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Application of the calculated electrophysiological parameters in early diagnosis of carpal tunnel syndrome

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Abstract

Objective: To investigate the application of the calculated electrophysiological parameters in early diagnosis of carpal tunnel syndrome (CTS). *Methods:* 44 patients (60 hands) with a diagnosis of CTS and 31 healthy volunteers (44 hands) were enrolled. Acquired indicators include median nerve distal motor latency (DML), complex muscle action potential (CMAP) amplitude, conduction velocity (MCV), median nerve sensory nerve action potential (SNAP) amplitude, and conduction velocity (SCV). Then the terminal latency index (TLI), the residual latency (RL), and the difference in peak sensory latencies between the median and ulnar nerves (ΔPSL) were calculated. *Results:* The two groups were matched in age and gender distribution. The CTS group showed significant difference in SCV, DML, SNAP, and CMAP compared with the control group. The sensitivity, specificity, cut-off value, Youden index, and area under the curve of each indicator are respectively as follows: TLI (0.733, 0.932, 0.622, 0.629, and 0.877), RL (0.750, 0.977, 1.334, 0.727, and 0.907), ΔPSL (0.950, 0.841, 0.150, 0.791, and 0.942), SCV (0.950, 0.796, 56.5, 0.746, and 0.946), DML (0.867, 0.932, 3.55, 0.799, and 0.930), SNAP (0.683, 0.932, 21.68, 0.615, and 0.844), and CMAP (0.683, 0.773, 8.76, 0.456, and 0.758).
Conclusion: The calculated electrophysiological parameters have higher sensitivities and specificities relative to a single electrophysiological parameter, which could greatly improve the accuracy of early diagnosis of CTS.

Keywords: Carpal tunnel syndrome (CTS); calculated electrophysiological parameters; early diagnosis.

INTRODUCTION

Carpal tunnel syndrome (CTS) is the most common syndrome of peripheral neuropathy.[1] It is mainly characterized by numbness on the three and a half fingers and the palm of the afflicted hand. Early diagnosis and treatment have a great significance in remission of the disease. Unfortunately, many CTS patients are misdiagnosed with cervical spondylosis, cerebral infarction, and other conditions, even using conventional electromyography parameters, such as the distal motor latency (DML), the action potentials (CMAP), the motor nerve conduction velocity (MCV), the sensory nerve action potentials (SNAP), and the sensory conduction velocity (SCV).[2] Calculated electrophysiological parameters, such as the terminal latency index (TLI), residual latency (RL), and the difference in peak sensory latencies between the median and ulnar nerves (ΔPSL), are developed to assess CTS severity in a recent study.[3] Therefore, this study aimed to investigate whether TLI, RL, and ΔPSL could identify CTS with high sensitivities and specificities in the early stage of the disease.

METHODS

Subjects

We recruited 131 subjects in the Department of Neurology, Affiliated ZhongDa Hospital of Southeast University between years of 2017 and 2018. Among of them, 75 subjects were CTS patients with the average age of 60.12±10.87 (27-80) years. Particularly, 17 subjects were bilateral CTS and 58 subjects were unilateral CTS. The control group consisted of 56 subjects with 78 hands. The average age was 59.62±13.89 (16-87) years. This study was approved by the Research Ethics Committee of Affiliated ZhongDa Hospital of Southeast University and written informed consents were obtained from all subjects.

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Diagnostic criterion

CTS was clinically diagnosed according to the following clinical diagnostic criteria from American Academy of Neurology[4-6]: (1) paresthesia, pain, swelling, weakness, or clumsiness of the hand provoked or worsened by sleep, sustained hand or arm position, or repetitive action of the hand or wrist mitigated by a change in posture or by shaking of the hand; (2) sensory deficits in the median nerve innervated regions of the hand; (3) motor deficit or hypotrophy of the median nerve innervated muscles; and (4) positive provocative clinical tests (positive Phalen and/or Tinel sign). The subjects were diagnosed CTS if he or she met item (1) together with one or more items from (2) to (4) above.

