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The diagnostic contribution of motor and sensory conduction studies of the wrist-palm segment in carpal tunnel syndrome

Karpal tünel sendromunda bilek-aya segmenti motor ve duysal iletim çalışmalarının tanıya katkısı

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Abstract

Aim: Sensory and motor segmental conduction studies have been performed to improve diagnostic sensitivity especially in cases with mild carpal tunnel syndrome, but there are very few studies comparing these methods. The purpose of this study was to determine the segmental conduction studies' contribution to the diagnosis of carpal tunnel syndrome (CTS), to compare the sensitivity and specificity of these methods.

Methods: Patients with suspected CTS referred to our electrophysiology laboratory and a control group was included. The data were collected prospectively. The following measurements made: median sensory conduction velocity wrist-digit 1 (W-1), median sensory conduction velocity wrist- digit 3 (W-3), median wrist-palm sensory conduction velocity (W-Ps), distoproximal ratio of velocity (D/P), median distal motor latency wrist- APB (MDML), median wrist- palm segment motor conduction velocity (W-Pm).

Results: The highest sensitivity for an electrodiagnostic CTS diagnosis were W- Pm (38%), D/P (33.3%), MDML (33.3%), W- 3 (31%), W- 1 (31%), W-Ps (24%), respectively. Seventeen out of 42 hands presented one or more abnormal results of routine electrophysiologic tests (W-1, W-3, MDML). Twenty-one patients were diagnosed CTS electrophysiologically after inclusion of D/P and 24 patients were defined CTS after inclusion of W- Pm. Twenty-five of 42 hands with CTS were defined as an electrophysiologically proven CTS using routine electrophysiologic tests together with both D/P and W-Pm segmental studies. That is; diagnostic sensitivity increased nearly by 50%.

Conclusion: The results of this study suggested that motor or sensory segmental studies have an important contribution to the diagnosis, particularly for mild subjects.

Keywords: Carpal tunnel syndrome, Segmental conduction study

Öz

Amaç: Özellikle hafif karpal tünel sendromu olan olgularda tanı duyarlılığını artırmak için duysal ve motor segmental iletim çalışmaları yapılmıştır, ancak bu yöntemleri birbiriyle karşılaştıran çok az sayıda çalışma vardır. Bu çalışmanın amacı segmental iletim çalışmalarının karpal tünel sendromu (KTS) tanısına katkısını saptamak, bu yöntemlerin duyarlılığını ve özgüllüğünü birbiriyle karşılaştırmaktır.

Yöntemler: KTS şüphesiyle elektrofizyoloji laboratuvarına gönderilen hastalar ile bir kontrol grubu dahil edildi. Veriler prospektif olarak toplandı. Bilek- 1. parmak median duysal iletim hızı (W-1), bilek- 3. parmak median duysal iletim hızı (W-3), median bilek- aya duysal iletim hızı (W- Ps), distoproksimal hız oranı (D/P), bilek- APB median distal motor latansı (MDML), median bilek- aya segmenti motor iletim hızı (W-Pm).

Bulgular: Elektrofizyolojik KTS tanısı için sensitivitesi en yüksekler sırasıyla W- Pm (%38), D/P (%33,3), MDML (%33,3), W- 1 (%31), W- Ps (%24)' di. 42 elden 17' sinde rutin elektrofizyolojik testlerde (W-1, W-3, MDML) bir veya daha fazla anormal sonuç elde edildi. D/P eklendikten sonra 21 hasta elektrofizyolojik olarak KTS tanısı aldı ve W- Pm eklendikten sonra 24 hasta KTS olarak değerlendirildi. Rutin elektrofizyolojik testlere ek olarak hem D/P, hem W- Pm segmental çalışmalarının eklenmesiyle 25 hastaya elektrofizyolojik olarak KTS tanısı kondu. Böylece; tanısal duyarlılık yaklaşık %50 arttı.

Sonuç: Bu çalışmanın sonuçları göstermiştir ki; özellikle hafif olgularda motor ve duysal segmental çalışmalar tanıya önemli katkı sağlamaktadır.

Anahtar kelimeler: Karpal tünel sendromu, Segmental iletim çalışması

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Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy of the upper extremities, due to compression of the median nerve as it travels through the wrist at the carpal tunnel [1-5].

