Electrophysiological evaluation of carpal tunnel syndrome

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Submitted: 19 December 2021; **Accepted:** 2 September
Online publication: 9 September 2022

Arch Med Sci
DOI: https//doi.org/10.5114/aoms/153468

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Abstract

Introduction: Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy in society. Based on the data obtained from basic conventional CTS studies, patients can be staged, and the changes in CTS severity can be followed according to the electrophysiological parameters derived from the data. This study aimed to assess the electrophysiological findings of CTS patients using the Bland and Padua grading systems and median terminal latency index (mTLI) and to evaluate the findings that may indicate the transition to the advanced stage.

Material and methods: The study included 822 patients. After electrophysiological examination, both hands of the patients were staged according to the grading systems proposed by Padua and Bland. Additionally, mTLI was calculated for each hand.

Results: With the increase in stages, a significant decrease was found in mTLI, median sensory nerve conduction velocity (mSNCV), median sensory amplitude (mSA), median motor nerve conduction velocity (mMNCV), and median motor amplitude (mMA), whereas a significant increase was observed in median sensory distal latency (mSDL) and median motor distal latency (mMDL) ($p < 0.001$) The parameter with the highest sensitivity regarding the indication of transition between stages was mSNCV; the sensitivity increased with the progression of stage, and a cut-off value of 40.5 m/s showed a sensitivity of 94.2% and a specificity of 90% regarding the indication of transition to the advanced stage.

Conclusions: Our results showed that with a cut-off value of 40.5 m/s, mSNCV is an accurate, sensitive and specific parameter regarding the indication of transition to the advanced stage.

Key words: neurophysiology, classification, index.

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathology, presenting with tingling, numbness, hand and arm pain, and muscle dysfunction [1, 2]. CTS is observed in approximately 3% of the general population, and its frequency and severity increase with age [3]. Electrophysiological examinations give reliable information to the physician and patient in confirming the diagnosis of CTS by excluding conditions that mimic CTS, and also provide objective findings about the severity of CTS that assist in treatment planning and recognize the new, changing and recurrent symptoms in the follow-up of patients [2, 4, 5].

Many staging methods, especially those defined by Bland and Padua, are used in the electrophysiological evaluation of CTS patients. Although these staging methods do not include any other electrophysiological findings other than distal latency (DL), they are an important guide in clinical follow-up and a strong indicator in predicting the postoperative prognosis [6]. While sensory conduction studies are the most sensitive studies in early stages, motor conduction studies are more sensitive than sensory conduction studies in advanced stages of CTS [7]. Some electrophysiological parameters derived from these conventional basic electrophysiological findings can also be used to evaluate and follow-up the patients. One of the commonly used derived motor parameters is the terminal latency index (TLI), which gives a motor DL (MDL) correction to nerve conduction velocity [7].

We aimed to evaluate the electrophysiological findings of CTS patients using the Bland and Padua grading systems and median motor TLI (mTLI), which have previously been shown to be correlated with clinical findings, and to assess the electrophysiological parameters that can be used to predict the increase in severity of the disease.

Material and methods

Between April 2013 and November 2017, 964 patients over the age of 18, who were referred to the electrophysiology laboratory of our hospital by clinicians for electrophysiological examination with a pre-diagnosis of CTS, were retrospectively analyzed. The study was approved by the local ethics committee. Patients with diabetes mellitus, cardiovascular disease, rheumatoid arthritis, gout, hypothyroidism, acromegaly, chronic renal failure, hereditary or acquired amyloidosis, a heavy occupational workload requiring repetitive handgrip tasks and vibrating tools, CTS due to trauma, and space-occupying lesions of the carpal canal were excluded from the study. A hundred and forty-two patients with polyneuropathy or radiculopathy and acute or chronic demyelinating disease were excluded through the electrophysiological evaluation, while the remaining 822 patients were included in the study.

