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Original Research

The Diagnostic Utility of Ultrasound and Electrodiagnostic Studies in The Young and Old

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Purpose: Carpal tunnel syndrome is the most common compressive neuropathy. The diagnostic parameters currently used for the general adult population may not be valid in elderly or younger cohorts. The purpose of this study is to determine the diagnostic accuracy of nerve conduction studies (NCS) and ultrasound (US) in different age groups utilizing the 6-item Carpal tunnel syndrome (CTS) symptoms scale (CTS-6) as the reference standard.
Methods: A retrospective database of patients who underwent US and NCS as part of the diagnostic work-up for suspected peripheral nerve compression was reviewed. Subjects were separated into three groups based on the median age of carpal tunnel syndrome patients (55 years of age) and two standard deviations (standard deviation 13.5 years) above and below the median. The young group was 28 years of age or less, the middle group was 29–71 years of age, and the old group was 72 years of age or greater. CTS-6 and Boston Carpal Tunnel Syndrome Questionnaire scores were recorded. Using CTS-6 as a reference standard, the sensitivity and specificity were calculated for NCS and US.
Results: A total of 295 hands were included in the analysis with 23 hands in the young group and 24 hands in the old group. NCS showed 31% sensitivity and 100% specificity in the young group compared to 54% sensitivity and 90% specificity for US. NCS showed 94% sensitivity and 25% specificity in the old group compared to 81% sensitivity and 38% specificity for US. Overall accuracy for US and NCS was 66% for both tests when looking at all age groups. The accuracy in the young group was 70% for US and 61% for NCS, whereas the accuracy in the old group was 67% for US and 71% for NCS.
Conclusions: US has comparable sensitivity and specificity to NCS in patients two or more standard deviations above or below the mean age for presentation of CTS. US may be more accurate in younger patients, although NCS limits the number of false positive tests. There remains a substantial amount of inaccuracy for both tests when using a validated clinical diagnostic tool (CTS-6) as the reference standard.
Type of study/level of Evidence: Diagnostic IV.

Carpal tunnel syndrome (CTS) is the most common compression neuropathy with a prevalence of around 5% of the general population.[1] The median age of patients with carpal tunnel syndrome is 55 years (standard deviation [SD] =13.5 years) of age; typically, the diagnosis is made based on history and clinical examination.[2–4] Some have suggested that diagnostic testing does not add value and does not improve outcomes over clinical diagnosis alone.[4,5] However, in patients presenting outside the typical age range or with a less clear history and exam, additional testing may prove valuable.

An important question in all studies examining the diagnostic accuracy of confirmatory testing is the reference standard. Prior studies have utilized the 6-item CTS symptoms scale (CTS-6) diagnostic tool as the reference standard as it is a validated diagnostic tool.[5] It is composed of two history components (numbness in median nerve distribution and nocturnal numbness) and four physical exam components (thenar atrophy and/or weakness, positive Phalen test, loss of two-point discrimination, and positive Tinel sign) that each are attributed a point value with the maximum

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Table 1
Summary of Groups

Clinical and Patient-Reported Measurements	All	Young N = 23	Middle N = 248	Old N = 24	*P* Value
Median Nerve (mm^2)	10.3	8.44 (SD 3.02)	10.38 (SD 3.02)	11.83 (SD 3.7)	<.05*
CTS-6	12.8	10.61 (SD 6.31)	12.87 (SD 6.31)	13.85 (SD 7.09)	.48
Distal Motor Latency (ms)	4.76	3.63 (SD 0.95)	4.74 (SD 1.75)	6.63 (SD 2.38)	<.05†
CMAP (mV)	10.8	16.8 (SD 19.2)	10.19 (SD 3.9)	7.41 (SD 9.44)	<.05*
Distal Sensory Latency (ms)	3.44	2.68 (SD 1.74)	4.58 (SD 2.65)	6.73 (SD 3.2)	<.05†
SNAP (uV)	34.2	72.1 (SD 55.5)	25.6 (SD 28.1)	10.4 (SD 13.9)	<.05†
BCTQ SSS	2.79	2.49 (SD 0.84)	2.85 (SD 0.01)	2.47 (SD 0.65)	<.05‡
BCTQ FSS	2.18	1.87 (SD 0.74)	2.19 (SD 0.84)	2.39 (SD 0.95)	0.12