In patients with mild form of the carpal tunnel syndrome (CTS), electrophysiological studies may fail to detect any abnormalities [6,7-12]. False negative conduction studies may result from the masking of the slowing in the proximal segment by the normal conduction velocity in the distal part of the tunnel, since conduction abnormality is confined to the segment of the median nerve within the carpal tunnel in mild CTS cases. Therefore, wrist-palm studies are considered to provide a more sensitive means of electrophysiological diagnosis for CTS [1,5,13]. In the present study, our aim was to examine the contribution of segmental conduction studies on the electrophysiological diagnosis of CTS.

Materials and methods

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/ or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Forty-two symptomatic arms from 29 patients referred to our EMG laboratory with a diagnosis of CTS based on history and examination were included in this study. Patients with nocturnal numbness and tingling on the hand or hands are accepted as carpal tunnel syndrome. Exclusion criteria included suspicious co-existence of polyneuropathy, plexopathy, or radiculopathy, and presence of systemic conditions associated with polyneuropathy or mononeuritis. Of the 29 patients, 26 were female and 3 were male, with an average age of 46.4 ± 8.4 years. All 42 arms had nocturnal paresthesia, while 4 had thenar atrophy, 6 had abductor pollicis brevis (APB) motor deficit, and 2 had sensory deficit in the median nerve territory.

Control subjects were the patients referred to the EMG laboratory with a pre-diagnosis of lumbar disc herniation who had no neurological complaints of the upper extremity and healthy volunteers employed in the neurology unit (23 healthy volunteers; 19 female, 4 male; average age 42.4 ± 10.5 years).

All patients were kept in a room with a temperature of 22 to 24 C for 15 minutes prior to the electrophysiological study. Subsequently, using an infrared thermometer (Exergen Dermatemp Infrared Temperature Scanner®) the extremity temperatures were measured and were maintained at a minimum temperature of 32 C using an infrared heater when needed.

A 4-channel Keypoint Electromyograph (Medtronic-Dantec) was used for electrophysiological tests, all of which were performed by the same investigator while the patient was in the supine position and the forearm was in extension and supination. All stimulations and recordings were performed with superficial electrodes. Before placement of electrodes, the skin was cleansed using alcohol-soaked cotton balls for minimizing skin resistance and electrode gel was utilized for the study. Two Velcro-band grounding electrodes were used, one on the wrist, the other on the metacarphophalangeal joint. Dry cotton balls were placed between the fingers to prevent contact. For recording, a Velcro-band ring electrode was used for sensory conduction and self-adhesive superficial electrodes were used for motor conduction measurements.

Sensory conduction studies

All sensory conduction measurements were performed antidromically. For the sensory conduction tests of the median nerve at the 1st finger, the active ring electrode was placed on the interphalangeal joint, while the reference ring electrode was placed on the distal phalanx, and median nerve was stimulated along its course at wrist level.

For the sensory conduction tests of the median nerve at the 3rd finger, the recorder ring electrode was placed in the middle of the middle phalanx of the third finger, while the reference ring electrode was placed in the middle of the distal phalanx. Separate stimulations were performed on the median nerve along its course at the wrist and palm.

For the sensory conduction test of the ulnar nerve at the 5th finger, the recorder ring electrode was placed on the middle of the middle phalanx of the fifth finger, while the reference ring electrode was placed on the middle of the distal phalanx. The electrical stimulation was performed along the course of the ulnar nerve in the wrist.

The amplitude of sensory action potentials were measured from peak to peak, and at least 10 measurements were averaged. The filtering frequency range was 20 to 2000 Hz.

Motor conduction studies

The superficial electrode was placed on the APB muscle at the thenar edge for median nerve motor conduction studies. The reference Velcro ring electrode was attached to the middle of the distal phalanx. Electrical stimulations were performed along the course of the median nerve in the wrist and palm. For stimulations at the palm, the anode was placed on an imaginary line connecting the cathode and the metacarpophalangeal joint of the fifth finger. This distal placement of the anode was for avoiding the stimulation of the recurrent thenar nerve beneath the anode that enters APB. The activation of the recurrent thenar nerve under the anode and cathode may lead to inaccuracy of the latency [1].