Electrophysiological examination

Electrophysiological studies were performed with a Dantec Keypoint EMG machine (Dantec Dynamics A/S, Skovlunde, Denmark). Recording of the median nerve compound muscle action potential (CMAP) was performed using 2 pre-gelled silver–silver chloride surface electrodes that were placed on the abductor pollicis brevis muscle at a distance of 8 cm from the stimulation point. Recording of the ulnar nerve CMAP was performed using 2 pre-gelled silver–silver chloride surface electrodes placed on the abductor digiti minimi muscle at a distance of 8 cm from the stimulation point. Sensory nerve action potentials (SNAPs) were obtained antidromically. The recordings were performed from the index finger for the median sensory nerve and the fifth finger for the ulnar sensory nerve with stimulation at the wrist. Ring electrodes at a distance of 16 cm from the stimulation points were used for sensory nerve recordings. If necessary, an ulnar versus median comparison study was recorded at the fourth finger with stimulation of both ulnar and median nerves at the wrist with equal distances, respectively. Stimulations were performed with 2 pre-gelled silver–silver chloride surface electrodes with the anode 2.5 cm proximal to the cathode. Studies were performed on both upper extremities, which were warmed up, if the skin temperature was under 32°C.

Electrophysiological criteria for CTS were: a) a median MDL (mMDL) of > 4.5 ms; b) prolongation of the median (index finger) sensory onset latency of > 3.2 ms; c) prolongation of the median (index finger) SNAP compared with ulnar (fifth finger) SNAP onset latency of > 0.5 ms; and d) prolongation of median fourth finger SNAP latency compared with ulnar fourth finger SNAP peak latency of > 0.5 ms.

Electrophysiological staging

Each hand was staged based on the Padua and Bland (B and P) grading systems [8, 9]. mTLI, which is a previously defined electrophysiological parameter for each hand, was calculated as suggested for the median motor nerve [7] (mTLI: terminal distance (mm)/[median motor nerve conduction velocity (mMNCV) (m/s) × mMDL (ms)]). According to the Padua classification: stage 0 (P0) – (negative) normal electrophysiological findings in all tests; stage 1 (P1) – (minimal) abnormal findings that can be detected by further examinations; stage 2 (P2) – (mild) slower median sensory finger-wrist segment and normal mMDL; stage 3 (P3) – (moderate) slower median sensory finger-wrist segment and abnormal mMDL; stage 4 (P4) – (severe) failure to obtain median SNAP and abnormal mMDL; stage 5 (P5) – (extreme) failure to obtain median SNAP and CMAP.

According to the Bland classification: stage 0 (B0) – no electrophysiological abnormality; stage 1 (B1) – (very mild) abnormal findings that can be detected by further examinations; stage 2 (B2) – (mild) slower median sensory finger-wrist segment and normal mMDL; stage 3 (B3) – (moderately severe) median SNAP obtained and mMDL in the range 4.5–6.5 ms; stage 4 (B4) – (severe)

failure to obtain median SNAP and mMDL in the range 4.5–6.5 ms; stage 5 (B5) – (very severe) mMDL > 6.5 ms; stage 6 (B6) – (extremely severe) failure to obtain median SNAP and CMAP.

Statistical analysis

The data obtained from the study were transferred to electronic media and analyzed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). In the evaluations, frequency distributions and mean and standard deviation values were used for descriptive statistics. The conformity of the data to normal distribution was evaluated with the Kolmogorov-Smirnov test. Kruskal-Wallis analysis of variance was used to compare the data according to B and P stages as the data did not follow a normal distribution. Pairwise comparisons were made using the Dunnett T3 test for each pair of groups. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the variables were estimated by receiver operating characteristic (ROC) curve analysis. Data were reported as mean ± standard deviation. A p-value ≤ 0.05 was considered statistically significant.

Results

The mean age of the 822 patients examined was 48.0 ±13.28 years. Three hundred and fifteen (38.3%) patients did not have CTS, while unilateral CTS was found in 104 (12.7%) and bilateral CTS in 403 (49%) of the patients. Of the patients with unilateral CTS, 74.4% had CTS in the right hand and 35.6% had CTS in the left hand. The electrophysiological findings of the 1644 hands examined according to the B and P staging are given in Tables I and II, and the distribution of gender and involved side is given in Figure 1 A, B.

