EDITOR'S CHOICE

A Prospective Comparison of Diagnostic Tools for the Diagnosis of Carpal Tunnel Syndrome

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Purpose Nerve conduction studies (NCS), CTS-6, Wainner, Kamath, and Lo are diagnostic tests that are used to diagnose carpal tunnel syndrome (CTS). To our knowledge, no study has compared the sensitivity and specificity of these 5 tests with one another. The purpose of this study is to compare NCS, CTS-6, Wainner, Kamath, and Lo using clinical diagnosis by a hand fellowship–trained orthopedic surgeon as reference standard.

Methods A hand fellowship–trained surgeon completed the CTS-6, Wainner, Kamath, and Lo diagnostic tools. Cutoff values for a positive test were based on values in the literature, if available. The NCS were performed by a certified electrodiagnostic physician according the standards of the American Association of Neuromuscular and Electrodiagnostic Medicine and were interpreted using absolute latencies, relative latencies, and combined sensory index. Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio were calculated for the tests using clinical diagnosis as the reference standard.

Results A total of 408 wrists from 250 patients were analyzed in the study. The NCS had the highest sensitivity (94%) but also the lowest specificity (50%) of any of the diagnostic tests. Using a cutoff of 18, CTS-6 had the highest specificity (99%). The NCS had the highest area under the curve at 74%, followed closely by the Kamath at 69%.

Conclusions The NCS were traditionally felt to be a strong confirmatory test given their high specificity. However, this prospective series demonstrated that NCS had the lowest specificity of any diagnostic test.

Clinical relevance Consideration should be given to using alternative diagnostic tests/tools based on the results of this study. *(J Hand Surg Am. 2018;43(9):833–836. Copyright © 2018 by the American Society for Surgery of the Hand. All rights reserved.)*

Key words Carpal tunnel syndrome, CTS-6, Kamath, Lo, Wainner.

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CARPAL TUNNEL SYNDROME (CTS) is a common musculoskeletal disorder, with an estimated prevalence of 6% in men and 9.2% in women.[1] The diagnosis of CTS is generally made through clinical history and physical examination findings. Symptoms include nocturnal paresthesias, numbness, tingling, and pain in the median nerve distribution, decreased grip strength, and thenar muscle atrophy. Although the diagnosis of CTS can be made on history and clinical findings, confirmation of CTS is commonly performed using nerve

conduction studies (NCS) to assess for median neuropathy.[2,3] The American Academy of Orthopaedic Surgeons Clinical Practice Guidelines indicate that NCS and clinical evaluation using the CTS-6 diagnostic tool and/or Katz Hand diagrams are interchangeable.[4]

The CTS-6, Wainner, Kamath, and Lo are diagnostic tools that use common physical examination and history findings to estimate the probability of CTS (Appendix A; available on the *Journal*'s Web site at www.jhandsurg.org). Individually, these tools have been shown to have potential to reasonably estimate the probability of CTS.[5–7] There have been limited follow-up studies in the literature to test the reliability of these diagnostic questionnaires.[8–11] Furthermore, there have been no studies in the literature that have directly compared these tools with one another. The purpose of this study is to compare the accuracy of the CTS-6, Wainner, Kamath, and Lo clinical diagnostic questionnaires in diagnosing CTS with clinical diagnosis by a hand fellowship–trained orthopedic surgeon (R.J.G. or J.R.F.) as reference standard.

METHODS

After institutional board review, patients were identified and recruited through an orthopedic hand surgery clinic. We enrolled patients who presented to our hospital orthopedic surgery clinic from October 2014 through March 2017. Our inclusion criteria included patients who returned to the office after being previously referred for electrodiagnostic testing for the assessment of CTS. Our exclusion criteria were patients younger than 18 years of age and the inability to comprehend English or give consent.

