An Evaluation of The Sensitivities and Specificities of The Comparative Techniques For Electrophysiological Diagnosis of Carpal Tunnel Syndrome

İlknur Aygün DEMIR¹, Ayşe OYTUN BAYRAK¹, Yüksel BEK², Musa Kazım ONAR¹

¹Ondokuz Mayis University, Faculty of Medicine, Department of Neurology, Samsun, Turkey
²Ondokuz Mayis University, Faculty of Medicine, Department of Biostatistics, Samsun, Turkey

Summary

Objective: The aim of this study was to determine the diagnostic value of the comparative techniques in carpal tunnel syndrome (CTS) at various electrophysiological stages.

Patients and Methods: One hundred hands of 61 patients and 100 hands of 50 healthy volunteers were examined electrophysiologically. The CTS was classified into four stages according to findings from routine nerve conduction studies. Three motor techniques and two sensory techniques were assessed. The motor techniques included the 2nd lumbricales to interossei distal motor latency difference (2LI-DMLD), the median-thenar to ulnar-hypothenar latency difference (THLD) and the median-thenar to ulnar-thenar latency difference (TTLD). The two sensory techniques included the digit 1 sensory latency difference (D1SLD) and the digit 4 sensory latency difference (D4SLD).

Results: From the electrophysiological assessment, we found that the CTS stage was mild in 47 hands, moderate in 47 hands and severe in 6 hands. The respective sensitivities and specificities of diagnosing CTS were 100% and 100% for D4SLD, 98% and 98% for THLD, 92% and 92% for 2LI-DMLD, 88.3% and 87% for D1SLD and 87% and 92% for TTLD. The most sensitive and specific technique were found to be D4SLD in mild cases, D4SLD and THLD in moderate cases and THLD and 2LI-DMLD in severe cases.

Conclusion: Comparative techniques can be easily performed and are useful in the diagnosis of CTS. The most valuable techniques were D4SLD in mild cases, D4SLD and THLD in moderate cases and THLD and 2LI-DMLD in severe cases.

Key words: Carpal tunnel syndrome, comparative techniques, electrophysiological stage

Karpal Tünel Sendromunun Elektrofizyolojik Tanısal Karşılaştırmalı Tekniklerinin Sensitivite ve Spesifikite Değerlendirilmesi

Özet

Amaç: Bu çalışmanın amacı karpal túnel sendromunda (KTS) karşılaştırmalı tekniklerinin tanısal değerlere farklı elektrofizyolojik evrelere göre belirlemektir.

Hastalar ve Metodlar: Alınmış bir hastanın 100 eli ile 50 sağlıklı gönüllünün 100 eli elektrofizyolojik olarak değerlendirildi. Rutin sinir iletim çalışmalara göre KTS dört evreye ayrıldı. Üç motor ve iki duysal karşılaştırmalı tekgini değerlendirildi. Motor teknikler; 2. lumbrikal-interosseus distal motor latans farkı (2LI-DMLF), median-tenar ulnar-hipotenar latans farkı (THLF) ve median-tenar ulnar-tenar latans farkı (TTLF) tekniklerini içermekte idi. İki duysal teknik ise 1. parmak duysal latans farkı (1PDLF) ve 4. parmak duysal latans farkını (4PDLF) içermekte idi.
Bulgular: Elektrofizyolojik değerlendirme sonucunda KTS 47 elde hafif, 47 elde orta ve 6 elde ağır evrede bulundu. Karşılaştırma testlerinin KTS tanısı için sensitivite ve spesiviteleri sırası ile 4PDLF için 100% ve 100%, THLF için 98% and 98%, 2LI-DMLF için 92% ve 92%, 1PDLF için 88.3% ve 87% ve TTLF için 87% ve 92% olarak bulundu. En sensitif ve spesifik teknik hafif olgularda 4PDLF, orta olgularda 4PDLF ve THLF ile ağır olgularda THLF ve 2LI-DMLF olarak bulundu.

Tartışma: Karşılaştırma teknikleri, kolayca uygulanabilen ve KTS tanısı için kullanılabilecek tekniklerdir. Tanisal açısından en değerli teknikler, hafif olgularda 4PDLF, orta olgularda 4PDLF ve THLF ile ağır olgularda THLF ve 2LI-DMLF'dir.

