Original Article

A comparison of the ultrasonographic median nerve cross-sectional area at the wrist and the wrist-to-forearm ratio in carpal tunnel syndrome

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Background: Electrophysiologic (EDX) study is the most valuable method in grading the severity of carpal tunnel syndrome (CTS), but it is invasive and painful. We evaluated the efficacy of ultrasound for this purpose. **Materials and Methods:** Eighty-one wrists of 52 consecutive patients with clinical evidences of CTS, confirmed and graded by EDX as mild, moderate, and severe, were examined by ultrasonography. Cross-sectional area (CSA) of the median nerve was measured at the distal wrist (CSA-D), and proximal forearm (CSA-P), and wrist-to-forearm ratio (WFR) was calculated for each hand. **Results:** The mean CSA-D was 0.12 cm^2 ± 0.03, 0.15 cm^2 ± 0.03 and 0.19 cm^2 ± 0.06 and the mean WFR was 2.77 ± 1.14, 3.07 ± 1.07 and 4.07 ± 1.61 in mild, moderate and severe groups respectively. WFR showed significant differences between the severe and none severe CTS groups (P < 0.001), but there was no significant difference between mild and moderate CTS groups (P < 0.381). CSA-D showed a significant difference between all groups (P < 0.0001). In the Receiver Operating Characteristic curve analysis, the optimal cut-off value of the CSA-D and WFR for detecting severe CTS were 0.15 (area under the curve 0.784, 95% confidence interval (CI): 0.662-0.898, P < 0.001, sensitivity of 68.2% and specificity of 70.9%) and 3 (area under the curve 0.714, 95% CI: 0.585-0.84, P = 0.001, sensitivity of 68.2% and specificity of 64.8%) respectively. All values were superior in CSA-D. **Conclusion:** Ultrasonography, can be complementary but not conclusive to the classification of CTS severities. CSA-D and WFR both increased in proportion to CTS severity, but neither parameter exhibited excellent performance in grading the severities.

Key words: Carpal tunnel syndrome, cross sectional area, carpal tunnel syndrome severity, ultrasonography, wrist-to-forearm ratio

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INTRODUCTION

Carpal tunnel syndrome (CTS) caused by compression of median nerve at wrist is the most common entrapment peripheral neuropathy[1] and a common indication for electrophysiologic (EDX) study, which has been the most valuable method in confirming the clinical diagnosis of CTS[2] and evaluating its severity.[3] Despite its role in evaluating the syndrome, EDX is known to be painful or unpleasant, and false negatives and false positives occur even if the most sensitive methods are used.[4] Recently, non-invasive high-resolution ultrasonography (US) has been increasingly used to evaluate entrapment neuropathies like CTS[5] that takes lower costs and lasts a shorter examination time.[6] Based on the promise that the median nerve is enlarged proximal to the site of entrapment due to swelling[7] many researchers went on tracing the circumference of median nerve in the carpal tunnel to use the cross-sectional area (CSA) of the nerve at distal wrist (CSA-D) as an index for CTS diagnosis,[8] although their methods were variable.[9] limits for CSA-D varied among reports ranging from 7 to 9.5 mm^2 in normal[10,11] and from 9 to 15 mm^2 in CTS patients[12] the variability may be due to difference in populations and measurement techniques. Area of a nerve is affected by variety of conditions like body weight[13] and specific diseases such as demyelinating hereditary motor sensory neuropathy[14] and a single measurement of CSA can lead to a false positive result. Won *et al*., showed although the area of median nerve is different between measured points along its path but the wrist-to-forearm ratio (WFR) (distal/proximal) did not correlate with demographic factors in normal population therefore enlargement of median nerve at the wrist as in CTS, enlarges the ratio.[15] Hobson-Webb *et al*., 2008, employed WFR to avoid mentioned causes of false positive result and use every patient as his own control. According to their study a WFR equal or >1.4 was 100% sensitive for detecting patients with CTS.[16]

Grading the severity of CTS is quite essential for treatment planning. Many grading are made based on

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clinical or EDX findings in CTS patients.[17-19] Bland showed that the strongest predictor for surgical outcomes is based on nerve conduction studies, and mid-range severity had better outcomes.[20] Ultrasonographic indexes such as CSA-D have been recently used to classify the severity of CTS and there are only few studies on WFR for this purpose.[21,22]

The purpose of this study is to assess the usefulness of WFR in comparison with CSA-D in grading of CTS severity according to EDX grading of its severity.