With the increase in stages, a statistically significantly decrease was found in mTLI, median sensory nerve conduction velocity (mSNCV), median sensory amplitude (mSA), mMNCV and median motor amplitude (mMA), while a significant increase was seen in median sensory distal latency (mSDL) and mMDL (p < 0.001, Tables I and II). The cut-off values of mSDL, mSNCV, mSA, mMDL, mMNCV and mTLI and sensitivity and specificity of all parameters during the transition from early stage (B1) to mild stage (B2), from mild stage (B2) to moderate stage (B3), and from moderate stage (B3) to advanced stage (stages over B3) were calculated using ROC analysis. The parameters with the highest sensitivity and specificity regarding the indication of transition between stages were mSNCV and mTLI among sensory and motor parameters, respectively (Table III). In univariate analysis, while mTLI was similar in groups B3 and B4 (p = 0.816), it was significantly different between the other groups (p < 0.001).

Discussion

Here we found that among several electrophysiological parameters of relevance, mSNCV is the parameter with the highest sensitivity and specificity regarding the indication of transition to the advanced stage in CTS patients.

In CTS, sensory fibers are affected earlier than motor fibers. Although the reason is unclear, it is thought that sensory fibers contain a higher amount of thick myelinated fibers with higher energy needs and therefore are more prone to ischemic damage [10, 11]. In the typical course of the syndrome, demyelination occurs in sensory

Table I. Hand distribution, mean age and electrophysiological findings of patients according to the Bland staging system

Parameter	B staging; Number of hands							*P*-value
	B0 734	B1 282	B2 224	B3 294	B4 12	B5 84	B6 14	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age [years]	45.38 ±13.54	47.57 ±12.91	49.12 ±11.88	51.27 ±12.60	57.25 ±11.54	54.11 ±11.55	66.29 ±9.46	< 0.0001*
mSNCV [m/s]	60.19 ±5.13	53.02 ±2.91	45.60 ±2.77	40.40 ±4.97	0	20.60 ±17.16	0	< 0.0001*
mSDL [ms]	2.67 ±0.23	3.02 ±0.17	3.52 ±0.23	4.03 ±0.52	0	2.94 ±2.45	0	< 0.0001*
mSA [μV]	31.40 ±12.30	26.90 ±13.45	19.77 ±8.64	15.63 ±13.65	0	5.30 ±5.78	0	<0.0001*
mMNCV [m/s]	54.48 ±3.76	53.84 ±3.73	53.44 ±4.32	51.40 ±4.95	49.40 ±4.24	47.03 ±6.01	0	< 0.0001*
mMDL [ms]	3.44 ±0.35	3.97 ±0.36	4.21 ±0.26	5.26 ±0.56	5.71 ±0.52	7.69 ±1.09	0	< 0.0001*
mMA [mV]	8.10 ±1.95	7.88 ±1.95	7.90 ±2.19	6.89 ±2.07	4.90 ±1.87	4.25 ±2.70	0	< 0.0001*
mTLI	0.43 ±0.05	0.38 ±0.04	0.36 ±0.03	0.30 ±0.04	0.29 ±0.03	0.23 ±.043	0	†‡**

*B – Bland staging, mSDL – median sensory distal latency, mSA – median sensory amplitude, mSNCV – median sensory nerve conduction velocity, mMDL – median motor distal latency, mMA – median motor amplitude, mMNCV – median motor nerve conduction velocity, mTLI – median motor terminal latency index. *Kruskal-Wallis test; **post-hoc comparison analysis (Dunnett T3 test); †p = 0.816 in comparison between B3 and B4; ‡p < 0.001 in comparison between other groups.*

Table II. Hand distribution, mean age and electrophysiological findings of patients according to the Padua staging system

Parameter	P staging; Number of hands						*P*-value
	P0 734	P1 282	P2 224	P3 346	P4 44	P5 14	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Age [years]	45.38 ±13.54	47.57 ±12.91	49.12 ±11.88	51.41 ±12.40	57.16 ±10.56	66.29 ±9.46	< 0.0001*
mSNCV [m/s]	60.19 ±5.13	53.02 ±2.91	45.60 ±2.77	39.36 ±5.87	0	0	< 0.0001*
mSDL [ms]	2.67 ±0.23	3.02 ±0.17	3.52 ±0.23	4.13 ±0.66	0	0	< 0.0001*
mSA [μV]	31.40 ±12.30	26.90 ±13.45	19.77 ±8.64	14.56 ±12.96	0	0	< 0.0001*
mMNCV [m/s]	54.48 ±3.76	53.84 ±3.73	53.44 ±4.32	50.79 ±5.14	47.30 ±6.90	0	< 0.0001*
mMDL [ms]	3.44 ±0.35	3.97 ±0.36	4.21 ±0.26	5.78 ±0.96	7.54 ±1.57	0	< 0.0001*
mMA [mV]	8.10 ±1.95	7.88 ±1.95	7.90 ±2.19	6.57 ±3.32	3.81 ±2.27	0	< 0.0001*
mTLI	0.43 ±0.05	0.38 ±0.04	0.36 ±0.03	0.29 ±0.42	0.24 ±0.59	0	†‡**