BCTQ, Boston Carpal Tunnel Syndrome Questionnaire.
* Significant difference between middle versus young and young versus old.
† Significant difference between middle versus young, young versus old, and middle versus old.
‡ Significant difference between middle versus young and middle versus old.

score of 26.[4,5] Wang et al[6] reported that a score of 12 has a sensitivity of 75% and specificity of 59%, whereas a score of 18 or greater has a sensitivity of 31% and specificity of 99%. Similar to a previous study by the senior author that compared the diagnostic accuracy of nerve conduction studies (NCS) and ultrasound (US), the current study used the CTS-6 set at a specific cutoff score to represent a positive reference standard for NCS and US measurements to be measured against in the two cohorts.[7]

The purpose of this study is to determine the diagnostic accuracy of NCS and US in patients two or more SDs above or below the mean age of carpal tunnel syndrome presentation using the CTS-6 as a reference standard. The null hypothesis is that there is no difference in diagnostic accuracy between the two tests.

Materials and Methods

Patients that presented to a hand surgery clinic with complaints of hand numbness were retrospectively reviewed through an institutional review board-approved database maintained by the senior author. Patients with a diagnosis other than carpal tunnel syndrome were specifically included in this database to allow determination of sensitivity and specificity of the diagnostic testing; the only inclusion criterion for the database was hand numbness at presentation. Patients underwent a history and physical examination and completion of the CTS-6 diagnostic evaluation. Subjects were separated into three groups based on the median age of carpal tunnel syndrome patients (55 years of age) and two SDs (SD = 13.5 years) above and below the median. The young group was 28 years of age or less, the middle group was 29–71 years of age, and the old group was 72 years of age or greater.

US of the median nerve was then performed as it has been described in previous studies.[8–12] Briefly, the patient was instructed to sit comfortably with the elbow flexed at 90° with the forearm in supination and fingers in a normal resting cascade. Using a 15-6 MHz linear array transducer, the median nerve cross-sectional area (CSA) was then measured inside the hyperechoic epineurium using the trace function at the level of the pisiform. All US examinations were performed by a fellowship trained hand surgeon. An a priori cutoff of 10 mm^2 or greater is considered positive in our practice.

All patients who previously had an US of the median nerve were subsequently referred for NCS as part of the senior author's routine preoperative, diagnostic work-up. Any patient that did not have an electrodiagnostic study performed was excluded from this study. Electrodiagnostic studies were performed by a certified electrodiagnostic medicine physician in accordance with the guidelines of the American Association of Neuromuscular and Electrodiagnostic Medicine. In general, a distal sensory latency greater than or equal to 3.2 ms or distal motor latency greater than or equal to 4.2 ms were considered to be diagnostic of CTS; however, the interpretation of the test by the electrodiagnostic physician was used as the diagnosis. For statistical analysis, a value of "no response" was replaced with a value of 10 ms for distal motor latency and/or distal sensory latency. Patients also completed the Boston Carpal Tunnel Syndrome Questionnaire with the Symptom Severity Scale and Functional Status Scale.

Using CTS-6 as the reference standard with a cutoff score of 12 indicating likely CTS, true positive, true negative, false negative, and false positive results were recorded for each test for each patient. CTS-6 was considered "positive" if it was $\geq$ 12.[4,5,7] The sensitivity and specificity of electrodiagnostic testing and US were then calculated using CTS-6 as the reference standard for carpal tunnel syndrome. The accuracy of US and NCS were defined as the rate of their respective agreement with the reference standard (CTS-6).