Anahtar Kelimeler: Karpal tünel sendromu, karşılaştırma teknikleri, elektrofizyolojik evre

INTRODUCTION
Carpal tunnel syndrome (CTS) is a common neuropathy that is caused by the entrapment of the median nerve at the wrist. The diagnosis of CTS is based on clinical history, physical examination and electrophysiological studies. Electrophysiological diagnosis of CTS is confirmed by identifying a slowing in the velocity of the median sensory nerve conduction across the wrist and median distal motor latency prolongation. In some patients with clinical symptoms and signs of CTS, the routine nerve conduction studies may be normal, so the electrophysiological diagnosis will be missed. The diagnosis may also be difficult in patients with severe CTS and in patients where the CTS is associated with polyneuropathy. Comparative techniques were developed as more sensitive methods of studying median nerve slowing in order to supplement routine nerve conduction studies. These techniques involve a comparison of the median nerve with another nerve in the same hand. In the previous studies which examined the sensitivity and specificity of these techniques in diagnosing CTS, the results were varied and diagnostic values of the techniques according to different electrophysiological stages were rarely studied. The aim of this study was to determine the diagnostic value of the most commonly used comparative techniques in CTS at various electrophysiological stages.

MATERIAL AND METHODS
Patients and controls:
The patient group consisted of 100 hands of 61 patients, who were referred to the neurophysiology laboratory and diagnosed as having CTS, both clinically and electrophysiologically. For the clinical diagnosis of CTS, the patients were questioned about the primary symptoms (paresthesias, needling, clumsiness, nocturnal symptoms) in the median nerve distribution. If they had only one of these symptoms, then at least two of the secondary symptoms (burning/cold, tightness, pain/discomfort, swelling) were explored. The clinical diagnosis was then confirmed electrophysiologically. The patients were excluded if they had any symptoms or signs of polyneuropathy and any systemic diseases or conditions potentially associated with polyneuropathy or a history of previous median nerve surgery.

The control group consisted of 100 hands of 50 healthy volunteers. Potential control subjects who had any of the symptoms or signs of CTS or had any systemic diseases or conditions that could be associated with polyneuropathy were excluded. All patients and control subjects were asked to provide signed informed consent, and a research committee at our institution approved the study.

Electrophysiological studies:
Routine nerve conduction studies for CTS assessment and comparative techniques
were performed in all patients and controls by using Neuropack-8 EMG equipment (Nihon Kohden, Tokyo, Japan) and standard techniques of supramaximal percutaneous stimulation. The skin temperature was maintained between 31 and 32°C. We compared the findings with the reference values used in our laboratory.

**Routine nerve conduction studies**

For electrophysiological CTS diagnosis we explored median nerve neuropathy related to the median nerve action potential latency abnormality at the palm-wrist segment\(^{(11)}\). For median nerve motor conduction studies, the recording electrode was placed over the motor point of the abductor pollicis muscle (APB) and the reference electrode over the distal interphalangeal joint. The median nerve was stimulated at the wrist 80 mm proximal to the recording electrode and the anteceubital fossa. For ulnar nerve conduction studies, the recording electrode was placed over the motor point of the abductor digiti minimi (ADM) muscle and the reference electrode over the middle phalanx of digit V. The ulnar nerve was stimulated at the wrist 80 mm proximal to the recording electrode and the elbow. The latencies of the median thenar and ulnar hypothenar compound muscle action potentials (CMAPs) were measured at the onset of the negative deflection.

The CTS was classified in to one of the following four stages according to the results of the electrophysiologic studies\(^{(16)}\):

1. **Mild CTS**, defined by slowing of digit-wrist segment and normal distal motor latency
2. **Moderate CTS**, defined by slowing of digit-wrist segment and abnormal distal motor latency
3. **Severe CTS**, defined by absence of median SNAPs and abnormal distal motor latency
4. **Extreme CTS**, defined by absence of thenar motor (and sensory) response

**Comparative techniques**

Three motor and two sensory comparative techniques were evaluated. The motor techniques included the 2nd lumbricales to interosseus distal motor latency difference (2LI-DMLD), the median-thenar to ulnar-hypothenar latency difference (THLD) and the median-thenar to ulnar-thenar latency difference (TTLD). The two sensory techniques included the digit 1 sensory latency difference (D1SLD) and the digit 4 sensory latency difference (D4SLD).

