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Research paper

Standard median nerve ultrasound in carpal tunnel syndrome: A retrospective review of 1,021 cases ☆

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ABSTRACT

Objective: Carpal tunnel syndrome (CTS) is diagnosed with electrodiagnostic (EDx) studies. Investigations have examined US cross sectional-area (CSA) and wrist to forearm ratio (WFR) cut-offs for screening EDx abnormalities in patients with suspected CTS. The objective of this study is to determine if these US parameters are effective in a real world population.

Methods: This is a retrospective review of patients presenting to the Duke Electromyography (EMG) Laboratory during 2013–2014 with a final diagnosis of CTS. US diagnosis of CTS was based upon median nerve cross-sectional area of >9 mm^2 and/or wrist-to-forearm ratio of >1.4. EDx studies were the gold standard for diagnosis.

Results: A total of 670 patients and 1,021 extremities were studied. US was positive in 97.6% of EDx confirmed CTS.

Conclusion: Median nerve US is nearly as sensitive as the gold standard for EDx testing for the diagnosis of CTS.

Significance: The data here suggest that US may have use as a screening tool prior to performing EDx testing for CTS.

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1. Introduction

Carpal tunnel syndrome (CTS) is the most frequent entrapment neuropathy and a common reason for referral to electrodiagnostic (EDx) laboratories. CTS causes pain, numbness, and tingling in the hands and is an important cause of work disability. Several factors have been associated with CTS and include chronic diseases (diabetes mellitus, rheumatoid arthritis, gout, hypothyroidism) or occupational factors associated with forceful and repetitive hand motions, awkward postures, mechanical stress at the base of the palm and vibration (Atcheson et al., 1998; Feldman et al., 1987). The gold standards for diagnosis are based largely on clinical pre-

sentation and EDx studies, however at least four studies have provided level I evidence for sonographic visualization of median nerve enlargement as a diagnostic alternative that is painless, non-invasive and inexpensive (Beekman and Visser 2003; Mhoon et al., 2012; Duncan et al., 1999).

CTS is widespread with a prevalence in the general adult population ranging from 2.7% to 5.8% (Atroshi et al., 1999). This condition also carries a high healthcare burden. A 1998 study examined health care expenditures and patterns of work disability by analyzing claims accepted by the US Department of Labor, Office of Workers' Compensation Programs (OWCP), from October 1, 1993, through September 30, 1994. CTS was the most costly diagnosis, accounting for 57% of expenditures. A mean of 84 workdays was lost for CTS and the average cost per patient was $4,941 (Atroshi et al., 1999). Given the frequency of CTS in the general population and its cost to society, inexpensive screening and diagnostic tools would be advantageous.

A prospective trial performed in 2012 at our institution assessed the utility of ultrasound (US) in screening for EDx abnormalities in patients with CTS symptoms. The results of this prospective study demonstrated 99% sensitivity for detecting EDx abnormality in patients with a median nerve cross sectional area

(CSA) of >9 mm^2 at the wrist and 97% sensitivity for a wrist-forearm ratio (WFR) of >1.4. There were no clinically significant correlations between US parameters and EDx severity. In this retrospective study, we performed a review of all diagnosed CTS patients evaluated between January 2013 and December 2014 to investigate the utility of our established median nerve US parameters in clinical practice (Mhoon et al., 2012).

2. Methods

The institutional review board of Duke University approved this retrospective study. Informed consent was not obtained, Exempt Research Application and an Application for Waiver of HIPAA Privacy Authorization were obtained.

2.1. Study group

This is a retrospective chart review of all patients who presented to the Duke Electromyography (EMG) Laboratory during January 2013–December 2014. The Duke EMG Laboratory database (ELMS) was queried to identify all patients with a final diagnosis of CTS. Our institutional standard is that CTS is diagnosed based upon EDx studies alone, irrespective of the US findings. However, we have no effective way of retrospectively looking at this data or to determine if the patient had clinical symptoms of CTS. Accompanying EMG findings and US findings were reviewed as described here.

After identifying patients with a final electrodiagnostic diagnosis of CTS, an electronic medical record review was completed on these patients to assess demographics including age, sex, handedness, height, weight, body mass index (BMI) and ethnicity. In addition, the presence of diabetes mellitus, hypertension, pregnancy and thyroid disease was recorded.

In total, 670 patients were included in this analysis. Of the 670 patients, 351 had studies to both upper extremities and 319 only had one extremity examined. Therefore, 1,021 extremity studies were included.