The sample size calculation was based on the following assumptions: 2-sided α of 0.05 and β of 0.20 (power of 80%), a predicted sensitivity and specificity of diagnostic tests ranging from 75% to 85%, and a difference in specificity and sensitivity of 20% being considered a clinically important difference. Tables from the study by Bujang and Adnan,[12] a study specifically examining power analyses for diagnostic tests, were utilized and a prevalence of CTS set at 10%. Based on these assumptions, 310 wrists were required with at least 31 having CTS.

A hand fellowship–trained surgeon (R.J.G. or J.R.F.) completed the CTS-6, Wainner, Kamath, and Lo diagnostic tools. The diagnostic questionnaires were completed with the patient during scheduled clinic visits by the treating surgeon. In general, absolute motor and/or sensory latencies, relative sensory latencies, and the combined sensory index were used to make the diagnosis of CTS using NCS.[13]

Stepwise cutoffs for a positive test were used for the diagnostic tests without a specified cutoff value (Lo, Wainner, CTS-6). Lo was tested at a cutoff value of 10 and 20; CTS-6 tested at 12, 14, 16, and 18; and Wainner tested at 3 and 4. The Kamath has a suggested threshold of 5 or more to replace NCS as a screening tool.[14] Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each test using clinical diagnosis by a hand fellowship–trained orthopedic surgeon (R.J.G. or J.R.F.) as the reference standard.

RESULTS

A cohort consisting of 408 consecutive wrists from 250 patients consented to the study, of which 69 were men and 181 women The sample consisted of 219 right wrists and 189 left wrists. The age range was 18 to 90 years, with a mean of 52 years (SD, 14). Diagnosis of CTS was made in 255 wrists (63%).

The NCS had the highest sensitivity (94%) and highest NPV (87%), but also the lowest specificity (50%) of any of the diagnostic tests (Table 1). Using a cutoff of 18, CTS-6 had the highest specificity (99%) and highest PPV (96%). The NCS (74%) had the highest area under the curve (AUC) (Table 2), followed closely by the Kamath (69%).

DISCUSSION

This study has found that commonly used diagnostic tests perform better than NCS when clinical diagnosis is used as the reference standard. The NCS had the lowest specificity of any of the diagnostic tools/tests, meaning it had the most false positives of the diagnostic tools/tests evaluated. This finding is in agreement with a growing body of literature, which has found a high rate of false-positive results for NCS.[15,16] Proponents of NCS will diagnose these patients with "asymptomatic carpal tunnel syndrome." However, a syndrome is, by definition, a constellation of signs and symptoms. If the patient does not have the signs and symptoms, then by definition, the patient does not have the syndrome in question.

The CTS-6 diagnostic tool, using a cutoff of 18, had a specificity of 99% and PPV of 96%. This makes sense because CTS-6 was originally designed to offer a probability of having a diagnosis of CTS. As the CTS-6 score increases, the probability of having a diagnosis of CTS increases. Based on the

TABLE 1. Comparison of Diagnostic Tools

Test	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)
Lo (cutoff, 10)	66 (59–71)	56 (47–65)	78 (72–83)	40 (33–48)
Lo (cutoff, 20)	22 (17–27)	94 (88–97)	90 (80–95)	33 (28–39)
CTS-6 (cutoff, 12)	75 (70–80)	59 (49–68)	82 (76–86)	50 (41–58)
CTS-6 (cutoff, 14)	56 (50–62)	59 (49–68)	77 (70–82)	36 (29–43)
CTS-6 (cutoff, 16)	56 (50–62)	71 (62–79)	83 (76–88)	40 (33–47)
CTS-6 (cutoff, 18)	31 (24–39)	99 (86–99)	96 (86–99)	67 (62–72)
NCS	97 (94–98)	50 (41–60)	83 (78–86)	87 (76–93)
Kamath (cutoff, 5)	74 (68–79)	64 (54–72)	83 (78–87)	50 (42–58)
Wainner (cutoff, 3)	70 (64–75)	64 (54–72)	82 (77–87)	47 (39–55)
Wainner (cutoff, 4)	22 (18–28)	91 (85–95)	86 (76–93)	33 (28–38)

95% CI, 95% confidence interval.