*P – Padua staging, mSDL – median sensory distal latency, mSA – median sensory amplitude, mSNCV – median sensory nerve conduction velocity, mMDL – median motor distal latency, mMA – median motor amplitude, mMNCV – median motor nerve conduction velocity, mTLI – median motor terminal latency index. *Kruskal–Wallis test, **post-hoc comparison analysis (Dunnett T3 test); p < 0.001 in comparison between whole groups.*

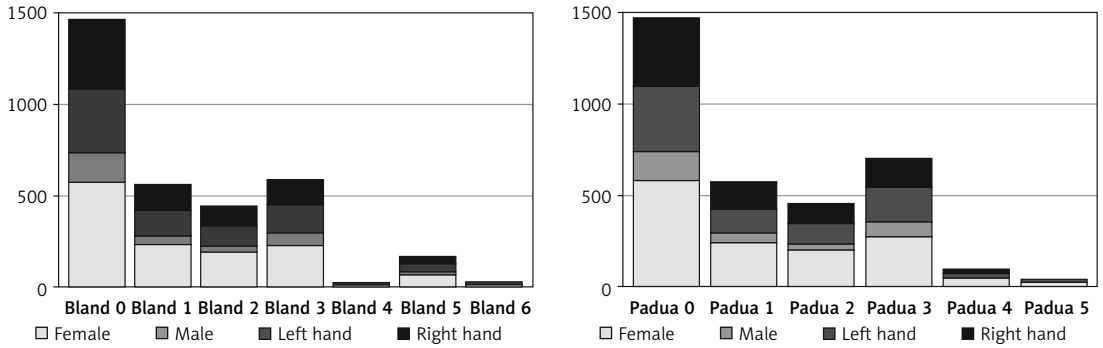

Figure 1. Electrophysiological findings of patients according to gender and localization distributions. **A** – Bland staging. **B** – Padua staging

Table III. Cut-off value, sensitivity and specificity of electrophysiological parameters in carpal tunnel syndrome staging systems

Parameter		Sensitivity %	Specificity %	PPV	NPV	AUC	LR +	LR –
Cut-off value from early to mild:								
mSNCV [m/s]	53.4	69.5	47.5	30.9	89.3	0.62	2.07	0.48
mTLI	0.37	58.5	63.5	52.1	34.8	0.75	2.57	0.64
Cut-off value from mild to moderate:								
mSNCV [m/s]	45.8	88.5	82.9	44.6	95.2	0.888	5.14	0.19
mTLI	0.34	87.1	76.8	76.8	88.1	0.893	4.83	0.21
Cut-off value from moderate to advanced:								
mSNCV [m/s]	40.5	94.2	90	50.7	97.3	0.973	5.65	0.18
mTLI	0.27	78.1	83.7	84.7	84.6	0.981	3.21	0.31

mSNCV – median sensory nerve conduction velocity, mTLI – median motor terminal latency index, PPV – positive predictive value, NPV – negative predictive value (NPV), LR+ – positive likelihood ratio; LR– – negative likelihood ratio, AUC – area under curve.

fibers of the median nerve, which is under pressure in the carpal tunnel in the early stages. With the increase in pressure, demyelination of sensory fibers increases and motor fibers begin to be affected. As the degree of demyelination increases, axonal degeneration towards the distal region and additional retrograde degeneration develops towards the proximal region. Many electrophysiological staging methods, including those proposed by Padua and Bland, are used in monitoring the

progress in CTS severity. The involvement of only DL among electrophysiological findings, different DL values used in staging, and not knowing how the transition between stages is determined are the most criticized issues of these staging methods [12]. The results of the present study indicated that the sensitivity and specificity of mSDL and mMDL decreased, while those of other electrophysiological parameters increased during the progression of the stage of CTS.