2.2. EDx testing

All nerve conduction studies (NCS) were performed at a skin temperature of 34 °C. For CTS, a minimum of median motor response over the abductor pollicis brevis, median mixed nerve action potential, and ulnar mixed nerve action potential recordings was performed. The median motor nerve conduction study was obtained by placing recording electrodes over the abductor pollicis brevis and stimulating the nerve 6.5 cm proximally at the wrist. Median and ulnar mixed nerve conduction studies were obtained by stimulating the nerves in the palm and recording 8 cm proximally over the respective nerves. A diagnosis of CTS was defined by a distal motor latency of >4.3 ms, a median mixed nerve latency of >2.2 ms, or a difference between median and ulnar mixed latencies of ≥0.4 ms. Distal median motor latency, median motor compound muscle action potential (CMAP) amplitude, median mixed nerve latency and median and ulnar mixed interlatency differences were recorded for all patients.

2.3. US testing

Median nerve US images were obtained by neurologists trained in peripheral nerve US. Images were collected on the same day as EDx testing using an Esaote MyLab 70 equipped with an 18–6 MHz linear array transducer. The median nerve was imaged in cross section at the distal wrist crease (carpal tunnel inlet) and 12 cm proximal to this point in the forearm. The cross-sectional area (CSA) was calculated using the continuous trace method by outlining

the perimeter just inside the hyperechoic epineurium. The CSA of any bifid nerve was calculated by adding the individual CSAs of the 2 components.

US findings were reviewed for median nerve CSA at the distal wrist crease and 12 cm proximal to the distal wrist crease. The wrist to forearm ratio (WFR) of CSA (wrist CSA/forearm CSA) was calculated. CSA >9 mm^2 and WFR >1.4 were used as cut-off values, based upon prior study.

2.4. Grading of CTS severity

CTS severity was graded based on two scales-EDX 3 (used at Duke EMG laboratory) and the internationally validated EDX 5 (Mhoon et al., 2012) . In the EDX 3 scale, severity is defined as no EDX evidence of CTS (0) if the median mixed and ulnar mixed nerve studies are normal, mild (1) if only the median mixed nerve action potential is abnormal or its latency is ≥0.4 ms longer than the ipsilateral ulnar mixed nerve action potential; moderate (2) if both the median mixed nerve conduction study and the median motor latency are abnormal or the median mixed nerve action potential is absent; and severe (3) if the median mixed nerve conduction study is abnormal and the median compound muscle potential amplitude and latency are abnormal. EDX 5 is as follows: Abnormalities of comparative (comparison of median nerve conduction through the carpal tunnel with the radial or ulnar nerve conduction in the same hand) and/or segmental studies (over a short conduction distance across the carpal tunnel) (1). Sensory nerve conduction velocity slowing in the digit-wrist segments (2), increase in distal motor latency (3), disappearance of the digit wrist sensory response (4), disappearance of motor response (5).

2.5. Statistical analysis

Statistical analysis was performed using JMP version 11 software (SAS, Inc., Cary, North Carolina). Pearson correlation coefficients were calculated to analyze the relationship between ultrasound findings and the clinical and EDx severity scales and clinical severity was analyzed in similar fashion. A correlation was considered clinically significant if $r > 0.4$ and $p < 0.05$ for a set of variables.

3. Results

3.1. Demographics/characteristics

The mean age of the 670 CTS patients was 56.6 ± 15 years. Mean BMI was 31.8 ± 8 in an area where 30% of all adults meet criteria for obesity (Ziswiler et al., 2005). The most commonly associated comorbidities were hypothyroidism (49.1%), followed by diabetes mellitus (41.9%). There were 233 (34.8%) men and 437 (65.2%) women examined. The majority of patients were right-handed (76.4%) and Caucasian (70.8%). These characteristics are described in Table 1. Differences between the three sub-groups (EDx abnormal/US normal, EDx and US normal and ED normal/US abnormal) are discussed in Table 2.

3.2. EDx/US findings

A total of 954 patients and 1,904 extremities had a diagnosis of CTS based on EDx studies.

Since not all physicians in the EMG laboratory are US trained, out of these 954 patients, 670 (70%) patients and 1,201 out of 1,904 extremities (53.8%) had both EDx and US studies done during CTS evaluation. Out of these 670 patients and 1,021 extremities,

Table 1
Patient characteristics.

Age (years ± SD)	56.6 ± 15
Gender	
Male	233 (34.8%)
Female	437 (65.2%)
Body mass index (±SD)	30.6 ± 23
Comorbidities	
Pregnancy	11 (1.6%)
Gout	179 (26.7%)
Hypothyroidism	329 (49.1%)
Diabetes mellitus	281 (41.9%)
Hypertension	152 (22.6%)
Rheumatoid arthritis	47 (7.0%)
Ethnicity	
Caucasian	475 (70.8%)
African American	156 (23.2%)
Other	39 (5.8%)

654 patients and 986 extremities had both EDx and US findings consistent with CTS (96.6% and 97.6% respectively).

