MUSCULOSKELETAL ULTRASONOGRAPHIC VALUES FOR DIFFERENT SEVERITIES OF CARPAL TUNNEL SYNDROME IN A PAKISTANI COHORT

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ABSTRACT

Objective: To identify the cutoff values suggested by musculoskeletal ultrasound for the diagnosis of different severities of carpal tunnel syndrome and compare the parameters among males and females and patients with and without comorbidities of hypertension, diabetes mellitus, and hypothyroidism.

Study Design: A cross-sectional study.

Place and Duration of Study: Department of Electrodiagnosis, Armed Forces Institute of Rehabilitation Medicine Rawalpindi, from Mar to Jun 2017.

Methodology: Adults (20-75 years) with clinical and electrodiagnostic diagnosis of carpal tunnel syndrome were grouped into having mild, moderate, and severe disease and examined through musculoskeletal ultrasound for cross-sectional area and flattening ratio. A cross-sectional area of >9.8 mm^2 was considered diagnostic of carpal tunnel syndrome.

Results: There were 11 (22.9%) males and 37 (77.1%) females (mean age: 47 ± 9 years). Based on electrodiagnostic studies, 4 (8.3%) patients had mild, 18 (37.5%) had moderate, and 26 (54.2%) had severe carpal tunnel syndrome. All patients had carpal tunnel syndrome based on the cutoff value of musculoskeletal ultrasound. There was no significant difference among mean values of cross-sectional area and flattening ratio for both genders and for individuals who had diabetes mellitus, hypertension, or hypothyroidism compared to those who did not have these diseases. The cross-sectional area cutoff value for mild carpal tunnel syndrome was ≤14.4 mm^2, for moderate carpal tunnel syndrome was 14.4 -15.55 mm^2, and for severe carpal tunnel syndrome was >15.55 mm^2.

Conclusion: Musculoskeletal ultrasound is a useful modality to determine severity of carpal tunnel syndrome with cross-sectional area values of ≤14.4 mm^2, 14.4-15.55 mm^2, and >15.55 mm^2 corresponding to mild, moderate, and severe carpal tunnel syndrome respectively.

Keywords: Carpal tunnel syndrome, Electrophysiology, Median nerve, Ultrasonography.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the entrapment neuropathy of median nerve (MN) at the carpal ligament characterized by symptoms of numbness, paresthesia, and/or pain in the distribution of MN beyond the carpal ligament[1]. The sensory symptoms may appear radiating proximally to right shoulder or even neck and may vary from mild to debilitating intensity[1]. At times, the motor symptoms also accompany the sensory symptoms and present as weakness of muscles in the thenar eminences. CTS is diagnosed clinically by symptoms of MN compression at wrist and presence of Phalen's Test, Reverse Phalen's Test, Carpal Tunnel Compression Tests, and/or Tinel's sign at the wrist[1]. The diagnostic investigations for CTS are the nerve conduction studies (NCS), electromyography, and musculoskel ultrasonography (MSUS)[2].

NCS remain the gold standard for the diagnosis of CTS[3], however, there are pros and cons associated with their use as a diagnostic utility. They definitely give details about nerve involvement and its severity, rule out coexisting polyneuropathy, cervical radiculopathy, and entrapment neuropathy of the same nerve at different levels or of other nerves in the arm and are also useful in making the decision for surgical decompression but the cons associated with NCS

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are also very worth-mentioning. They are almost always uncomfortable and invasive if electromyography is also included. They do not give the anatomical reason for compression of MN, cannot appreciate anatomical anomalies of MN that are sometimes falsely taken as positive MN compression, and have a considerable false-negative rate of 10-20%[4]. High-resolution MSUS has emerged as a feasible, simple, relatively low cost, rapid, accurate, comfortable, and noninvasive imaging method for evaluation of MN in the carpal tunnel to detect changes in the nerve shape and exclude anatomical variants and space occupying lesions e.g. ganglion cysts and tenosynovitis[4]. The MSUS evaluation of a peripheral nerve involves evaluation of its cross-sectional area (CSA), the flattening ratio (FR), nerve vascularity, its echogenicity, and mobility[5]. The use of MSUS for diagnosis of CTS has been limited in Pakistan. To the best of our knowledge, there has been only a single published Pakistani[6], that has investigated the correlation between MSUS and NCS. The study, however, did not give the idea about the range of values for MSUS to diagnose and quantify CTS. The aim of this study was to determine the values of important MSUS parameters in patients diagnosed with CTS and observe the cut-off values suggested by MSUS for the diagnosis of different severities of CTS. Comparison of values among males and females and among individuals with and without comorbidities of hypertension, diabetes mellitus (DM), and hypothyroidism were secondary goals of the study.