Statistical comparisons of the median nerve CSA, CTS-6 with score of 12 as a threshold, distal motor latency (DML), distal sensory latency (DSL), functional severity score (FSS), and symptom severity score (SSS) were performed across young, middle, and old groups using a Kruskal–Wallis analysis of variance given nonparametric data.[6] Tukey's test was used for multiple comparisons.

Results

A total of 295 hands were included in the analysis with 23 hands in the young group and 24 hands in the old group. Table 1 presents a summary of the mean and SD for US CSA, DML, DSL, compound motor action potential (CMAP), sensory nerve action potential (SNAP), SSS, FSS, and CTS-6 results for the three groups. There was a statistically significant difference in median nerve CSA, DML, DSL, CMAP, and SNAP between the young and old groups. In general, CSA, DML and DSL increased with increasing age, and CMAP and SNAP decreased with increasing age. The Boston Carpal Tunnel Questionnaire SSS and FSS were less affected by increasing age.

Tables 2 and 3 present a summary of the diagnostic accuracy of US and NCS, respectively. The overall prevalence of CTS among the patients included in this study was determined to be 65%. NCS showed 31% sensitivity and 100% specificity in the patients in the young group compared to 54% sensitivity and 90% specificity for US. NCS showed a 94% sensitivity and 25% specificity in the old group compared to 81% sensitivity and 38% specificity for US. Overall accuracy for US and NCS was 66% for both tests when looking at all ages. The accuracy in the young group was 70% for US and 61% for NCS, whereas the accuracy in the old group was 67% for US and 71% for NCS (Figs. 1 and 2).

Table 2
Sensitivity and Specificity of Ultrasound

Statistical Measure	All (95% CI)	Young (95% CI)	Middle (95% CI)	Old (95% CI)
Sensitivity	72.2% (65.2% to 78.5%)	53.9% (25.1% to 80.8%)	72.8% (65.1% to 79.6%)	81.3% (54.4% to 95.9%)
Specificity	56.5% (46.6% to 66%)	90% (55.5% to 99.8%)	54.4% (43.6% to 65%)	37.5% (8.5% to 75.5%)
Positive Predictive Value	74.2% (69.5% to 78.4%)	87.5% (50.5% to 97.9%)	73.7% (68.7% to 78.2%)	72.2% (59.1% to 82.4%)
Negative Predictive Value	54% (46.9% to 60.9%)	60% (44.6% to 73.7%)	53.3% (45.3% to 61.0%)	50% (20.5% to 79.5%)
Accuracy	66.4% (60.7% to 71.8%)	69.6% (47.1% to 86.8%)	66.1% (59.9% to 72%)	66.7% (44.7% to 84.3%)

CI, confidence interval.

Table 3
Sensitivity and Specificity of Electrodiagnostic Testing

Statistical Measure	All (95% CI)	Young (95% CI)	Middle (95% CI)	Old (95% CI)
Sensitivity	74.3% (67.5% to 80.4%)	30.8% (9.1% to 61.4%)	76% (68.5% to 82.4%)	93.8% (69.8% to 99.8%)
Specificity	50.9% (41.1% to 60.7%)	100% (69.1% to 100%)	47.8% (37.1% to 58.6%)	25% (3.2% to 65.1%)
Positive Predictive Value	72.4% (68% to 76.4%)	100% (39.8% to 100%)	71.9% (67.3% to 76%)	71.4% (62.2% to 79.2%)
Negative Predictive Value	53.4% (45.8% to 60.9%)	52.6% (43.6% to 61.5%)	53.1% (44.33% to 61.7%)	66.7% (17.5% to 95%)
Accuracy	65.8% (60% to 71.2%)	60.9% (38.5% to 80.3%)	65.7% (59.5% to 71.6%)	70.8% (48.9% to 87.4%)

CI, confidence interval.

