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Peripheral Nerve

Characteristics of Patients with Clinical Signs and Symptoms of Carpal Tunnel Syndrome but Negative Diagnostic Testing

Luke D. Latario, MD
John R. Fowler, MD

Background: Carpal tunnel syndrome (CTS) is a clinical diagnosis involving numerous confirmatory diagnostic tools, including patient questionnaires, ultrasound (US), and electrodiagnostic studies (EDX.) Patients may experience clinical symptoms of CTS with false negative diagnostic testing. The purpose of this study was to identify characteristics of patients with clinical symptoms of CTS with negative diagnostic testing.

Methods: An existing database of 295 hands containing the six-item CTS-6, US of the median nerve, and EDX was queried. Patients with symptoms of carpal tunnel scoring 12.5 or higher on CTS-6 were sorted into those with all positive testing or negative testing.

Results: In 60 patients, 103 hands had both positive US and EDX and a CTS-6 of 12.5 or higher. Twenty-nine hands in 25 patients had a CTS-6 of 12.5 or higher and both negative ultrasound and EDX. There was a significantly younger average age of 43 ($P = 0.007$) and lower average BMI of 28 ($P < 0.0001$) of patients in the negative diagnostic study group, compared with the average age of 53, and a body mass index (BMI) of 34 in the positive diagnostic study.

Conclusions: In this series, patients with symptoms of carpal tunnel syndrome and negative diagnostic studies were on average younger and had a lower BMI. These patients may warrant more careful consideration of CTS clinical diagnosis and counseling regarding a higher risk of false-negative confirmatory testing. Further studies are needed to determine possible effects of age and BMI on electrodiagnostic studies and ultrasound testing in CTS. *(Plast Reconstr Surg Glob Open 2024; 12:e5816; doi: 10.1097/GOX.0000000000005816; Published online 15 May 2024.)*

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common compressive neuropathy with an estimated community prevalence of 5%.[1] CTS is frequently attributed as a work-related injury at a rate as high as 67%,[2] and the diagnosis and treatment of CTS can have significant cost to healthcare system.[3,4] There is currently no accepted standard for diagnosis with clinicians utilizing electrodiagnostic (EDX) studies, clinical questionnaires, and ultrasound (US) as diagnostic aids.[4–9]

From the Department of Orthopaedic Surgery, University of Pittsburgh, Pittsburgh, Penn.

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Six-item CTS scale (CTS-6) is a validated clinical tool used to assess the probability of diagnosis CTS.[6,10] CTS-6 has been shown to have a high positive predictive value of up to 96%[11] and has even been proposed as an outcome measure in clinical trials for CTS.[12]

US is increasingly advocated as a diagnostic study in CTS.[1,6,7,9,13–15] In comparison to a standard reference of clinical diagnosis[6] or EDX testing, US performs well. US is also a lower cost study than EDX and providers can be rapidly and effectively instructed in its use.[16] The American Academy of Neuromuscular and Electrodiagnostic Medicine supported the use of US in the diagnosis of CTS in its 2012 evidence-based guidelines.[13]

Concerns regarding the use of US for definitive diagnosis have centered around reliability and the lack of standardized methodology for US measurement of median nerve compression and interpretation.[5,14,15,17] A 9% mean error in measurement of median nerve is seen and may not be significantly decreased with user experience.[16,17] In US diagnosis of carpal tunnel, there is moderate

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interrater and intrarater reliability among orthopedic trained physicians.[18]

Despite the significant research and technological development progress in ancillary and confirmatory testing for CTS, patients may have clinical CTS not detected by confirmatory testing. Work by Pimentel et al[9] showed that in a series of 115 patients, with 90% experiencing relief of paresthesia following carpal tunnel release, there was a sensitivity of 84.6% and 92.3% for US and nerve conduction studies, respectively. This gave a negative predictive value of only 36% for US and 55.6% for nerve conduction studies.[9] Other work has shown higher negative predictive values of 82% for US and 80% for EDX studies. The EDX study has been shown to have high sensitivity but relatively poor specificity when compared with examination and history-based clinical tools,[11] and diagnostic studies complement and do not supplant detailed history and clinical evaluation.[6,15,19] Patients with both negative US and EDX testing but clinical signs of CTS may have unique features not previously reported in studies evaluating the sensitivity and specificity of individual US or EDX studies. The purpose of this study is to identify characteristics of patients with clinical symptoms of CTS based on validated clinical questionnaires who have negative diagnostic testing.

Takeaways

Question: What are the characteristics of patients with carpal tunnel syndrome (CTS) clinically but with negative diagnostic confirmatory testing?

Findings: A total of 295 patients presenting for evaluation of CTS were analyzed. Patients with CTS based on the six-item CTS scale but negative ultrasound and electrodiagnostic studies (n = 29) had a younger average age of 43 years ($P = 0.007$) and lower average body mass index of 28 ($P < 0.0001$) compared with patients with six-item CTS scale scores greater than 12.5 and both positive ultrasound and electrodiagnostic studies (n = 103).