PATIENTS AND METHODS

The study protocol was approved by the Ethics Committee of Isfahan University of medical sciences with Research Project number of 391262 and informed consent was obtained from all patients.

Eighty-one wrists of 52 consecutive patients (45 female and 7 male, mean age 51.8 ± 10.8, range 24-78 years) with clinical evidences of CTS (such as weakness of grip, pain or parenthesis in digits I-III, loss of sensation in the hand, weakness or atrophy of the thenar eminence, wrist pain) who were referred to the Electromyography (EMG) Laboratory in Alzahra University Hospital from November 2012 to July 2013, were examined [Table 1]. Diagnosis was confirmed by clinical findings such as Phalen's and Tinel's signs and electrodiagnostic criteria. Patients with cervical spondylosis, plexopathy, history of wrist fracture or a previous surgery and injections in the wrist, bifid median nerve and having a motor neuron disease were not included. None of the patients were pregnant or suffered from neuropathies other than CTS. 7 patients were diabetics, and 4 of them had a history of hypothyroidism. All patients underwent electrodiagnostic study by experienced neurologist on a Synergy Electromyograph (Medelec Synergy, Oxford Instruments, Abingdon, UK). Skin temperature on the hand was measured and maintained between 32.0 and 34.0_C. All CTS severity was classified according to EDX results as.

Table 1: Patients' demographic and ultrasonographic data according to electrophysiologic grading of CTS severity

Variables	Mild CTS	Moderate CTS	Severe CTS
Number (%)	26 (32.1)	32 (39.5)	23 (28.4)
age (years)	46.05±10.49	54.10±9.31	55.12±10.82
sex (male/female)	2/15	3/16	2/14
Height (cm)	158.88±7.7	157.68±7.62	160.00±8.01
csa-d (cm^2)	0.12±0.03	0.15±0.03	0.19±0.06
csa-p (cm^2)	0.053±0.02	0.053±0.01	0.051±0.01
wfr	2.77±1.14	3.07±1.07	4.07±1.61

CTS = Carpal tunnel syndrome; CSA-D = Cross sectional area at distal wrist; CSA-P = Cross sectional area at proximal forearm; WFR = Wrist-to-forearm ratio. Results are presented as mean ± standard deviation or number (%)

Mild

Prolonged distal sensory latency (DSL) and/or median mixed nerve latency (MNL), and; normal or minimally prolonged distal motor latency (DML), and; Amplitudes of all responses within normal range, and; No conduction block (CB) or mild CB, and No thenar EMG abnormalities (if tested).

Moderate

Prolonged DSL, MNL, and DML (if all tested), and; Amplitudes of all tested responses may be diminished, typically a relative decrease (but not required), and; CB may be present, and; Minor thenar EMG abnormalities may be present.

Severe

Unobtainable median sensory nerve action potentials (or low amplitude and very prolonged DSL), and; low-amplitude or unobtainable median mixed nerve response and if present, very prolonged MNL, and; low-amplitude or unobtainable median compound muscle action potential and if present, very prolonged DML, and; CB may be present and pronounced (i.e., >70%), and; Thenar EMG abnormalities often present.[23]

Sonographer was blinded to the grade of severity in each patient, but not to the diagnosis. US examination was done by a 13 MHz linear transducer sonosite machine (SonoSite Ltd., Alexander House, Hitchin, Hertfordshire, SG4 0AP UK). The patients were seated near the examiner with their arms stretched; hands in a supine position, wrists resting on a flat surface and fingers were semiflexed. To avoid causing any artificial nerve deformity no additional force was applied other than the weight of the probe. The CSA of median nerve was measured at the proximal inlet of carpal tunnel at level of the pisiform bone as a landmark and 12 cm proximal in the forearm by tracing a continuous line around the inner hyperechoic rim of the median nerve with electronic calipers. The CSA was measured 3 times, and the average value was used for analysis.

Statistical analysis

We adopted the IBM SPSS version 22 statistical software (IBM SPSS, Chicago, IL, USA) for statistical analysis. Means and standard deviations (SD) were calculated for each variable. For comparison of continuous variables between groups analysis of variance was used, including least significant difference (LSD) *post-hoc* test for multiple comparisons. Correlations between ultrasonographic values and electrodiagnostic severities were tested using Pearson's correlation coefficient. Using Receiver Operating Characteristic (ROC) curves we investigated the optimal possible cut-off values of the ultrasonographic data according to electrodiagnostic severities, and specificity and sensitivity were obtained.