Exclusion criteria

The exclusion criteria of this study were: (1) Subjects with endocrine abnormalities (such as diabetes and hypothyroidism), chronic renal failure, malnutrition, and other diseases that may cause peripheral neuropathy; (2) Subjects who received a closed injection in the carpal tunnel, or had an acute injury or a significant mass in the wrist during the past month.

Nerve conduction examination

Electrophysiological examinations were conducted by Nicolet EDX (Natus Neurology Incorporated, USA) in a quiet, warm (30-32°C), and shielded room. The subjects were relaxed and in a supine position. Nerve conduction test: the surface electrode and the finger ring electrode were used for detection of motor and sensory nerve conduction. The sensory nerve conduction test was performed by retrograde conduction measurement with the back of the hand grounded. The stimulation mode is square wave stimulation (wave width 0.1ms) with filtering range of 2 – 2000 Hz, scanning speed of 2 – 5 ms/D, and sensitivity of 5 mv/D for motor nerve or 5 – 20 μv /D for sensory nerve.

Conventional nerve conduction detection

Conventional nerve conduction detection in this study includes DML, CMAP, MCV, SNAP, and SCV. Particularly, the DML of the thumb abductor muscle, the CMAP amplitude, and the MCV of the compound muscle were recorded at wrist level after stimulation of the median nerve. For sensory conduction detection, the ring electrode was placed on the index finger. The SNAP amplitude and SCV were recorded after stimulation of the median nerve at wrist level.

The calculated electrophysiological parameters

The TLI[7-10], RL[8,11], and ΔPSL[12] were calculated by following equations:

$$TLI = \text{distal conduction distance distal MCV} \times \text{DML} \quad (1)$$

$$RL = DML - \text{distal conduction distance distal MCV} \quad (2)$$

$$\Delta PSL = \text{peak sensory latencies in median nerve} - \text{peak sensory latencies in ulnar nerve} \quad (3)$$

Statistical analysis

Statistical analysis was performed using SPSS 20.0 software. Quantitative data were presented as mean ± standard deviation. Independent sample t-test was used to compare quantitative data between the two groups. The $\chi 2$ test was used to compare qualitative data between the two groups. Sensitivity and specificity were analyzed by receiver operating characteristic (ROC) curves. The Youden index, a statistic tool to estimate the performance of a dichotomous diagnostic test, was used to determine the cut-off value for each electrophysiological parameter. The Youden index was calculated according to equation (4). The statistical threshold was set at $p < 0.05$.

$$\text{Youden index} = \text{sensitivity} + \text{specificity} - 1 \quad (4)$$

RESULTS

Between-group comparison of conventional electrophysiological parameters

As shown in Table 1, compared with the control group, the CTS group exhibited a significantly slower SCV (t = -11.12, p = 0.001), prolonged DML (t = 8.71 p = 0.001), decreased SNAP amplitude (t = -6.21, p = 0.001), and CMAP amplitude (t = -4.79, p = 0.001). The CTS group showed a significantly increased TLI (t = -7.91, p = 0.001), decreased RL (t = 7.80, p = 0.001), and decreased ΔPSL (t = 9.82, p = 0.001) compared with the control group (Table 2).

Diagnostic performances between conventional electrophysiological parameters and the calculated electrophysiological parameters

In conventional neurophysiological parameters, the sensitivity, specificity, Youden index, cut-off value, and area under the curve (AUC) of SCV were 0.950, 0.796, 56.5, 0.746, and 0.946, respectively. The sensitivity, specificity, cut-off value, Youden index, and AUC of DML were

Table 1: Demographic data and conventional neurophysiological parameters of subjects

	CTS subjects (N = 60)	Control subjects (N = 44)	Statistics	*P* value
Age (years)	60.28±10.08	57.66±15.55	1.043	0.3
Gender (M/F)	12/48	15/29	2.622	0.105
SCV	43.33±8.94	60.80±6.23	-11.124	0.001
DML	4.56±1.11	3.07±0.29	8.710	0.001
SNAP	19.52±14.35	35.63±11.08	-6.208	0.001
CMAP	7.95±2.79	10.35±2.10	-4.792	0.001

Abbreviations: CTS, carpal tunnel syndrome; M, male; F, female; SCV, sensory conduction velocity; DML, distal motor latency; SNAP, sensory nerve action potential; CMAP, complex muscle action potential. Quantitative variables were analyzed by the student *t* tests, gender distribution were analyzed by the chi-square test.