TABLE 2. Area Under the Curve

Diagnostic Tool	Area Under the Curve (%)
Lo (cutoff, 10)	61
Lo (cutoff, 20)	58
CTS-6 (cutoff, 12)	67
CTS-6 (cutoff, 14)	58
CTS-6 (cutoff, 16)	64
CTS-6 (cutoff, 18)	65
NCS	74
Kamath (cutoff, 5)	69
Wainner (cutoff, 3)	67
Wainner (cutoff. 4)	57

results of this study, the CTS-6 diagnostic tool is the strongest confirmatory test.

Confirmatory tests should have a high specificity to decrease the likelihood of a false positive. Screening tests should have a high sensitivity to decrease the likelihood of a false negative. The NCS has historically been regarded as a strong confirmatory test owing to the high specificity found in multiple studies.[3,13] Despite NCS being the most commonly used confirmatory test for CTS, it had the lowest specificity of all the tests/tools evaluated in this study. This should call into question the routine use of NCS as a confirmatory test.

The NCS were found to have the highest sensitivity, which is curious given that many physicians would agree that NCS should not be utilized as a "screening test." The reasons for the high sensitivity are unclear. It could be the high prevalence population used in this study (63% of patients in this study carried a clinical diagnosis of CTS. It could also be the use of relative sensory latencies and the combined sensory index (CSI). The CSI combines the median-ulnar ring finger antidromic latency difference at 14 cm, median-radial thumb antidromic latency difference at 10 cm, and median-ulnar midpalmar orthodromic latency difference at 8 cm. If this sum is greater than 1.0, then it is considered positive.[17] The CSI likely identifies many "borderline" cases of CTS that may not be clinically relevant.

The NCS (74%) had the highest AUC, but nearly all of the diagnostic tests were within 10% of NCS. The high AUC for NCS is likely related to its high sensitivity in this study.

There are several limitations to this study. The most important limitation is the high prevalence sample used in this study that will artificially elevate the sensitivity and specificity of diagnostic tests/tools. This is always an issue in studies performed by hand specialists and high-volume centers. However, as health care becomes more specialized, the high-volume and high-prevalence centers will be the ones performing these diagnostic tests. It is possible that the results of this study would be different if performed in the general population with a lower prevalence of CTS. However, Atroshi et al[16] found a similar high rate of false-positive NCS in a general population. A second limitation is using clinical diagnosis as the reference standard. It is often difficult to standardize the criteria used for a clinical diagnosis of CTS; however, this is a pragmatic approach. Physicians must make clinical diagnoses based on signs and symptoms on a daily basis and there is

always the potential that one physician uses a slightly different set of criteria than another physician. This could affect the sensitivity and specificity of the diagnostic tests.

Carpal tunnel syndrome is a common diagnosis that results in significant cost to the health care system through diagnostic testing and lost time from work. By using clinical diagnostic tools such as the CTS-6, it would be possible to decrease health care costs by decreasing the utilization of NCS in the majority of cases. It is also possible that the use of NCS results in a higher rate of false-positive tests than the other diagnostic tools, thereby leading to increased rates of treatment, including carpal tunnel release, which would increase costs further.

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APPENDIX A. Kamath Questionnaire

Has the pain in the wrist woken you up at night?
Yes 1 No 0
Has tingling and numbness in your hand woken you at night?
Yes 1 No 0
Has tingling and numbness in your hand been more pronounced first thing in the morning?
Yes 1 No 0
Do you have any trick movements to make the tingling, numbness, go from your hand?
Yes 1 No 0
Do you have tingling and numbness in your little finger at any time?
Yes 0 No 3
Has tingling and numbness presented when you were reading a newspaper, steering a car, or knitting?
Yes 1 No 0
Do you have any neck pain?
Yes - No 0
If applicable, has the tingling and numbness in your hand been severe during pregnancy?
Yes 1 No -1 N/A (0)
Has it helped the tingling and numbness on wearing a splint on your wrist?
Yes 2 No 0 N/A
Total score _____