For the 2LI-DMLD the active electrode was placed at the motor point, localized slightly lateral to the mid-point of the third metacarpal and the reference electrode was placed over the proximal inter-phalangeal joint of the second digit. The median and ulnar nerves were stimulated at the wrist at an equal distance (range; 8-10cm) from the active electrode. The difference between the two distal latencies was then calculated\(^{(19)}\).

For sensory comparative techniques, the antidromic technique was used. For D4SLD ring electrodes placed over digit 4 and identical distances (11-13cm) were used for median and ulnar stimulation at the wrist. For D1SLD, ring electrodes...
placed over digit 1 and identical distances (11-13cm) were used for median stimulation at the wrist and radial stimulation at the wrist along the lateral border of the radial bone.

**Statistical Analyses:**

Statistical analyses were performed by using SPSS Version 15.0 for Windows (SPSS, Chicago, IL, USA). The descriptive data are standard deviation (SD), or median (minimum-maximum) when presented as mean necessary, according to the normal distribution of parameters. The Shapiro-Wilk test was used to analyze the normal distribution of quantitative outcomes. The variables which were not met normality assumption compared by using non-parametric tests such as Mann-Whitney-U test. P values less than 0.05 were considered statistically significant. The categorical variables were assessed by using chi-square tests for cross-tables.

A receiver operating characteristics curves (ROC) analysis was performed to assess the efficiency of the comparative techniques in the diagnosis of CTS for different electrophysiological stages, and to determine the sensitivities, specificities and the cutoff points. ROC analysis was calculated using the NCSS-PASS program (PASS 2005; NCSS 2004, Kaysville, UT, USA).

**RESULTS**

One hundred hands of 61 patients (45 women and 16 men) and 100 hands of 50 healthy volunteers (35 women and 15 men) were included in the study. Thirty nine patients (26 women and 13 men) had CTS bilaterally. The mean age of the patients was 45 years (range: 31-58 years), and the mean age of the control subjects was 44 years (range: 32-58 years). No significant differences in age or gender were observed between the patients and controls.

The latencies of median CMAPs and SNAPs were longer in the CTS group than the control group, and the amplitudes and conduction velocities were less in the CTS group than the control group. These differences were statistically significant. In the electrophysiological evaluation, we found that the CTS stage was mild in 47 hands, moderate in 47 hands, severe in 6 hands, and extreme in none.

The sensitivity and specificity of the comparative techniques, the area under curve and the cutoff points for each technique for diagnosing CTS are summarized in Table 1. In addition, the sensitivity and specificity of the comparative techniques for the different electrophysiological stages of CTS are summarized in Table 2. The data of the ROC curves indicated superior diagnostic performance of the D4SLD (Figure 1). According to the electrophysiological stages, D4SLD in mild cases, D4SLD and THLD in moderate cases and THLD and 2LI-DMLD in severe cases were found to be the most sensitive and specific techniques. In addition, TTLD was found to be the least sensitive technique in mild cases.
Table 1. The sensitivity and specificity of the comparative techniques, the area under curve and the cut off points for each technique.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Cut off</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>D4SLD</td>
<td>0.45</td>
<td>100</td>
<td>100</td>
<td>1.000</td>
</tr>
<tr>
<td>D1SLD</td>
<td>0.30</td>
<td>88.3</td>
<td>87.0</td>
<td>0.950</td>
</tr>
<tr>
<td>THLD</td>
<td>0.75</td>
<td>98.0</td>
<td>98.0</td>
<td>0.988</td>
</tr>
<tr>
<td>TTLD</td>
<td>0.30</td>
<td>87.0</td>
<td>92.0</td>
<td>0.925</td>
</tr>
<tr>
<td>2LI-DMLD</td>
<td>0.45</td>
<td>92.0</td>
<td>92.0</td>
<td>0.985</td>
</tr>
</tbody>
</table>

2LI-DMLD: 2nd lumbricales to interossei distal motor latency difference, THLD: Median-thenar to ulnar-hypothenar latency difference, TTLD: Median-thenar to ulnar-thenar latency difference, D1SLD: Digit 1 sensory latency difference, D4SLD: Digit 4 sensory latency difference, AUC: Area under curve

Table 2. The sensitivity and specificity of the comparative techniques for the different electrophysiological stages of CTS