0.867, 0.932, 3.55, 0.799, and 0.930, respectively. The sensitivity, specificity, cut-off value, Youden index, and AUC of SNAP were 0.683, 0.932, 21.68, 0.615, and 0.844, respectively. The sensitivity, specificity, cut-off value, Youden index, and AUC of CMAP were 0.683, 0.773, 8.76, 0.456, and 0.758, respectively. By contrast, In the calculated neurophysiological parameters, the sensitivity, specificity, cut-off value, Youden index and AUC of TLI were 0.733, 0.932, 0.622, 0.629, and 0.877, respectively; the sensitivity, specificity, cut-off value, Youden index and AUC of RL were 0.750, 0.977, 1.334, 0.727, and 0.907, respectively; the sensitivity, specificity, cut-off value, Youden index and AUC of ΔPSL were 0.950, 0.841, 0.150, 0.791, and 0.942, respectively. Therefore, TLI and RL yield the highest specificity for early diagnosis of CTS, with ΔPSL and DML in turn (Figure 1 and Table 3). ΔPSL yield the highest sensitivity for early diagnosis of CTS, with TLI, RL, and DML in turn (Figure 1 and Table 3). The AUC of ΔPSL showed no significant difference when compared with that of TLI and RL (TLI vs. ΔPSL, $p = 0.079$; RL vs. ΔPSL, $p = 0.294$). We also determine the cut-off value for each indicator, as shown in Table 3.

DISCUSSION

CTS refers to a syndrome of sensory abnormalities and dysfunction due to a compression of the median nerve in the carpal tunnel.[13] It accounts for approximately 90% of all compression induced peripheral neuropathies.[14] Typical clinical symptoms include numbness and/or pain in the hand, together with experiences of nighttime awakening or swelling of the hand. Although these symptoms could be temporarily relieved by hand rubbing or certain movements of the wrist, CTS would progressed more severely to thumb and palm weakness and muscle atrophy if no intervention were performed timely.[15] Therefore, early diagnosis and treatment are important for the prevention of irreversible nerve damage. This study indicated a significant prolonged DML, a slower SCV, and a significant decrease of TLI and RL in the CTS group compared with the control group. Further analysis of ROC curve showed a larger AUC for ΔPSL followed by RL and TLI. These results indicate that the calculated electrophysiological parameters have better sensitivities and specificities for CTS diagnosis relative to conventional parameters.

Electrophysiological examination is the golden standard for diagnosis of carpal tunnel syndrome.[16] Although SCV and DML have larger AUCs when compared to other indicators, they are susceptible to diverse confounding factors, such as height, age, skin temperature, nerve conduction velocity, and other peripheral neuropathies. Thus, using SCV or

Table 2: The calculated electrophysiological parameters between the CTS and control groups

	CTS group	Control group	Statistics	*P* value
TLI	0.56±0.14	0.76±0.10	-7.91	0.001
RL	2.11±1.11	0.76±0.34	7.80	0.001
ΔPSL	1.12±0.74	-0.06±0.33	9.82	0.001

Abbreviations: CTS, carpal tunnel syndrome; TLI, terminal latency index; RL, residual latency;PSL, median / ulnar nerve peak sensory latencies difference.

Table 3: Diagnostic values of conventional neurophysiological parameters and the calculated electrophysiological parameters

	SCV	DML	SNAP	CMAP	TLI	RL	ΔPSL
sensitivity	0.950	0.867	0.683	0.683	0.733	0.750	0.950
specificity	0.796	0.932	0.932	0.773	0.932	0.977	0.841
cut-off value	56.5	3.55	21.68	8.76	0.632	1.334	0.15
Youden index	0.746	0.799	0.615	0.456	0.665	0.727	0.791
Area under the curve	0.946	0.930	0.844	0.758	0.877	0.907	0.942

SCV, sensory conduction velocity; DML, distal motor latency; SNAP, sensory nerve action potential; CMAP, complex muscle action potential; TLI, terminal latency index; RL, residual latency; PSL, median / ulnar nerve peak sensory latencies difference.