For the motor conduction tests of the ulnar nerve, the superficial electrode was placed at the hypothenar edge on the abductor digiti minimi (ADM) muscle. The reference Velcro ring electrode was placed on the middle of the middle phalanx of the fifth finger. The electrical stimulation was provided on the course of the ulnar nerve at the wrist.

The latency of the compound muscle action potentials (CMAP) were recorded as the time from the onset of stimulus artifact to the onset of the potential. The filtering frequency range was 20 to 10000 Hz.

The amplitude of CMAP was estimated from peak to peak. The sum of the negative and positive CMAP areas was recorded as the CMAP area.

Bilaterally, the following measurements and estimations were performed in all cases.

- median nerve sensory conduction velocity wrist- 1st finger (W-1)
- median nerve sensory conduction velocity wrist- 3rd finger (W-3)
- median nerve sensory conduction velocity palm- 3rd finger (P-3)
- median 1st finger sensory nerve action potential amplitude (W-1 . amp)
- median 3rd finger sensory nerve action potential amplitude (W-3 amp)
- median nerve sensory conduction velocity wrist-palm (W-Ps) was . calculated as follows: (wrist-palm distance)(mm)/ (W-3 latency- P-3 latency) (ms)
- distoproximal velocity ratio (D/P) was calculated as follows: (P-3)/(W-Ps) (Figure 1)
- distoproximal amplitude ratio was calculated as follows: median sensory nerve action potential amplitude (SNAP2 amp) obtained by palm stimulation divided by the median sensory nerve action potential amplitude obtained by wrist stimulation (W-3 amp).
- ulnar nerve sensory conduction velocity wrist-5th finger (W-5)
- ulnar sensory nerve action potential amplitude (UAMP)
- median distal motor latency wrist-APB (MDML)
- median wrist segment motor conduction velocity (W-Pm) was calculated as follows: the compound muscle action potential 1 (CMAP1) from wrist stimulation and the compound muscle action potential 2 (CMAP2) from palm stimulation were recorded (Wristpalm distance) (mm)/(CMAP1 latency-CMAP2 latency) (ms) (Figure 2).
- compound muscle action potential amplitude obtained by median motor stimulation at the wrist (CMAP1 amp)
- compound muscle action potential amplitude obtained by median motor stimulation at the palm (CMAP2 amp)
- distoproximal amplitude ratio was estimated as follows: CMAP2 amp/CMAP1 amp
- compound muscle action potential area obtained by the motor stimulation of the median nerve at the wrist (CMAP1 area)
- the compound muscle action potential area obtained by the motor stimulation of the median nerve at the palm (CMAP2 area)
- distoproximal area ratio (CMAP2 area/CMAP1 area).
- ulnar nerve distal motor latency wrist ADM (UDML) .



Figure 1: Mediansensory segmental nerve conduction study. Distoproximal velocity ratio=P-3/W-P



Figure 2: Median motor segmental nerve conduction study

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The patient and control groups were comparable with regard to age, as determined by the Student's t test (p > 0.05). The data from patients and healthy controls had normal distribution. In healthy controls, there were no significant differences between right and left sided measurements, and the normal limits were estimated using the average of the electrophysiological parameters (± 2 SD) from healthy volunteers. The patient data lying outside these limits were considered abnormal. For each electrophysiological parameter tested, a positive predictive value, a negative predictive value, specificity and sensitivity were estimated. In order to examine the multiple diagnostic performances of these electrophysiological parameters, a logistic regression analysis was performed. Odds ratio, Youden's Index and likelihood ratio were used to determine the parameters with the best positive predictive value, negative predictive value, specificity and sensitivity.

Results

Table 1 shows the comparative test results in CTS patients and controls. Table 2 shows amplitude and area results in controls and CTS subjects. Table 3 shows the sensitivity, specificity, positive predictive value and negative predictive value of the tests for CTS diagnosis.