RESULTS

Patients were divided into three groups according to neurophysiologic study: Mild (n = 26), moderate (n = 32) and severe CTS (n = 23). The mean CSA at proximal was 0.053 cm^2 ± 0.025 (SD), 0.053 cm^2 ± 0.019 and 0.051 cm^2 ± 0.013 in mild group, moderate group and severe group respectively and showed no significant difference between the groups (P = 0.898). The mean CSA-D was 0.12 cm^2 ± 0.03, 0.15 cm^2 ± 0.03 and 0.19 cm^2 ± 0.06 in mild, moderate and severe groups respectively showing significant difference between all groups by using the LSD *post-hoc* analysis ($P < 0.0001$). The mean WFR was 2.77 ± 1.14, 3.07 ± 1.07 and 4.07 ± 1.61 in a mild group, moderate group and severe group. *Post-hoc* analysis using LSD correction showed significant differences between severe group and moderate group ($P < 0.001$) but showed no significant difference between mild and moderate CTS groups ($P < 0.381$) [Table 1].

In the correlation analysis using Pearson's correlation coefficient, electrodiagnostic severities were significantly correlated with CSA-D ($r^2 = -0.554$, $P < 0.001$) and WFR ($r^2 = -0.373$, $P < 0.001$). Correlation with CSA-D was higher.

Receiver Operating Characteristic curves were used to obtain the optimal possible ultrasonographic cut-off values to differentiate mild CTS and moderate CTS from severe CTS according to electrodiagnostic severities [Figure 1]. The area under curve of CSA-D and WFR in severe CTS were 0.784 (95% confidence interval [CI]: 0.662-0.898) and 0.714 (95% CI: 0.585-0.84) respectively ($P < 0.01$). Area under ROC curve showed higher values in CSA-D. The optimal cut-off values of CSA-D and WFR in severe CTS were 0.15 (specificity 70.9% and sensitivity 68.2%) and 3 (specificity 64.8% and sensitivity 68.2%) respectively. The sensitivity and specificity of the optimal possible cut-off value were slightly better in the CSA-D [Table 2].

DISCUSSION

The diagnosis of CTS usually is based on typical clinical signs and symptoms and EDX examinations are used to confirm the diagnosis and also in grading the severity of CTS which is essential in treatment planning and in follow up.[2,3,24] Recently, US as an additional approach has been used in the diagnosis of CTS and other entrapment neuropathies. CSA at distal wrist showed correlations with clinical symptoms and high concordance with nerve conduction study (NCS) in defining CTS severity.[8,25,26] CSA of nerve is affected by variety of conditions such as differences in populations, measurement techniques, specific diseases and body weight

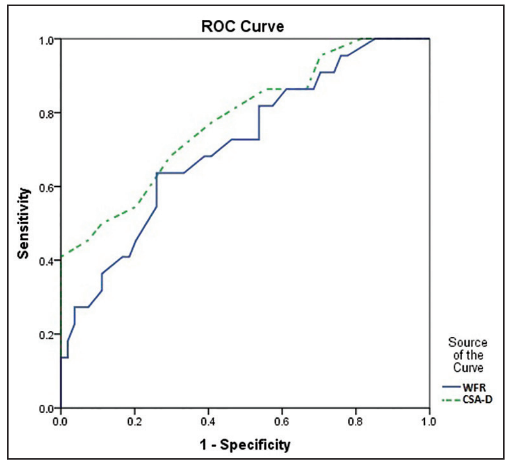

Figure 1: Receiver Operator Characteristic curves showing the relationship between sensitivity and specificity for wrist-to-forearm ratio and cross sectional area-distal wrist in detecting severe carpal tunnel syndrome patients

Table 2: Sensitivity and specificity of ultrasonographic nerve measurement in detecting severe CTS patients from none severe cases

Ultrasonographic findings	Sensitivity (%)	Specificity (%)
Cut off points for CSA-D		
0.15 (cm^2)	68.2	70.9
0.105 (cm^2)	100	20.0
0.195 (cm^2)	40.9	100
Cut off points for WFR		
3	68.2	64.8
1.937	100	14.8
5.650	13.6	100