METHODOLOGY

This study was carried out in the department of electrodiagnosis (EDX), Armed Forces Institute of Rehabilitation Medicine Rawalpindi, Pakistan, from March 2017 to June 2017. A sample size of 47 was calculated using a sample size calculator[7], while using a sensitivity of 42.3%[8], specificity of 91.4%[8], expected prevalence of 4.9%[9], desired precision of 0.07, and confidence level of 90%.

The sample comprised all cases with symptoms and signs suggestive of CTS belonging to both genders within the age group of 20 to 75 years. The age group was selected because children have a smaller diameter of MN as compared to adults and elderly have arthritic changes in carpal joints. After permission from the Institutional Ethics Committee and written consent from the inductees, the sample was raised using non-probability consecutive sampling.

The clinical inclusion criteria were symptoms of numbness, paresthesia or pain at least in the distribution of MN distal to carpal tunnel during any time of the day or night with positive Phalen's test and positive Tinel's sign and/or carpal tunnel compression test at wrist. Patients with a history of trauma to forearm or surgery of the forearm/post-surgical release cases of CTS were excluded.

The NCS were performed using an XLTEK Neuromax 1004 EMG 4-channel unit (Xltek, Ontario, Canada). The measured EDX parameters were distal motor latency (DML), sensory peak latency (SPL), sensory conduction velocity (SCV), motor conduction velocity (MCV), sensory nerve action potential (SNAP), motor unit action potential (MUAP), and shape, size and recruitment patterns of MUAPs during voluntary muscle activation of thenar muscles. For median sensory studies, recording was carried out at the index finger using adhesive electrodes with G1 placed over the metacarpophalangeal joint and G2 placed 3-4 cm distally over the distal interphalangeal joint, while the nerve stimulation was carried out at the middle of the wrist [between the tendons to the flexor carpi radialis (FCR) and palmaris longus] and at a distance of 13 cm from G1. The ground electrode was attached between the stimulating and recording electrodes. The median motor study was performed by placing G1 over the muscle belly of abductor pollicis brevis (APB) and G2 placed over the first metacarpophalangeal joint. The distal stimulation site was middle of the wrist between the tendons to the FCR and palmaris longus at a distance of 7 cm from the recording electrode while the proximal stimulation site was at the antecubital fossa. For completing the NCS protocol; ulnar motor and sensory studies, median and ulnar nerve

(UN) F-responses, and radial nerve sensory studies were also carried out. Diagnosis was based on prolongation of DML of >4.4 msec for the MN and/or of SPL of >3.5 msec or reduced CMAP amplitude to <4 mV and abnormal electromyography with no abnormalities in the UN and in the proximal MN. If the MN studies were completely normal or equivocal, we proceeded with the median-versus ulnar nerve comparison tests preferably the MN versus UN digit 4 sensory studies. The recording site in this study was the metacarpophalangeal joint of the ring finger with G2 placed 3-4 cm distally over the distal interphalangeal joint. Median nerve was stimulated at the wrist between the tendons to FCR and palmaris longus while UN was stimulated at wrist adjacent to the flexor carpi ulnaris tendon. The distance was 12-14 cm (same distance for both studies). A latency difference of ≥0.5 msec was considered significant.

The severity of CTS was classified based on NCS as; negative (normal findings on all tests including comparative test); mild (abnormal comparison studies/median sensory nerve abnormalities); moderate (prolonged DML to APB with normal APB CMAP amplitude); and severe CTS (above plus either reduced median to APB CMAP amplitude and/or abnormal needle electromyography in the thenar muscles)[3]. The patients with negative CTS, accessory MN, evidence of chronic inflammatory demyelinating polyneuropathy, mononeuritis multiplex, chronic polyneuropathy, and thoracic outlet syndrome were excluded for MSUS examination.