The mean overall CSA was 12.6 mm^2 ± 4.7. The mean overall WFR was 2.1 ± 0.93. The correlation with BMI was statistically significant, but did not meet criteria for clinical significance ($r = 0.179$, $p < 0.001$).

3.3. Median nerve CSA and electrodiagnostic severity

EDx severity was graded on 2 scales: a 3-point scale used at the Duke EMG laboratory (EDX 3), and an internationally accepted 5-point scale (EDX 5). Statistically, but not clinically, significant correlations were present between median nerve CSA at the wrist and the EDX 3 ($r = 0.226$, $p < 0.001$) and EDX 5 ($r = 0.239$, $p < 0.001$). There also was a statistically, but not clinically significant correlation between median nerve CSA at the wrist and median nerve distal latency ($r = 0.180$, $p < 0.0001$). There was no correlation between median nerve CSA at the wrist and median CMAP amplitude ($r = -0.006$, $p = 0.89$). In summary, median nerve CSA could not be used to predict EDX severity using either scale.

3.4. Median nerve CSA and co-morbidities

Patients with hypothyroidism had a slightly larger CSA compared to patients without thyroid disease (12.45 mm^2 vs. 12.15 mm^2, $p = 0.013$). There was no difference in nerve size, however, between patients with and without diabetes ($p = 0.4$).

3.5. EDx negative US abnormal group

There was a small group (n = 79) of patients with normal EDx studies and abnormal US studies that received a final diagnosis of CTS. This subgroup was not included in the overall analysis as their studies did not meet criteria of CTS based on the EDx criteria that we were using as gold standard. Slightly more than half of these patients were men (n = 42, 53.1%). The mean age was 55.7 years. The average weight and BMI were similar to that of the overall group at 84.7 kg and 30.6, respectively. Most were Caucasian (n = 58, 73.4%). There were 2 (2.5%) pregnant patients, 16 (20.5%) had gout, 32 (40.5%) had hypothyroidism, 39 (49.4%) had HTN, 26 (32.9%) had DM and 9 (11.4%) had RA. EDx and US studies were in line with the average for the group overall with the average CSA was 11.3 mm^2 and the mean WFR was 1.9. The main difference between this group and the main group (Edx abnormal/US abnormal) was the increased proportion of men and the smaller mean CSA and WFR values. Given the retrospective nature of this study, is difficult to say for certain what prompted evaluation for these patients but presumably it was based upon clinical suspicion by treating physician. The mean CSA of these patients was smaller than the main group, so it is possible that despite having some inflammation to the median nerve, the EDx had not yet been affected, yielding an abnormal US with a normal EDx results.

3.6. EDx positive US negative group

A small group of patients (n = 16/670 – 2.4%, n = 31/1,021 – 3.1%) had a normal US study despite positive EDx testing. This consisted mostly of female patients (n = 9, 56.2%). The average age was 55.8 years. The average weight was 85.5 kg and average BMI was 32.4. Half of the patients were Caucasian (n = 8, 50%) and most were right-handed (n = 13, 81.3%). One (6.3%) patient was pregnant, 4 (25%) had gout, 7 (43.8%) had hypothyroidism, 5 (31.3%) had HTN, 8 (50%) had DM2 and 1 (6.3%) had RA. The average CSA was 8.5. The WFR was 1.2. Both mean CSA and WFR values were smaller than the main group (EDx abnormal/US abnormal) ($p < 0.001$).

3.7. Bifid median nerves and other findings

Bifid median nerves were found in 66 (4.6%) of the 1425 patients studied with US. Bilateral bifid nerves were present in 5 (0.35%) patients. Two (0.14%) patients had unilateral trifid median nerves at the wrist. There were 7 instances of persistent median artery (PMA). These variants did not influence the CTS determination via US.

Table 2
Clinical and sonographic features of patient cohort.