CTS = Carpal tunnel syndrome; CSA-D = Cross sectional area at distal wrist; WFR = Wrist-to-forearm ratio

and a single measurement of nerve cross-section area can lead to false positive results.[13,14] Therefore, some authors preferred to use WFR and ΔCSA (difference between CSA-D and CSA at proximal) for this purpose to eliminate the false results.[22,27]

Previous studies had assessed concordance of US and CTS severity. Bayrak *et al*. showed an inverse relationship between the estimation of motor unit number of abductor pollicis brevis muscle and CSA at proximal and middle segments of carpal tunnel. Lee *et al*. showed that the swelling of the median nerve was correlated with NCS findings. Karadag *et al*. showed that CTS severity could be classified as normal, mild, moderate and severe according to CSA of the median nerve by US. Giannini *et al*. reported a significant relationship between the neurophysiological impairment of CTS and CSA of the median nerve.[17,25,28,29]

In this study, we compared the WFR and CSA-D of median nerve area between CTS patients according to EDX grading of severities. WFR and CSA-D both showed correlation with severity of CTS and their values increased according to EDX severity. CSA-D showed higher correlation. Mild CTS and moderate CTS and severe CTS showed significant differences in CSA-D mean, while mild CTS and moderate CTS did not show significant difference in WFR but the significant difference was observed between severe CTS and mild to moderate CTS. The sensitivity and specificity, obtained by the ROC curve, were slightly superior in CSA-D.

Prior US based studies were done to discriminate the different grades of CTS severity. Kang *et al*.[22] derived a cut-off value of 9.5 mm^2 for CSA-D and achieved sensitivity of 96.4% and specificity of 92.1%, for WFR a cut-off value of 1.34 was 99.9% sensitive and 100% specific in diagnosis of CTS but these ultrasonographic indexes could not show such an excellent power in discriminating the different grades of CTS (sensitivity of 69% and 72% and specificity of 68% and 72% for CSA-D and WFR respectively in detecting severe CTS patients). Klauser *et al*.[27] found a 2 mm^2 difference between CSA at distal and proximal (ΔCSA = 2 mm^2) 100% specific and 99% sensitive in detecting the patients from healthy controls, they also derived a cut-off CSA-D of 12 mm^2, 94% sensitive and 95% specific in diagnosis of patients but in terms of discriminating between wrists with mildly positive CTS findings based on electrodiagnostic study and wrists with highly positive findings, neither parameter exhibited excellent performance. Although values of both parameters tended to be greater in wrists with highly positive, parameters did not show significant differences (area under ROC curve A = 0.7592 for CSA-D and A = 0.7503 for ΔCSA).[27]

Lacking a control group this study was unable to compare diagnostic values of CSA-D and WFR. In terms of discriminating the different grades of CTS severity, none of the two parameters obtained excellent performance and a large difference between the parameters was not seen [Table 2].

A limitation of this study is the small sample size. Nonsignificant difference between mild and moderate groups in WFR may be due to small sample size in each group. Correlations were not performed with body mass index, which can influence the CSA.[30] Other US parameters, which can influence the CTS syndrome like flattening ratio of the median nerve in the distal carpal tunnel, bulging of the transverse carpal ligament, and median nerve echogenicity and mobility were not accessed in this study.[30]

CONCLUSION

Ultrasonography which is noninvasive and takes shorter time and lower cost, in addition to EDX study, can be complementary but not alternative for the classification of CTS severities. US provides anatomic information of the nerve and its surrounding structures, while the EDX study provides information on the level of the lesion and the function of the nerve. CSA-D and WFR both increased in proportion to CTS severity, although the sensitivity and specificity were superior in CSA-D.

AUTHORS CONTRIBUTION

FA contributed in the conception of the work, clinical studies, literature search, data acquisition, conducting the study, and agreed for all aspects of the work. BZ contributed in the conception of the work, literature search, data analysis, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. KB contributed in the conception of the work, conducting the study, revising the draft, approval of the final version of the manuscript, EDX study and agreed for all aspects of the work. MG contributed in the conception of the work, revising the draft, approval of the final version of the manuscript, ultrasonography and agreed for all aspects of the work. MM contributed in the conception and design of the work, conducting the study, data acquisition and agreed for all aspects of the work.

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