A Comparison of 6 Diagnostic Tests for Carpal Tunnel Syndrome Using Latent Class Analysis

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Abstract

Background: Nerve conduction studies (NCS), ultrasonography (US), Carpal Tunnel Syndrome 6 (CTS-6), Wainner, Lo, and Kamath are clinical diagnostic tools that can be used to diagnose carpal tunnel syndrome (CTS). Latent class analysis (LCA) is a proven statistical technique that can be used to evaluate diagnostic tests in a lack of a reference standard. Given that there is no accepted reference standard, we elected to perform an LCA to evaluate the 6 clinical diagnostic tests. **Methods:** One hundred eighty-seven wrists were prospectively evaluated by a board-certified hand surgeon using US, the CTS-6, Wainner, Lo, and Kamath. The NCS were performed by an electrophysiologist according to the standards of the American Association of Neuromuscular & Electrodiagnostic Medicine. The LCA was performed to evaluate individual performance and pairwise combinations of the tests. **Results:** The NCS demonstrated the highest estimated sensitivity of 97%, and the Wainner had the highest estimated specificity of 97%. Alternatively, the Lo had the lowest estimated sensitivity (36%), and NCS had the lowest estimated specificity (40%). When evaluating pairwise combinations, positive US and NCS demonstrated the highest overall sensitivity at 86%, and negative US and NCS had a specificity of 83%. **Conclusions:** There is no perfect clinical diagnostic test, with the 6 clinical diagnostic tests having differing sensitivities and specificities. Pairwise combinations of the test can be used to complement one another.

Keywords: carpal tunnel syndrome, CTS-6, latent class analysis, ultrasonography, Wainner, Kamath, Lo

Introduction

Carpal tunnel syndrome (CTS) is a common musculoskeletal disorder with an estimated prevalence of 6% in men and 9.2% in women.¹ It is diagnosed clinically through history and physical examination and is often confirmed with nerve conduction studies (NCS). However, given a reported false-negative rate of 16% to 34% in some series, NCS cannot be considered as a reference standard for diagnosis of CTS.² Furthermore, Glowacki et al³ and Graham⁴ have independently demonstrated that NCS do not provide additional information, nor change clinical outcomes after carpal tunnel release to an extent that is clinically relevant.

Several tests have been compared with NCS for the diagnosis of CTS. Fowler et al⁵ found ultrasonography (US) to have similar sensitivity and specificity as NCS when clinical diagnosis was used as the reference standard. Wang et al⁶ compared 5 clinical diagnostic tests (Carpal Tunnel Syndrome 6 [CTS-6], Wainner, Kamath, Lo, and NCS) and demonstrated CTS-6 to be the superior confirmatory test given its higher specificity. Ultimately, direct comparison of NCS with other clinical tests has been challenging due to lack of a universally accepted reference standard.

In cases where there is not an accepted reference standard, latent class analysis (LCA) is a useful statistical technique that identifies associations between tests to estimate the probability of the disease. Fowler et al⁷ performed LCA to evaluate 3 diagnostic tests for CTS: NCS, US, and CTS-6. The study demonstrated that US and CTS-6 had similar sensitivity and specificity compared with NCS, and that NCS studies had the lowest sensitivity and specificity among the 3 tests. The LCA examines the relationships between tests, and the more tests included, the more accurate the analysis. The purpose of this study is to expand on that analysis and to conduct an LCA using 6 diagnostic studies: NCS, US, CTS-6, Wainner, Kamath, and Lo.

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Table 1. Individual Test Scores Using Latent Class Analysis.

Diagnostic Test	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Kamath	77 (66-89)	72 (57-85)
Wainner	35 (25-48)	97 (90-100)
Lo	36 (26-51)	94 (86-99)
Carpal Tunnel Syndrome 6	75 (65-84)	61 (46-76)
Nerve conduction studies	97 (92-100)	40 (26-58)
Ultrasonography	89 (80-97)	72 (52-91)

Note. CI = confidence interval.