All patients underwent MSUS examination using LOGIQ C5 Premium (General Electric Medical Systems (China) Co. Ltd, Jiangsu, P.R China) with high resolution linear array transducers (10-12 MHz) following the standard MSUS guidelines[10]. To ensure unbiased examination, the examiner was requested not to inquire about symptoms and the patients were asked not to speak about their problem during examination. Musculoskeletal ultrasonographic examination was done either on the same day or within 3 days of NCS. Musculoskeletal ultrasonographic examination was performed with the patient seated in a comfortable position facing the sonographer, with the affected forearm supported by the examination table and the palm facing up in the neutral position and fingers in extension. The volar wrist crease was used as an initial external reference point, with subsequent modifications during scanning using carpal bony landmarks and internal reference points. The full course of the MN in the carpal tunnel was assessed in both transverse and longitudinal planes. The size, shape, echogenicity, and relationship of MN to the surrounding structures and overlying retinaculum were observed. The amount of synovial fluid and the presence or absence of any mass were noted. The continuity of MN and any area of constriction were assessed in both the longitudinal and transverse planes. Two cases of CTS were excluded after MSUS i.e. one with bifid MN and persistent median artery and the other one with a large ganglion adjacent to the MN.

Measurements were taken for MN at the level of pisiform bone to measure CSA of MN, which was calculated by measuring the anteroposterior and transverse diameters of MN and entering the values in the Ellipse formula to calculate CSA. A value of >9.8 mm^2 was considered diagnostic for CTS. The FR (defined as the ratio of the major transverse axis of the MN to its minor longitudinal axis) was also assessed at the level of pisiform bone.

Analysis of data was done using Statistical Program for Social Science, version 20 (SPSS Inc., Chicago, Illinois, USA) and Med Calc (Med Calc Software, Ostend, Belgium). The CSA and FR were evaluated for normality using Shapiro Wilk test. CSA was distributed normally while FR did not follow a normal distribution. Comparison between groups for CSA was done by independent samples t-test and ANOVA. While for FR, it was done by Mann-Whitney U-test and the Kruskal-Wallis one-way ANOVA. The Spearman correlation analysis was performed to examine the correlation between CSA and CTS severities. Receiver operating characteristic (ROC) curves were also applied to determine the cutoff points

of MN CSA and FR in mild, moderate, and severe CTS levels described by NCS. The level of statistical significance was set at the *p*-value ≤0.05.

RESULTS

Fifty-two cases were included in the study over a period of 06 months. Three patients were excluded based on history of trauma or surgery of the forearm. One patient had accessory MN. The mean age was 47 ± 9 years (range 34 to 65 years). There were 11 (22.9%) males and 37 (77.1%) females. In 29 (60.4%) patients right hand was examined while in 19 (39.6%) patients, left hand was examined. Nine (18.8%) patients were diabetic, 10 (20.8%) were hypertensive, and nine (18.8%) had hypothyroidism. The mean values for DML, SPL, CMAP, and SNAP were 6.03 ± 1.39 msec (range: 4.3 to 10.2 msec), 5.91 ± 4.54 msec (range: 3-22 msec), 6.48 ± 3.21 mV (range: 0.7 to 16 mV), and 16.67 ± 7.9 µV (range: 3.8-33µV) respectively. The mean CSA for MN was 16.52 ± 3.28 mm² (range: 10.2 to 24.59 mm²) and the mean value for FR ratio for the MN was 4.59 ± 1.13 (range: 3.17 to 8).

