.001	-0.091/ 0.357	0.268/ 0.008	0.128/ 0.109	0.481/ 0.001	0.450/ 0.001
r: correlation coefficient, FSS: Functional status scale, BSSS: Boston symptom severity scale.							

presence of paresthesia (r=0.351, p=0.001) and loss of dexterity (0.268, p=0.008) and BSSS scores (r=0.450, p=0.001).

DISCUSSION

There have been many studies in recent years on the use of ultrasonography in the diagnosis, severity and evaluation of the disease characteristics of CTS[13,20,21]. Mechanical compression of the median nerve in the carpal tunnel leads to the proliferation of fibrous tissue proximal to the compression site, which causes swelling of the nerve and an increase in its cross-sectional area (CSA) ultrasonographically[22]. The increase in the cross-sectional area of the median nerve indirectly provides insight into the severity of the disease, which can be detected by electrophysiologic findings[21]. Recent studies have shown that carpal tunnel outlet measurements are more sensitive, but the results are contradictory[23,24].

In this study, median nerve SNAP and CMAP decreased in correlation with the increase in proximal and distal median nerve CSA. In addition, a positive correlation was found between prox-distal median nerve CSA and CTS clinical stage (Hi-Ob). Similar to our study, some publications in the literature show a correlation between median nerve cross-sectional area and the Hi-Ob scale[16,20,25]. Padua et al. showed that the proximal median nerve CSA correlated with electrophysiologic disease severity and disease severity assessed by the Hi-Ob scale. Lee et al. reported that the median nerve CSA at the level of the proximal carpal tunnel correlated with electrophysiologic findings[26]. Beverlie et al. also reported that ultrasonographic measurement of the proximal median nerve CSA is an important method to evaluate disease severity[27]. Another result of our study was that proximal and distal median nerve CSA correlated with functionality but not with symptom severity. Aktürk et al., in a study of 41 patients (51 hands) reported a positive correlation between proximal median nerve CSA and functionality and symptom severity, similar to our study[28]. In contrast, Kaymak et al. reported that electrophysiologic measurements were more effective in predicting functionality and symptom severity than sonographic proximal median nerve CSA measurements[29].

As described above, almost all studies have been performed with proximal median nerve CSA. This paper is the first large-scale study to show the relationship between distal median nerve CSA and disease in a group of patients with CTS. The median nerve branches exiting the carpal tunnel make it difficult to measure. Our study compared proximal and distal CSA measurements and provided similar results. Therefore, we can say that proximal CSA measurement, which can be seen more superficially, is no different from the distal CSA measurement in terms of its relationship with electrophysiology and functionality.

In our study, in addition to the sonographic measurement of the median nerve CSA, we measured the skin thickness of the wrist, which has not been measured ultrasonographically in patients with CTS before. We performed this measurement because we hypothesize that increased skin thickness may increase compression and decrease carpal tunnel compliance. In the literature, studies show that increased skin thickness due to fibrosis of the skin in scleroderma patients causes median nerve neuropathy due to mechanical compression of the median nerve[30-32]. Based on these studies, we evaluated the relationship between increased wrist skin thickness and disease severity in patients with CTS without scleroderma. In our study, there was no correlation between electrophysiologic findings and hand-wrist skin thickness on the CSA of the proximal median nerve. In contrast, the increased thickness was associated with paresthesia, loss of dexterity, and severe disease symptoms.

The median nerve contains motor, sensory and autonomic fibers[33]. It has been shown that autonomic symptoms such as dry hands, temperature changes, and skin ulcerations may occur without electrophysiological findings due to mechanical compression of the median nerve[34]. Peripheral autonomic neuropathy is difficult to detect electrophysiologically because most sympathetic postganglionic fibers are composed of slow-conducting C fibers[33]. For this reason, in our study, wrist skin thickness did not correlate with electrophysiological findings but positively correlated with symptoms related to sensory and autonomic fiber functions such as paresthesia and loss of fine dexterity. At the same time, the increase in wrist skin thickness was positively correlated with the functional status scale and symptom severity scores. We think that sonographic measurement of wrist skin thickness in patients with CTS, which is the first in the literature, may lead to more comprehensive studies. Studies comparing wrist skin thickness with healthy individuals and measuring skin stiffness using elastography in patients with CTS will give more reliable and valuable results.

CONCLUSION

Ultrasonographic measurements, including median nerve CSA and wrist skin thickness, are associated with functionality in patients with CTS. Moreover, wrist skin thickness is closely associated with symptom severity.

Conflict of interest: Authors of this work declare no conflict of interest.

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