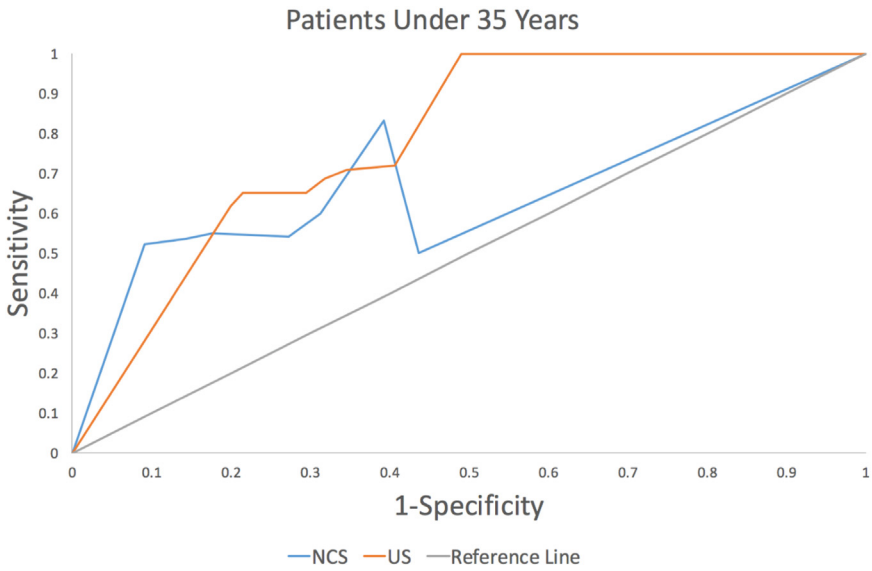

Figure 1. Receiver operating characteristic curve for US and NCS in the patient group under 35 years old.

Discussion

The main finding of this study is that US is a more specific test in nearly all situations but does have a higher rate of false positives, particularly in the young age group. In this study, we retrospectively reviewed young (< 28 years of age) and elderly (> 72 years of age) patients that are two SDs outside the mean age for carpal tunnel syndrome presentation and specifically examined the accuracy of the diagnostic testing that was performed after obtaining an initial history and physical examination. These patients often present a diagnostic challenge as some will have classic symptoms with normal diagnostic tests, whereas other have minimal symptoms with grossly abnormal diagnostic tests. The hallmark of a quality confirmatory test is its specificity for a given condition. The specificity of US was greater than that of NCS in all scenarios except the old age group.

The CTS-6 tool developed by Graham converts qualitative attributes from the physical exam and subjective information from the patient's history into a quantitative value that can be used to determine the likelihood a patient has carpal tunnel syndrome.[3,4] Graham et al[4] noted that a CTS-6 score of 12 resulted in an approximately 80% chance of having carpal tunnel syndrome based on Bayesian statistics. Previous studies from our institution determined that a score of 12 has a sensitivity of 75% and specificity of 59%.[7] The reference standard is of the utmost importance when attempting to determine the sensitivity and specificity of a diagnostic test. There is no agreed upon reference standard for diagnosis of carpal tunnel syndrome; however, CTS-6 has been used in numerous previous studies and is a validated diagnostic tool. Of note, it has not been specifically studied as related to variations in different age groups, which may be appropriate for future study.

The clinical impetus for this study was that the senior author noticed many patients presenting to the hand surgery clinic with diagnostic testing that did not correlate with their history and physical examination. For example, many young patients would present with clinical evidence of carpal tunnel syndrome and have normal diagnostic testing. Many older patients would present with minimal signs and symptoms of carpal tunnel syndrome yet have