There were 4 (8.3%) patients with mild CTS, 18 (37.5%) patients with moderate CTS, and 26 (54.2%) patients with severe CTS. All patients had CTS based on the cutoff value of MSUS used for the diagnosis of CTS. The mean values of CSA of the MN for mild, moderate, and severe CTS were 11.52 ± 1.94 mm², 14.57 ± 1.37 mm², and 18.63 ± 2.68 mm², respectively (p<0.001). The mean values for FR ratio of the MN for mild, moderate, and severe CTS were 3.7 ± 0.48, 4.07 ± 0.74, and 5.1 ± 1.19, respectively (p=0.002). A higher degree of positive correlation between CTS severities and CSA was observed (Spearman rank correlation coefficient = 0.79). There was no significant difference among mean values of CSA and FR for both genders and for individuals who had DM, hypertension, or hypothyroidism and those who did not have these diseases (table-I).

Table-I: Comparison of cross-sectional areaand flattening ratiovalues among different genders, and patients with and without diabetes mellitus, hypertension, or hypothyroidism.

Variables	Cross-Sectional Area	*p*-value	Flattening Ratio	*p*-value
Gender				
Male	15.44 ± 3.22	0.219	5.2 ± 1.44	0.071
Female	16.83 ± 3.28		4.43 ± 0.98	
Hypothyroidism				
Yes	18.34 ± 3.6	0.063	4.95 ± 1.27	0.291
No	16.09 ± 3.1		4.52 ± 1.1	
Diabetes Mellitus				
Yes	17.47 ± 2.66	0.337	4.64 ± 1.56	0.509
No	16.3 ± 3.4		4.6 ± 1.04	
Hypertension				
Yes	16.2 ± 2.58	0.737	4.96 ± 1.39	0.454
No	16.6 ± 3.49		4.52 ± 1.07	

Table-II: Cutoff values of cross-sectional areafor different carpal tunnel syndrome severities.

Category of Carpal Tunnel Syndrome	Area Under the Curve	95% CI	Cross-Sectional Area value in mm²	Sensitivity	95% CI	Specificity	95% CI
Mild	0.943	0.836 to 0.989	≤14.4	100%	39.8-100.0	77.27%	62.2-88.5
Moderate	0.824	0.687 to 0.919	≤15.55	94.4%	72.7-99.9	90%	57.7-90.1
Severe	0.942	0.835 to 0.989	>15.55	94.44%	69.8-97.6	76.67%	77.2-99.9

The ROC curve for MSUS and different severities of CTS is shown in figure.

DISCUSSION

We found that the majority of patients reporting with symptoms of CTS were females. The females had been found to be reporting with CTS symptoms more likely than males in earlier Pakistani studies[6,11-13]. This is because of the causal pathway between gender and CTS and may include some determinants such as hormo-

nal factors, anthropometric characteristics, and non-occupational exposure to biomechanical overload (e.g. household tasks)[14].

We found that the majority of patients had severe form of CTS. Another Pakistani study also found similar findings[15]. An earlier study from the same institute found moderate CTS to be the most prominent disease entity[12]. Two other Pakistani studies found mild and mild to moderate CTS to be the most frequent grade in patients presenting with CTS symptoms[11,13]. A Saudi study found mild CTS to be the most prevalent while a Thai study observed moderate CTS to be the most common grade of CTS on NCS[16,8].

a sensitivity of 94.4% (95% CI: 72.7-99.9) and specificity of 90% (95% CI: 57.7 - 90.1) at CSA of ≤15.55 mm^2. The CSA value for severe CTS was >15.55 mm^2 with a sensitivity of 94.44% (95% CI: 69.8-97.6) and specificity of 76.67% (95% CI: 77.2-99.9). Phongamwong *et al*[8] reported a value of 14 mm^2 for CSA to sufficiently rule in moderate and severe CTS, with a specificity of 91.4% and sensitivity of 42.3%. Some other studies primarily focused on establishing a cutoff value to use MSUS as a screening test for CTS. Mhoon *et al*[18] suggested a CSA of 9 mm^2 as the cutoff with a sensitivity of 99% and specificity of 22%. The study of Moran *et al*[19] suggested CSA of 9.8 mm^2 (sensi-