Lo Carpal Tunnel Questionnaire

Gender
Male (0) Female (−5)
Duration
< 2 months (0) 2−12 months (7) > 12 months (11)
Nocturnal symptoms Neck Pain
Yes (6) No (0) Yes (−6) No (0)
Wrist Pain
Yes (−5) No (0)
Median nerve distribution sensory symptoms
Yes (7) No (0)
Abductor pollicis brevis weakness Thenar Atrophy
Yes (7) No (0) Yes (7) No (0)
2-point discrimination
Normal (0) Abnormal in median nerve distribution (10)
Abnormal only thumb/index (2) Abnormal fingers 2−4 (1)
Can't feel anywhere (−11) Abnormal in ulnar nerve distribution (−1)
Total score _____

Wainner Clinical Prediction Rule

1. Do your symptoms improve with moving, "shaking," or positioning your wrist or hands?
Yes No
2. Patient age _____ (Positive if > 45 y)
3. 2-pt discrimination thumb _____ (Positive if ≥ 6 mm)
2-pt index _____ 2-pt middle _____ (not part of rule, just for info)
4. Calculate the patient's wrist-ratio index by measuring the AP and mediolateral wrist width in centimeters. Divide the AP wrist width by the ML wrist width.
AP _____ cm ML _____ cm Ratio _____ (Positive if > 0.67)
5. Boston Symptom Severity Scale Result _____ (Positive if > 1.9)
(See Boston SSS Form)

Boston Carpal Tunnel Questionnaire

Symptom Severity Section (SSS)

The following questions refer to your symptoms for a typical 24-hour period during the past 2 weeks (circle 1 answer to each question).

How severe is the hand or wrist pain that you have at night?
1. I do not have hand or wrist pain at night.
2. Mild pain
3. Moderate pain
4. Severe pain
5. Very severe pain

How often did hand or wrist pain wake you up during a typical night in the past 2 weeks?
1. Never
2. Once
3. Two or 3 times
4. Four or 5 times
5. More than 5 times

Do you typically have pain in your hand or wrist during the daytime?
1. I never have pain during the day.
2. I have mild pain during the day.
3. I have moderate pain during the day.
4. I have severe pain during the day.
5. I have very severe pain during the day.

How often do you have hand or wrist pain during the daytime?
1. Never
2. Once or twice a day
3. Three to 5 times a day
4. More than 5 times a day
5. The pain is constant.

How long, on average, does an episode of pain last during the daytime?
1. I never get pain during the day.
2. Less than 10 minutes
3. Ten to 60 minutes
4. Greater than 60 minutes
5. The pain is constant throughout the day.

Do you have numbness (loss of sensation) in your hand?
1. No
2. 1 have mild numbness.
3. I have moderate numbness.
4. I have severe numbness.
5. I have very severe numbness.

Do you have weakness in your hand or wrist?
1. No weakness
2. Mild weakness
3. Moderate weakness
4. Severe weakness
5. Very severe weakness

Do you have tingling sensations in your hand?
1. No tingling
2. Mild tingling
3. Moderate tingling
4. Severe tingling
5. Very severe tingling

How severe is numbness (loss of sensation) or tingling at night?
1. I have no numbness or tingling at night.
2. Mild
3. Moderate
4. Severe
5. Very severe

How often did hand numbness or tingling wake you up during a typical night during the past 2 weeks?
1. Never
2. Once
3. Two or 3 times
4. Four or 5 times
5. More than 5 times

Do you have difficulty with the grasping and use of small objects such as keys or pens?
1. No difficulty
2. Mild difficulty
3. Moderate difficulty
4. Severe difficulty
5. Very severe difficulty

Total Score _____ Total Score/ 11 =_____

CTS-6

Numbness predominantly or exclusively in median nerve distribution 3.5
Nocturnal numbness 4.0
Thenar atrophy and/or weakness 5.0
Positive Phalen test 5.0
Loss of 2-pt discrimination 4.5
Positive Tinel sign 4.0
Total Score _____