Materials and Methods

After institutional review board approval, a sample of 187 wrists were included in the study. Inclusion criteria for the study were patients who presented to the clinic who were previously referred to obtain NCS for suspected CTS. Participants were enrolled between October 2014 and March 2017. A complete electrodiagnostic examination was performed according to the standards of the American Association of Neuromuscular & Electrodiagnostic Medicine by a certified physician. Absolute motor and/or sensory latencies, relative sensory latencies, and the combined sensory index were used to make the diagnosis of CTS.⁸ The interpretation of the certified electrodiagnostician was used for the determination of a positive or negative test.

At the time of the clinic visit, a board-certified, hand fellowship-trained surgeon, who was blinded to the results of the NCS, completed the CTS-6, Wainner, Kamath, and Lo clinical diagnostic questionnaires as well as an US evaluation of the cross-sectional area of the median nerve at the level of the carpal tunnel inlet using a 15-6 MHz linear transducer (Sonosite X-porte, Bothell, Washington). The cross-sectional area of the median nerve was measured using the “trace function.” These 5 diagnostic tests were all performed by the treating surgeon. Exclusion criteria for the study were patients who were younger than 18 years old, who had an inability to consent to the study, and who were unable to complete all 6 diagnostic tests.

The LCA was carried out through Bayesian methods in WinBUGS (<http://www.mrc-bsu.cam.ac.uk/software/bugs>).⁹ Our latent class models assume a fixed number of disease states, with the simplest being binary: positive or negative. The disease states are parameterized based on the probabilities of true positives (sensitivity) and true negatives (specificity). In the absence of a reference standard, simplified assumptions were made to make parameter estimation for disease states.^{10,11} Flat priors were used for all model parameters, meaning all parameter values were assumed to be equally likely and to be uniformly distributed between 0 and 1. Sensitivity and specificity estimates were performed

Table 2. Pairwise Combinations of the 6 Diagnostic Tests.

Diagnostic Test	Estimated sensitivity, %		Estimated specificity, %	
	AND	OR	AND	OR
Kamath/Wainner	27.2 (5.8)	85.1 (4.4)	99.0 (0.9)	69.0 (7.3)
Kamath/Lo	28.4 (6.0)	85.5 (4.3)	98.2 (1.1)	66.8 (7.0)
Kamath/CTS-6	58.1 (6.2)	94.3 (2.0)	88.6 (4.0)	43.5 (7.8)
Kamath/NCS	75.0 (5.9)	99.3 (0.5)	82.8 (5.5)	29.1 (7.5)
Kamath/US	68.9 (6.7)	97.5 (1.3)	91.7 (4.1)	51.3 (9.7)
Wainner/Lo	13.0 (3.9)	58.7 (6.5)	99.8 (0.3)	90.5 (4.4)
Wainner/CTS-6	26.4 (5.2)	83.7 (3.7)	98.6 (1.2)	58.8 (7.9)
Wainner/NCS	34.0 (5.9)	98.1 (1.3)	98.0 (1.7)	39.2 (8.3)
Wainner/US	31.3 (5.8)	93.0 (3.0)	99.0 (0.9)	69.2 (9.8)
Lo/CTS-6	27.5 (5.3)	84.1 (3.7)	97.5 (1.5)	56.9 (7.6)
Lo/NCS	35.5 (6.1)	98.1 (1.3)	96.2 (2.0)	37.9 (7.9)
Lo/US	32.7 (6.0)	93.0 (3.0)	98.2 (1.1)	67.0 (9.3)
CTS-6/NCS	72.8 (4.8)	99.3 (0.5)	76.5 (6.5)	24.8 (6.8)
CTS-6/US	66.9 (5.4)	97.3 (1.3)	88.6 (5.2)	43.8 (9.3)
NCS/US	86.4 (5.0)	99.7 (0.3)	82.6 (7.6)	29.5 (9.1)

Note. CTS-6 = Carpal Tunnel Syndrome 6; NCS = nerve conduction studies; US = ultrasonography.

of pairwise “and/or” combinations of the 6 clinical diagnostic tests.