Meaning: Patients who are younger and with lower BMI may have clinical CTS but false-negative confirmatory diagnostic testing.

METHODS

This study retrospectively queried a database collected with institutional review board approval from 2015 to 2018 on patients presenting for evaluation of CTS. All patients were adults, and demographic data on age, sex, height, weight, race, and presence of diabetes were recorded. All patients were evaluated using the CTS-6 tool and confirmatory diagnostic testing with US and EDX nerve studies were obtained.

US studies were performed by a trained orthopedic surgeon, measuring the area of greatest cross-sectional area of the median nerve at the level of the distal wrist crease. The cutoff of 10 mm^2 was used as a positive test for presence of carpal tunnel.[13,14] EDX studies were performed by board-certified physicians trained in electrophysiology. Patients having either motor distal latencies greater than 4.5 or sensory latencies greater than 3.3 were considered abnormal and a positive EDX. These cutoffs were used based on the 2020 American Association of Neuromuscular and Electrodiagnostic Medicine reference values.[20] CTS-6 data collection was performed by a hand and upper-extremity surgery fellowship-trained surgeon.

Statistical analysis was performed using GraphPad Prism v10.03. The Fisher exact test was used for categorical data and an unpaired *t* test was performed for continuous data of age and body mass index (BMI).

RESULTS

An existing database of 295 instances of patients presenting with CTS was sorted to include patients with a CTS-6 score of 12.5 or higher indicating the presence of signs and symptoms of CTS.[8] One hundred seventy-nine wrists had a CTS-6 of 12.5 or higher, and 116 cases were excluded. (Fig. 1) The 179 patients were stratified into those with positive or negative confirmatory testing studies of EDX and US. One hundred three hands in 60 patients had both positive US and EDX studies (Fig. 1). Twenty-nine hands in 25 patients had a CTS-6 of 12.5 or higher and also negative US and EDX testing (Fig. 1). Only one patient in the negative diagnostic study group had a contralateral hand with positive confirmatory testing.

Analysis of demographics showed a statistically significant difference in age, with a mean age of 53 years in the positive diagnostic study group compared with 43 years in the negative diagnostic study group (Table 1). Patients also had a lower average BMI in the negative diagnostic study group of 28 compared with 34 in the positive diagnostic study ($P < 0.0001$) (Table 1). No difference was found between the groups in their demographics of race, sex, or diagnosis of diabetes.

DISCUSSION

Debate remains on the best criteria for diagnosis of CTS.[4,11,13] Like all clinical tests, US and EDX diagnostic tests have limitations in their diagnostic accuracy and may result in false-negative results in patients with clinical signs and symptoms of CTS.[6] The aim of this study was to compare demographics of patients with signs and symptoms of CTS as measured using CTS-6 who have positive and negative diagnostic testing. This study showed that patients with negative US and EDX who had signs and symptoms of CTS (as measured using CTS-6) are on average 10 years younger than the patients with positive studies. They also on average have a lower BMI (Table 1). No other difference in sex, race, or presence of diabetes was found between the two groups.

In our study, patients with normal US EDX with CTS were younger than those with abnormal US and EDX suggestive of CTS. Work has shown that age and sex in adults does affect EDX studies, with increasing latencies and slowed conduction velocity found in older adults and men.[21] It is possible that younger patients with CTS experience clinical symptoms, but the neurologic insult does not reach the threshold for diagnostic confirmation using broader population-based parameters. Similarly, it