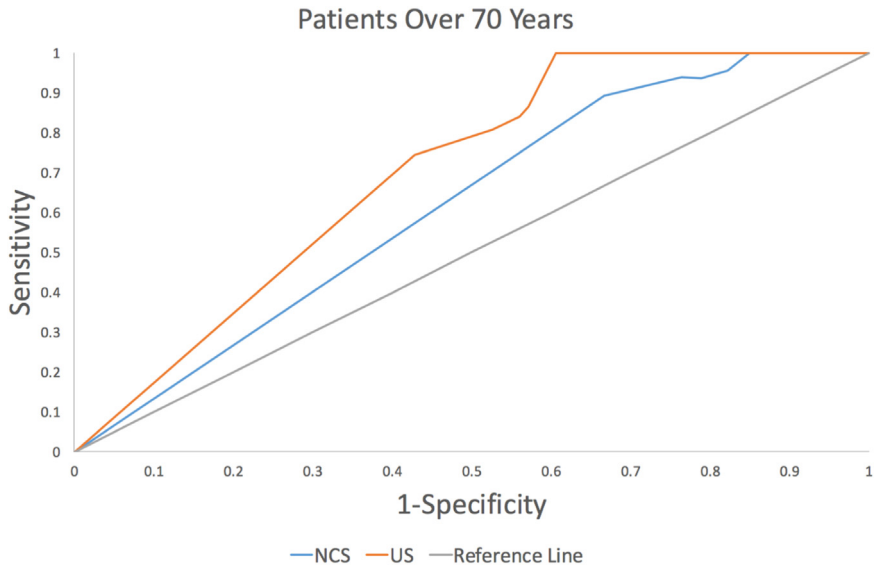

Figure 2. Receiver operating characteristic curve for US and NCS in the patient group over 70 years old.

severe findings on diagnostic tests. Büttner et al[13] demonstrated that inflammation and aging decreases Schwann cell regeneration and leads to a decrease in myelin production. It is possible that this explains why the DML and DSL are delayed in the elderly cohort compared to the younger and middle cohorts. Distal motor and sensory latency are essentially measures of nerve myelination.[14] Therefore, in younger patients, one could reason that they are too early in the disease process to manifest meaningful demyelination, and NCS would not be as sensitive in this group. It also explains the 100% specificity of NCS in the young group as the presence of demyelination in a younger patient may signify more severe compression of the median nerve rather than it being a part of the normal aging process in the elderly.

Studies examining electrodiagnostic and sonographic differences between elderly patients and younger patients have demonstrated that median nerve CSA is a less sensitive diagnostic tool in the elderly population compared to NCS. For example, Mulroy and Pelosi[15] demonstrated that the false negative rate of US in patients aged 80–95 years old is as high as 40%. Studies by Miwa et al[16] and Moschovos et al[17] similarly found that with increasing age there is increasing severity of CTS based on NCS, but the median nerve CSA either decreased in size or was not significantly different compared to patients 65 years old or younger. The current study demonstrated that the median nerve CSA in the elderly cohort was significantly larger than the middle and young cohorts. Additionally, the sensitivity of US in this age group was higher than in the young and middle age groups, which is directly related to the number of false negatives (as the number of false negatives increases, the sensitivity decreases). The lack of increasing median nerve CSA as severity increases may be due to atrophy and fibrosis of the nerve.[17] Measures such as the wrist:forearm ratio may be beneficial in these scenarios rather than using an absolute value.[18,19]

This study has several limitations. First, this is a retrospective study and subject to the bias of missing data and inclusion bias. Second, these patients were evaluated by hand surgeons for numbness in the hands. The findings in this group of patients may not be generalizable to the general population with no numbness in the hands. Third, we selected clinically utilized but likely imperfect cutoff values for NCS and US. Utilizing different cutoff values could have resulted in different diagnostic accuracy; however, we attempted to use clinically relevant values. Fourth, the CTS-6 diagnostic tool was used as a reference standard; however, this questionnaire has not been explicitly validated in the age groups of interest. Lastly, the number of young and old patients was relatively small, which could decrease the power, accuracy, and reproducibility of the study.

Disclaimer

Given his role as Editor-in-Chief of *The Journal of Hand Surgery Global Online*, Dr. Fowler had no involvement in the peer review of this article and had no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Aviram M. Giladi, MD, MS.

Conflicts of Interest

No benefits in any form have been received or will be received related directly to this article.

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