Results

Individually, NCS demonstrated the highest estimated sensitivity of 97% and the Wainner had the highest estimated specificity of 97%. Alternatively, the Lo had the lowest estimated sensitivity (36%) and NCS had the lowest estimated specificity (40%). See Table 1 for individual test sensitivities and specificities.

When comparing the 15 pairwise combinations among the 6 clinical diagnostic tests, positive US and NCS demonstrated the highest overall sensitivity at 86%, and negative US and NCS had a specificity of 83%. Similarly, when Wainner or US is positive, sensitivity and specificity are estimated to be 93.0% and 69.2%, respectively. See Table 2 for pairwise combination of tests and their estimated sensitivity and specificity.

Discussion

Comparison of diagnostic studies for CTS is challenging as there is no accepted reference standard for diagnosis. Although most cases of CTS may be diagnosed through history and physical examination, there is lack of standardization among surgeons in their evaluation and clinical impression.¹² The use of NCS as a reference standard has its own inherent limitations given the rate of false negatives and false positives.² The LCA is a statistical method used to

compare diagnostic tests in the absence of an accepted reference standard.

The use of LCA has been previously used in orthopedic research studies and is an accepted statistical method. Fowler et al⁷ evaluated the accuracy of US, CTS-6, and NCS for diagnosis of CTS. Duckworth et al¹³ used LCA for testing 4 physical examination findings for the diagnosis of scaphoid fractures. Buijze et al¹⁴ used LCA to evaluate the accuracy of specific radiographic parameters in diagnosing scaphoid fractures.

If we assume there is no accepted reference standard for CTS, NCS demonstrated the highest sensitivity compared with the other tests. However, NCS also demonstrated the lowest specificity among the 6 clinical diagnostic tests. Alternatively, the Wainner demonstrated the highest specificity. This finding puts into question the common practice of using NCS as a confirmatory test when evaluating for CTS. Furthermore, this finding is consistent with our study evaluating the efficacy of these clinical diagnostic tests using a fellowship-trained hand surgeon as a reference standard.⁶ The sensitivity of CTS-6 (75%) and NCS (97%) in the current study is almost exactly the same as the values reported in the previous study. The specificity of CTS-6 (61%) was similar; however, the specificity of NCS (40%) was even lower than the Wang et al study.

When US was combined with NCS, the overall sensitivity and specificity was highest among other pairwise combinations when both tests were positive. This finding suggests that the use of both diagnostic US in the clinic and NCS can be appropriate to maximize the diagnostic efficacy of CTS when the clinical diagnosis is unclear. A survey study published in 2017 that evaluated the preferences and usage of US in an upper extremity surgeon's practice found that only 55% of the respondents used US for diagnosing CTS, with the primary reason due to the belief that US was not as accurate as NCS.¹⁵ Our study demonstrates that there are differences in the sensitivity and specificity profiles of NCS and US, which may beneficially complement one another when used together.

This study has a few limitations. There is a high prevalence of carpal tunnel in our study sample given that patients were recruited from hand surgery clinic. It is possible that the high prevalence of CTS in our sample may affect the results of the study and falsely elevate the sensitivity and specificity of these tests. However, as medicine becomes more specialized, the diagnosis and treatment of CTS is being funneled to hand surgery specialists. Therefore, the prevalence of carpal tunnel in this study may mirror the prevalence in a typical hand surgery office. With LCA, there is the chance that unknown associations exist between the tests that are not detected by this statistical technique. By using 6 different diagnostic tests, we hoped to add additional information to the model. Finally, several of the clinical diagnostic tests (CTS-6, Lo, Wainner, Kamath) share common

criteria. It is possible that these shared data points overestimate the diagnostic accuracy of these tests in the LCA.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Statement of Informed Consent

All participation in the study was voluntary and informed consent was obtained from all patients who agreed to participate in the study.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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