Table 1: Conduction velocity results in CTS and control subjects

	Controls (n=46) Mean±SD	Mean±2SD	CTS (n=42) Mean±SD
W-1 (m/s)	59.40±7.50	44.95- 74.95	50.20± 8.10
W-3 (m/s)	58.00 ± 6.00	46.13-70.05	51.10 ± 7.70
W-Ps (m/s)	57.40 ± 9.70	37.88-76.92	46.70 ± 12.80
D/P	1.02 ± 1.17	0.70-1.34	1.20 ± 0.30
MDML (ms)	3.40 ± 0.30	2.73-4.13	4.00 ± 0.70
W-Pm (m/s)	41.90 ± 8.00	25.84- 57.96	33.40 ± 11.50
W-5 (m/s)	59.30 ± 6.70	45.87-72.79	59.90 ± 5.00
UDML (ms)	2.50 ± 0.50	1.60-3.56	2.40 ± 0.20

W-1: Median nerve sensory conduction velocity in the 1st finger W-3: Median nerve sensory conduction velocity in the 3rd finger W-Ps: median nerve wrist-palm conduction velocity, D/P: median nerve sensory distoproximal velocity ratio; MDML: median motor distal latency, W-Pm: median wrist-palm motor velocity, W-5: ulnar nerve sensory conduction velocity, UDML: ulnar motor distal latency

Table 2: Amplitude and area results in controls and CTS subjects

	Controls (n=46)		CTS subjects (n=42)
	Mean±SD	Mean±2SD	Mean±SD
SNAP amp	41.20 ± 16.00	9.09- 73.37	26.80±12.50
SNAP2 amp/W-3Amp	1.10 ± 0.20	0.71-1.59	1.20 ± 0.30
CMAP1 amp	11.00 ± 3.60	3.86-18.14	9.00 ± 3.00
CMAP2 amp/CMAP1 amp	1.20 ± 0.25	0.70- 1.70	1.20 ± 0.20
CMAP1 area	34.30 ± 10.80	9.70- 58.90	28.20 ± 12.10
CMAP2 AREA/ CMAP1 area	1.24 ± 0.34	0.56- 1.92	1.40 ± 0.60

Table 3: The sensitivity, specificity, positive predictive value, and negative predictive value of the tests for CTS diagnosis

			Positive	Negative
	Sensitivity	Specificity	predictive	predictive
Tests	%(n)	%	value %	value %
W-1	31.0(13)	100.0	100.0	61.3
SNAP amp	4.8(2)	100.0	100.0	53.5
MDML	33.3(14)	95.7	87.5	61.1
CMAP1 amp	2.4(1)	97.8	50.0	52.3
W-Pm	38,0(16)	100.0	100.0	55.4
W-3	31.0(13)	100.0	100.0	61.3
W-Ps	23.8(11)	100.0	100.0	59.0
W-5	0	97.8	0	51.7
D/P	33,3(14)	100.0	100.0	64
SNAP2 amp/W-3Amp	7.1(3)	100.0	100.0	54.1
CMAP2 amp/CMAP1 amp	4.8(2)	97.8	66.7	53
CMAP1 area	0	97.8	0	51.1
CMAP2 area/CMAP1 area	9.5(4)	97.8	75	53.5

Specificity: the percentage of those with normal test results within the control group; sensitivity: the percentage of patients with an abnormal test result; negative predictive value; the percentage of controls among those with a normal test result; positive predictive value: the percentage of patients within those with an abnormal test result

The tests with highest sensitivity were median motor wrist-palm velocity (38%), median sensory distoproximal velocity ratio (33.3%), median motor distal latency (33.3%), median sensory 3rd finger velocity (31%), median sensory 1st finger velocity (31%), and the median sensory 3rd finger wrist-palm segment velocity (24%).

The following 7 tests had a specificity and positive predictive value of 100%: median sensory 1st finger velocity, median sensory 1st finger amplitude, median motor wrist-palm velocity, median sensory 3rd finger velocity, median sensory 3rd finger wrist-palm segment velocity, median sensory 3rd finger distal to proximal velocity ratio, and median sensory 3rd finger distal amplitude to proximal amplitude ratio.

The tests with highest negative predictive value included the median sensory 3rd finger distoproximal velocity ratio (64%), median motor wrist-to palm latency (63.4%), median sensory 1st finger velocity (61%), median motor latency (61%), median sensory 3rd finger velocity (61%).

Median sensory 1st finger velocity was abnormal in 13 of the 42 hands with CTS, although it was not the sole abnormality in any of these 13 patients.

Median sensory 1st finger amplitude was abnormal in 2 patients, although it was not the sole abnormality in any of these cases. Wrist-palm segment median motor velocity was abnormal in 16 patients; in 3 of these, other electrophysiological tests revealed normal results and only the wrist-palm segment motor velocity was abnormal.