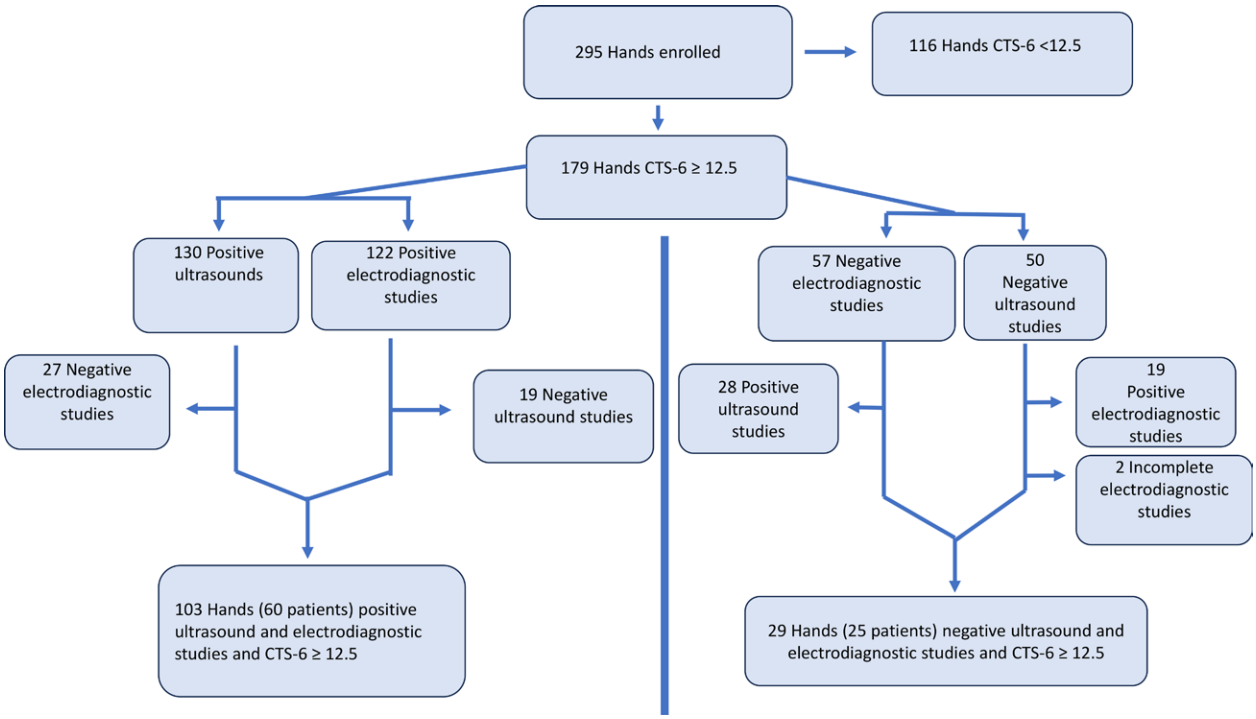

Fig. 1. Flow chart showing the inclusion and exclusion of patients with CTS based on CTS-6 and US and EDXs. Cross-sectional areas of the median nerve measured on US greater than 10 mm^2 were considered positive and motor latencies greater than 4.5 milliseconds or sensory latencies greater than 3.3 milliseconds were considered positive.

Table 1. Demographic Comparison of Patients Scoring Greater than 12 on CTS-6 and Having Both EDX Study and US-positive or -negative Studies

	EDX and US Positive	EDX and US Negative	*P*
N	103	29	
Mean age (y)	53	43	**0.0007** *
Mean BMI	34	28	**0.0001** *
Female (%)	79 (77%)	24 (83%)	0.6152†
White	66 (64%)	21 (72%)	0.5077†
African American	37 (36%)	8 (28%)	
Diabetic	17 (17%)	4 (14%)	>0.9999†

Statistically significant *P* values ($P<0.05$) are in bold font.
*A *P* value calculated using unpaired Student *t* test.
†A *P* value calculated using the Fisher exact test.

is known that diabetic neuropathy and male sex increases median nerve cross-sectional area, but this did not have a measured significant effect between groups in our study.[22] In regard to US, a review by Ng et al[22] showed variability in the median nerve cross-sectional area based on age, but these results were heterogenous between studies and appears inconclusive at this time.

Lower BMI was associated with an increased likelihood of having a negative US and EDX in the presence of CTS. Research has shown increasing BMI is correlated with increased median nerve cross-sectional area.[23] Our studies show patients with lower BMI are more likely to have signs and symptoms of carpal tunnel without increases in median nerve cross-sectional area reaching diagnostic thresholds. Therefore, patients with lower BMI may be more likely to have false-negative US studies despite positive CTS-6.

Limitations of this study include those inherent to retrospective studies utilizing an existing database without postoperative patient-reported outcomes. Additionally, the presence of signs and symptoms relied on the CTS-6 score, and as with any clinical test, adjusting parameters of diagnostic thresholds affect the sensitivity and specificity of the test. Adjusting the cutoff of 12 used in this study may affect sample sizes in our cohorts. However, the cutoff score of 12 used is consistent with published for diagnosis of CTS.[24] Similarly, other cutoff parameters for US and EDX could affect the number of false-negative tests in this study. Our parameters of 10 mm^2 and motor and sensory latency are consistent with previously published work.[14,20] It is possible patients may have symptoms of CTS from the contralateral and may confuse or misreport their symptoms, increasing the number of false-negative studies. However, only one patient in the negative diagnostic testing group had a contralateral positive diagnostic test.

In this study, patients with signs and symptoms of CTS but negative US and EDX were younger and had lower BMI than patients with findings of CTS on US and EDX studies. The continuing debate on the best criteria and algorithm in diagnosing CTS underscores the importance of clinical circumspection in the diagnosis of this common condition. Younger patients with lower BMI warrant more careful examination, history taking, and independent interpretation of the results of diagnostic studies. Further studies could explore the effect of age and BMI on US and

EDX and possible roles for other ancillary tests in younger patients with low BMI.

Luke D. Latario, MD
UPMC Passavant, McCandless Campus
9104 Babcock Blvd, Suite 4111
Pittsburgh, PA 15237
E-mail: Luke.Latario@gmail.com

DISCLOSURES

Dr. Fowler is a paid consultant of Integra LifeSciences. The other author has no financial interest to declare.

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