In the literature, there are many electrophysiological parameters derived from basic conventional CTS studies, the availability of which in the diagnosis and follow-up of the disease has been investigated. These studies focused on the parameters derived from motor fibers due to the fact that they can be evaluated up to the advanced stage of CTS and the most studied parameter is mTLI. It has been claimed that an mTLI below 0.35 in clinical CTS patients may help with the diagnosis of CTS without the need for additional electrical stimulation [13]. Subsequent studies have shown that the diagnostic sensitivity and specificity of parameters including mTLI derived from the electrophysiological findings of motor fibers are lower than those obtained from conventional studies [14–18]. In the study of Park *et al.* [18], it was found that mTLI correlated with the increase in the severity of CTS and could be used in electrophysiological follow-up. Our study showed that the sensitivity of mTLI is low in the early stages of CTS where sensory involvement is dominant, and it increases in the moderate and advanced stages when motor involvement is prominent; however, using mTLI alone in the follow-up, severity of the disease cannot be a reliable parameter as it cannot distinguish patients with similar motor involvement but different sensory involvement in the moderate and advanced stages.

Sensory involvement is dominant in the early stages of CTS and motor fibers begin to be affected in the later stages, and there may be differences in the involvement of sensory and motor fibers between patients. These differences affect the clinical course of CTS and treatment response. Some small-series studies reported that pre-operative electrophysiological evaluation was not predictive of surgical treatment response; however, a large-series study showed that detection of advanced stage disease by pre-operative electrophysiological examination is an indicator of poor prognosis [19]. According to this study, the patients in B3 had the most benefit from surgical treatment whereas the surgical treatment response of the patients in more advanced stages (B4, B5 and B6) was poor. Based on this study, Bland included patients with an mMDL > 6.5 ms from whom the median SNAPs could be obtained in stage 5. According to the results of our study, the first finding showing the difference in the involvement of sensory and motor fibers is that 15% of the patients who were evaluated as stage 3 with the Padua staging method had an mMDL > 6.5 ms and they were included in the Bland stage 5 group. Another study showed that electrophysiological evaluation at 12 months post-operatively could be used to predict the improvement of clinical outcome in CTS patients. This study showed the improvement in grip strength and the scores of the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire at 6 months post-operatively in patients with an mSNCV > 38.5 m/s [20].

The second finding showing the difference in the involvement of sensory and motor fibers is that the total loss of sensory fibers is earlier in some patients with an mMDL > 4.5 from whom the median SNAPs could be obtained. While median SNAPs were obtained in 96.6% of patients with an mMDL in the range 4.5–6.5 ms (B3 and P3), it could not be obtained in 3.4% (B4 and P4) of the patients. Our findings show that if electrophysiological follow-up is performed based on parameters that only evaluate motor fibers such as mTLI, the patients in advanced stage (3.4%) with an mMDL between 4.5 and 6.5 ms from whom the median SNAPs cannot be obtained can be mistakenly classified as moderate stage. According to the results of our study, the parameter with the highest sensitivity and specificity regarding the indication of transition to the advanced stage is mSNCV, and a decrease in mSNCV below 40.5 m/s (sensitivity: 94.2%, specificity: 90%) significantly supports the transition to the advanced stage.

The fact that the total loss of sensory fibers occurs in very late stages in some of the patients in the advanced stage is the last finding that shows the difference in the involvement of sensory and motor fibers. While a sensory response was obtained in 61.9% of patients with an mMDL > 6.5 ms (B5 and P3), it could not be obtained in 38.1% (B5 and P4) of the patients. Therefore, if electrophysiological follow-up is performed based on parameters that evaluate only motor fibers, such as mTLI in these patients, these two groups, which are in the advanced stage but have different severity levels, cannot be distinguished.

One of the shortcomings of this study is its retrospective nature, and another is that the clinical findings were not evaluated. However, the classification of the patients according to the staging systems, which has been proven to be correlated with clinical findings, has eliminated this deficiency [8, 9].

In conclusion, although there is a need for large-series studies evaluating the correlation between electrophysiological findings and prognosis, the results obtained from the conventional basic CTS studies currently used in clinical electrophysi-

ology laboratories should be evaluated individually independent of staging. We believe that the use of mSNCV, which is one of the electrophysiological parameters, could be an important guide in monitoring the increase in the severity of disease in CTS patients.

Conflict of interest

The authors declare no conflict of interest.

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