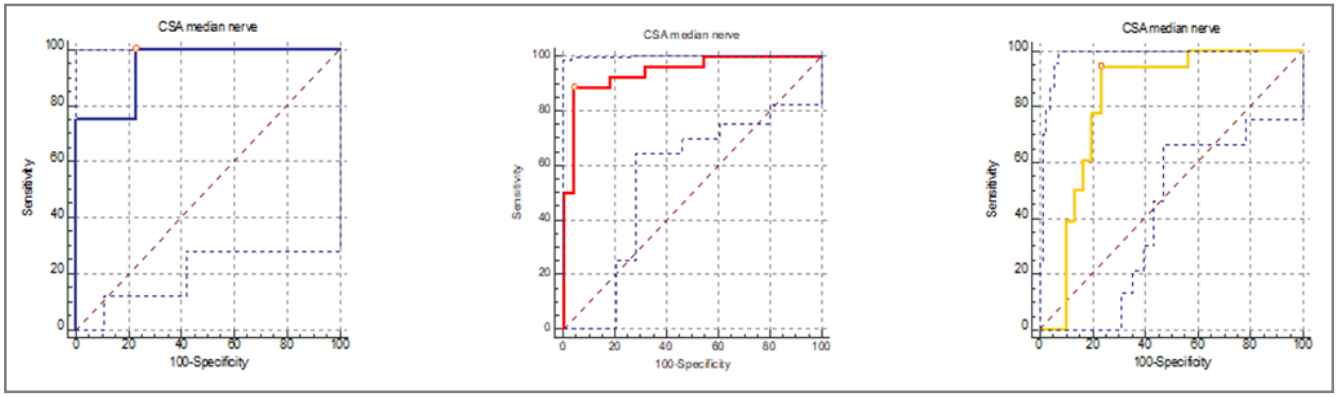

Figure: ROC Curve for musculoskeletal ultrasonography and different severities of carpal tunnel syndrome.

We did not find significant difference in CSA or FR among different genders, patients with and without DM, hypertension, and hypothyroidism; which infers that the findings observed in our study can be used as reference for the whole sample. The present study revealed a positive correlation between CSA and CTS severities (r_s=0.79). Previous studies have also reported similar correlation[8,17-19]. Phongamwong *et al*[8] reported a correlation coefficient of 0.56. The studies of Mhoon *et al*[18] and Moran *et al*[19] reported positive correlation coefficients of 0.52 and 0.61 respectively.

As all patients had CTS based on our used diagnostic criteria, we found that the CSA cutoff value for mild CTS was ≤14.4 mm^2 with a sensitivity of 100% (95% CI: 39.8-100) and specificity of 77.27% (95% CI: 62.2-88.5) (table-II). The CSA value for moderate CTS was 14.4-15.55 mm^2, with

tivity of 92% and specificity of 45%) and 12.3 mm^2 (sensitivity of 62% and specificity of 95%) as the cutoff to rule out and to rule in CTS, respectively. The study by Mohammad *et al*[20] showed 84% sensitivity and 100% specificity at a 9.5 mm^2 cutoff value for the mean CSA at the level of pisiform bone. Mehrpour *et al*[21] observed the sensitivity and specificity of MSUS in the diagnosis of CTS as 45% and 95.8%, respectively, with a CSA cutoff point of 9.8 mm^2. Sonbol *et al*[22] observed a diagnostic sensitivity of 93.3% and specificity of 98.3% for CSA cutoff value of 10 mm^2.

Musculoskeletal ultrasonography is considered a substitute method for the diagnosis of CTS according to many recently published studies[4,8,17-25], restricting the role of NCS to people with advanced axonal loss and suspected for differential diagnosis[25]. However, no exact normal ranges for MN CSA and cutoff point for

detecting CTS have been developed, mainly due to variations in equipment, measurement techniques, and patients' characteristics, and thus the variable location of maximum CSA or MN swelling. Therefore, to develop diagnostic criteria for MSUS diagnosis and quantification of CTS severity for Pakistani population, more studies with larger sample size are needed.

CONCLUSION

Musculoskeletal ultrasonography is a useful modality to determine the severity of CTS. Patients with ≤14.4 mm^2 of MN CSA at pisiform bone had a high probability for mild CTS. The CSA value for moderate CTS was 14.4-15.55 mm^2 and for severe CTS was >15.55 mm^2. The mean values of CSA did not differ significantly among genders and patients with and without DM, hypertension, or hypothyroidism.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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