Median motor distal latency was abnormal in 14 patients, though never on its own. Median motor amplitude was abnormal in only 1 patient, and it was not the sole electrophysiological abnormality.

Median sensory 3rd finger velocity was abnormal in 13 patients, although it was not the sole abnormality in any of these cases. Median sensory 3rd finger wrist-palm segment velocity was abnormal in 10 patients. However, it was not the sole abnormality in any of these cases. Median sensory 3rd finger distoproximal velocity ratio was pathological in 14 patients. In one of these patients, it was the only abnormal electrophysiological finding. Median sensory 3rd finger distoproximal amplitude ratio was abnormal in three patients. In one of these patients, it was the only abnormal electrophysiological finding.

Median motor distoproximal amplitude ratio was abnormal in only 2 patient. In both patients, there were additional electrophysiological abnormalities. Median motor distoproximal area ratio was abnormal in 4 patients. In all these patients, there were additional electrophysiological abnormalities.

In 17 hands, at least one of the electrophysiological studies routinely used in the electrophysiology laboratory (i.e. median sensory1st finger velocity, median sensory 3rd finger velocity, median motor distal latency) was abnormal. When median sensory 3rd finger distoproximal velocity ratio was added to these tests, the number of hands with abnormality increased to 21, and when the wrist-palm velocity was added this number increased to 24. The use of these two parameters in addition to routine electrophysiological tests allowed an electrophysiological diagnosis of CTS in 25 of the 42 hands with CTS.

Discussion

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CTS is a clinical diagnosis, supported by electrophysiological tests when differential diagnosis is required or when surgery is planned. Sensitivity of EMG is never close to 100%, and since in cases with mild CTS the conduction abnormality is confined within the segment of the median nerve in the carpal tunnel, the normal conduction in the distal segment may obscure the slowing in the shorter segment [14]. Therefore, in patients with normal conventional results, wrist-palm segment tests are recommended [1,3].

The tests used in the current study included the median nerve sensory conduction in the thumb and third finger, wristpalm segment sensory conduction with 3rd finger recording, median nerve motor conduction and wrist-palm segment motor conduction, ulnar nerve fifth finger sensory conduction, and ulnar nerve motor conduction.

The median motor wrist-palm velocity emerged as the test with highest sensitivity (38.0%) followed in the decreasing order by the median sensory distoproximal velocity ratio (33.3%), distal motor latency (33.3%), median nerve 3rd finger velocity (31.0%), median sensory 1st finger velocity (31.0%), and median sensory 3r finger wrist-palm segment sensory velocity (24.0%).

In a study by Padua et al. involving 43 patients (50 hands) and 36 healthy volunteers (40 hands), the sensitivity of routine electrophysiological tests was compared with that of the distoproximal velocity ratio and found that the test with the lowest sensitivity was the median nerve distal motor latency (44%). On the other hand, the sensitivity of the median nerve 1st finger sensory velocity was 66%, and the sensitivity of the median nerve 3rd finger sensory velocity was 64%. In 38 of the hands with CTS (76%), the median nerve sensory conduction velocity was below 45 m/s. In that study the test with the highest diagnostic value was the distoproximal velocity ratio, which was below 1.0 among 40 control hands, while above 1.0 in 49 of the 50 hands with CTS (sensitivity 98%).

However, despite the high diagnostic sensitivity of the distoproximal velocity ratio for CTS, the authors pointed out to the possibility of obtaining misleading results if the tests are not performed in a standardized manner, since the area of interest spans only a short distance [6].

In a study by Chang et al. [1] involving wrist-palm segment motor conduction velocity, the results of the electrophysiological tests were compared in 160 hands with CTS. Of these 160 hands with CTS, 11 had normal electrophysiological test results (7%). In 139 (87%) and 129 (81%) hands the wrist-palm segment motor and sensory conduction velocity were abnormal, respectively. In 92% of the cases, at least one of these two tests yielded an abnormal result. They concluded that the wrist-palm segment motor conduction velocity appeared to be a more sensitive and practical technique as compared the sensory conduction velocity, and therefore the combined use of these two tests may improve the diagnostic yield.