DML alone may contribute to missed diagnosis of CTS. Furthermore, single parameters alone cannot comprehensively reflect the median nerve function, thus remarkably reducing sensitivity of the parameters in CTS diagnosis. Relative to the conventional neurophysiological parameters, TLI is the distance-corrected proximal conduction time and end conduction time ratio, and RL is the distance-corrected proximal conduction time and end conduction time difference. Both parameters accounts for the above confounding factors. They reflect the median nerve function more objectively and comprehensively, thus yield higher sensitivity and specificity in CTS diagnosis.[7] Therefore, using TLI and RL would increase the accuracy for diagnosing CTS, especially when using them together with ΔPSL. Studies demonstrated that patients with chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) showed significantly reduced TLI, as the nerve damage site is located at the end of nerve.[17] RL is shown to be highly sensitive to peripheral nerve damage given abnormal glucose tolerance.[18] The main cause of CTS is dysfunction of the median nerve due to ischemia and hypoxia induced by compression of the median nerve in the carpal tunnel[19], which explains why TLI was significantly reduced and RL was significantly increased in CTS patients in our results.

In addition, in our study, although ΔPSL showed the highest sensitivity, its cut-off value is 0.15 that is lower than other studies. Thus, misdiagnosis would occur if we use this indicator alone in this study. These results suggest that the calculated electrophysiological parameters could increase the accuracy of CTS diagnosis when we use them together.

In summary, our findings suggest that TLI, RL and ΔPSL are better indicators for early diagnosis of CTS compared with conventional electrophysiological parameters, given their higher sensitivity and comparable specificity

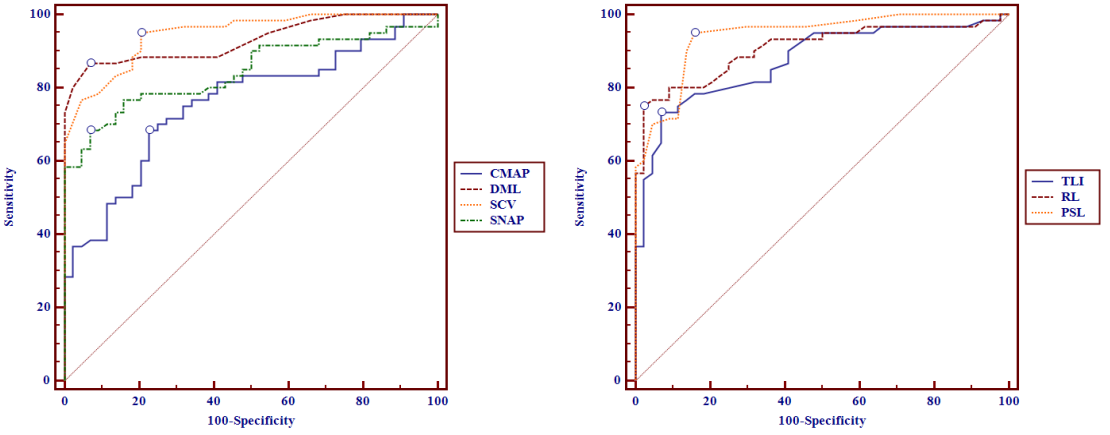

Figure 1. ROC curve analysis of conventional neurophysiological parameters and the calculated electrophysiological parameters. SCV: sensory conduction velocity of median nerve; DML: distal motor latency of median nerve; SNAP: sensory nerve action potential of median nerve; CMAP: complex muscle action potential of median nerve; RL, residual latency of median nerve; TLI, terminal latency index of median nerve; PSL, the difference in peak sensory latencies between the median and ulnar nerves.

to median nerve dysfunction. Using these three indicators together would greatly improve the sensitivity of early diagnosis of CTS. This study limitation was that there was no subgroup analysis based on disease severity and subject's age. Future studies should further enlarge the sample size and perform subgroup analyses to assess the clinical significance of relevant parameters.

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DISCLOSURE

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Conflict of interest: None

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