	EDx+/US− N = 16	EDx+/US+ N = 670	EDx−/US+ N = 79
Age (years)	55.8	56.6	55.7
Weight (kg)	85.5	86.3	84.1
Diabetic (n/%)	8 (50%)	273 (41.70%)	26 (34.2%)
Hypothyroidism (n/%)	5 (31.3%)	322 (47.60%)	32 (42.1%)
Handedness (n/%)	Right-13 (81.3%)	Right-499 (76.8%)	Right-67 (84.8%)
	Left-2 (12.5%)	Left-150 (23.1%)	Left-9 (11.4%)
	Ambidexterous1 (6.3%)	Ambidextrous 5 (0.77%)	Ambidexterous-3 (3.8%)
Gender (n/%)	Female-9 (56.2%)	Female-428 (65.4%)	Female-37 (46.8%)
	Male-7 (43.8%)	Male 226 (34.5%)	Male-42 (53.2%)
Ethnicity (n/%)	Caucasian-8 (50%)	Caucasian-467 (71.4%)	Caucasian-58 (73.4%)
	African American-5 (31.3%)	African American-151 (23.0%)	African American-11 (13.9%)
	Other-3 (18.8%)	Other-36 (5.5%)	Other-10 (12.7%)
Wrist CSA mm^2	8.5	12.6 (p < 0.4)	11.3 (p < 0.5)
WFR	1.2	2.1 (p < 0.001)	1.9 (p < 0.001)

4. Discussion

In the current retrospective study, US and EDx data from patients diagnosed with CTS were examined to determine if our previously established US criteria work well in clinical practice. The existing reference values were established through a prospective study at our medical center by Mhoon et al., but potentially biased by the study methods (Mhoon et al., 2012). The patient cohort analyzed here represents a broader patient population and is less susceptible to bias by study entry criteria.

Upon review, the patients in the Mhoon et al. study and the current study are remarkably similar in many ways. There were no differences in the average age, weight, gender and ethnicities of the patients. Despite these cohort similarities, the results did differ outside the setting of a prospective trial. Compared to the Mhoon et al. study, the incidence of thyroid disease was much higher in the current study, as efforts were made to exclude patients with thyroid disease from the initial study. The mean CSA and WFR were slightly larger in the Mhoon study (13.4 mm^2 vs. 12.6 mm$^{2;}$ 2.2 vs. 2.1, respectively), but the findings did not provide any evidence that our previously established cut-off values (CSA >9 mm^2, WFR >1.4) should be increased (Mhoon et al., 2012). Correlations with EDX severity were present here ($r = 0.23$), but were not as robust as Mhoon et al. (Mhoon et al., 2012).

The major strength of our study is the large number of patients from a representative clinical population consecutively referred to the electromyography laboratory. All were tested through a standardized EDx and US approach. However, our study is limited by its retrospective nature and the fact that data collection was limited to chart review. Additionally, not all patients with CTS had an US. This was due to the fact that not all clinicians in our laboratory perform US, as opposed to selection bias for only certain patients to receive the test. This is not expected to have altered the findings. It is also clear that the clinic population has a higher than normal incidence of obesity, diabetes mellitus and thyroid disease. This reflects the clinical complexity of patients at a tertiary care center and health care issues specific to our geographic area. This may limit the generalization of findings to other populations.

Prior studies have examined the utility of US in diagnosing CTS and have determined sonography to be a useful adjunct with EDx testing and multiple studies have found US to have high utility in the diagnosis of CTS (Kele et al., 2003; Ziswiler et al., 2005). A meta-analysis by Fowler et al. analyzed the role of US in CTS, including 19 articles with a total of 3,131 wrists. This meta-analysis revealed the composite sensitivity and specificity of CTS diagnosis to be 77.6% and 86.8%, respectively, but was unable to set exact diagnostic cut-off values due to wide variations of sensitivities and specificities reported in the literature (Fowler et al., 2011).

In the analyzed study population, the chance of having carpal tunnel syndrome based on clinical suspicion alone was very good (1,904/2,042 = 93%). However, currently, most clinicians consider EDx studies to be the gold standard for CTS diagnosis. Numerous, relatively small prospective trials have demonstrated its utility, but there have been doubts regarding its use in a typical patient population. In the current study, it is clear that US can be used to screen for and possibly diagnose CTS in an unselected patient population, but provides no meaningful information regarding EDX severity. This reinforces our assertion that US and EDx testing should be used in a complementary manner.

Our data has implied that there is not a significant correlation between US and EDx findings in regards to the severity of the CTS. However patients with CTS as determined by the gold standard of EDx largely had an abnormal US (97.6%), which likely is due to inflammation and edema which is often seen in median neuropathy of the wrist. In clinically symptomatic patients, if median nerve CSA is 9 mm^2 or less, it is highly unlikely that EDx testing will reveal abnormalities consistent with CTS and needle EMG for cervical radiculopathy might be the most appropriate next step. However, a limitation of this study is that we cannot comment on the specificity of an abnormal CSA (>9 mm2) or WFR (>1.4) in screening asymptomatic individuals. Regardless, with these above factors in mind, the data here does still suggest that US may have use as a screening tool prior to performing EDx testing for CTS. This approach might reduce the cost of care for suspected CTS.

Conflict of interest

Santoshi Billakota and Lisa Hobson-Webb: None.

Acknowledgments

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