In another study by Chang et al. [15] the sensitivity of the wrist-palm segment motor conduction velocity was compared with other sensory conduction techniques. In 32 of the 360 hands (8.9%) electrophysiological tests were normal. The tests with highest sensitivity were as follows: median-ulnar sensory latency difference (87.2%), median-radial sensory latency difference (86.7%), wrist-palm motor conduction velocity (81.7%), wrist-palm sensory conduction time (80.8%), wrist-palm sensory conduction velocity (73.6%). Thus, although wrist-palm segment motor conduction velocity was more sensitive than the sensory conduction time, a comparison of the sensory latency differences between the median and radial or ulnar nerves provided the highest sensitivity.

Sheu et al. [16] found that the distoproximal latency ratio of the median 3rd finger sensory conduction was the most sensitive test (77.9%) in their study, followed by the medianradial sensory latency difference (74.0%) and median-ulnar sensory latency difference (70.2%). The authors proposed that segmental tests provided a more practical and more sensitive means of diagnosis vs. tests based on comparison.

In a subsequent study by Lee et al. [17] median-radial and median-ulnar sensory latency differences were the tests with highest sensitivity (84.3% and 85.7%, respectively). These authors recommended the use of these comparative tests instead of segmental studies, in patients with normal median-sensory distal latency and median motor distal latency results. In their study, the other tests and their sensitivities are as follows: the wrist-palm segment sensory conduction time (77.0%), median distal sensory latency (74.3%), wrist-palm segment motor conduction velocity (69.1%), distoproximal conduction time difference (63%), distal motor latency (61.3%), and the distoproximal conduction time ratio (46.5%).

As compared to those reported by Chang and Padua, the results of the conduction tests in CTS patients in our study are closer to normal values, which may be explained by the inclusion of milder cases of CTS. All patients in our study, i.e. 42 symptomatic hands from 29 patients, described symptoms such as paresthesia involving the whole hand or the first four fingers that awakened the patients and that relieved with moving or shaking of the hand or by suspending the hand at the bed-side. Only 6 patients had permanent physical examination findings extending into day hours. On the other hand, the addition of D/P and W-Pm to the standard three tests (i.e. W-1, W-3, and DML) improved the sensitivity of electrophysiological tests from 40% to 59.5%, implying an approximately 50% increase in diagnostic sensitivity. Considering the fact that milder cases of CTS were included in our study, it may be assumed that segmental tests may be associated with a significant diagnostic contribution, particularly in very mild cases.

Entrapment neuropathies may also lead to slowing of the conduction through segmental demyelination as well as conduction block in some patients. Since entrapment neuropathies represent chronic conditions, conduction block is significantly less frequent as compared to the slowing of the conduction. In this study, 4 patients in sensory conduction tests and 2 patients in motor conduction tests had conduction block at the wrist segment. In only one case, block was the only electrophysiological finding, and it was associated with other signs in other cases. Although it may occur as a solitary condition, presence of motor or sensory conduction block should also be examined when segmental conduction studies are carried out.

In our study, some healthy individuals had slower median nerve conduction velocity at the wrist level as compared to more distal segments. In fact, a reduction in conduction velocity from proximal to distal segments is a physiological phenomenon [18]. Despite this, the conduction velocity may also slow down due to presence of segments with anatomic narrowing even in healthy subjects, as clearly exemplified by the ulnar nerve conduction. In healthy individuals, a motor nerve conduction velocity of 63 m/s in the arm and 61 m/s in the forearm is reduced to 51 m/s at the elbow segment [19]. Studies examining the segmental conduction in the median nerve are much less in number. In some of these studies, a slowing down of motor or sensory conduction was shown in healthy individuals at the level of the wrist-palm. In our study, the sensory D/P among healthy controls was between 0.6 and 1.3. Although Padua et al. [6] suggested that these ratio should always be less than 1, some healthy individuals may also have a ratio greater than 1. With a \pm 2 SD, this ratio could reach 1.3 among our healthy controls.

Limitations

Our patients are selected according to the clinical features therefore; a few normal individuals might be assessed as carpal tunnel syndrome.

Conclusions

The results of this study show that sensory and motor segmental nerve conduction studies may electrophysiologically provide significant diagnostic contributions, particularly in patients with new onset or mild disease.

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