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Stage I</th>
<th>Stage II</th>
<th>Stage III</th>
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<tbody>
<tr>
<td>Number of cases</td>
<td>47</td>
<td>47</td>
<td>6</td>
</tr>
<tr>
<td>D4SLD</td>
<td>Sensitivity(%)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Specificity(%)</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>D1SLD</td>
<td>Sensitivity(%)</td>
<td>86</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Specificity(%)</td>
<td>80</td>
<td>95</td>
</tr>
<tr>
<td>THLD</td>
<td>Sensitivity(%)</td>
<td>96</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Specificity(%)</td>
<td>97</td>
<td>100</td>
</tr>
<tr>
<td>TTLD</td>
<td>Sensitivity(%)</td>
<td>80</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Specificity(%)</td>
<td>83</td>
<td>95</td>
</tr>
<tr>
<td>2LI-DMLD</td>
<td>Sensitivity(%)</td>
<td>92</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Specificity(%)</td>
<td>90</td>
<td>97</td>
</tr>
</tbody>
</table>

2LI-DMLD: 2nd lumbricales to interossei distal motor latency difference, THLD: Median-thenar to ulnar-hypothenar latency difference, TTLD: Median-thenar to ulnar-thenar latency difference, D1SLD: Digit 1 sensory latency difference, D4SLD: Digit 4 sensory latency difference
DISCUSSION

In this study we evaluated the specificity and sensitivity of the comparative techniques used for diagnosing CTS of different electrophysiological stages. Because many techniques are used by physicians, we chose to assess only those techniques that are frequently used and showed the highest specificity and sensitivity in previous studies.

According to our results, the respective sensitivities and specificities in diagnosing CTS were 100% and 100% for D4SLD, 98% and 98% for THLD, 92% and 92% for 2LI-DMLD, 88.3% and 87% for D1SLD and 87% and 92% for TTLD. According to electrophysiological stages, D4SLD in mild cases, in D4SLD and THLD moderate cases and THLD and 2LI-DMLD in severe cases were found to be the most sensitive and specific comparative techniques.

Previously, the upper latency difference limit was reported to range from 0.4 to 1 ms for D4SLD, and from 0.3 to 1 ms for D1SLD. In our study, the cutoff values for D4SLD and D1SLD were found to be 0.45 ms and 0.3 ms, respectively, and these values were similar to those reported in the literature. However, the sensitivity and specificity values that we obtained for the sensorial techniques differed from previous studies. Atroshi et al. compared the SNAP latencies of the median nerve with the ulnar and radial nerves and similar to our observations, found D4SLD was to be the most sensitive. Uncini et al. evaluated D4SLD, 2LI-DMLD and

![ROC Curves](image)

Figure 1: ROC curves for each comparative techniques. (2LI-DMLD: 2nd lumbricales to interossei distal motor latency difference, THLD: Median-thenar to ulnar-hypothenar latency difference, TTLD: Median-thenar to ulnar-thenar latency difference, D1SLD: Digit 1 sensory latency difference, D4SLD: Digit 4 sensory latency difference)
differences between median and ulnar mixed nerve latencies from palmar stimulation. Similar to our findings, the most sensitive technique was found to be D4SLD and the cutoff points of D4SLD and 2LI-DMLD were 0.5 and 0.6, respectively. The authors explained the greater sensitivity of D4SLD by the funicular topography and consequently greater susceptibility to compression of the cutaneous fibers at the distal carpal tunnel. In another study, the authors evaluated patients with underlying axonal polyneuropathy, in which patients were divided into CTS cases and controls, using D4SLD, 2LI-DMLD and mixed palmar sensory latency difference. The diagnostic cutoffs were reported to be >0.8 and >0.4 for the 2LI-DMLD and D4SLD, respectively, which are similar to our findings. However, the respective sensitivities and specificities in diagnosing CTS were reported to be 71% and 81% for D4SLD while 80% and 85% for 2LI-DMLD, which differ from our findings. The greater diagnostic accuracy for D4SLD in our study may be explained by the fact that most of our cases were mild cases with an absence of underlying axonal polyneuropathy.

Demirci et al. evaluated only mild CTS cases and found D1SLD (sensitivity 94%, cutoff 0.3 ms) to be more sensitive than D4SLD (sensitivity 85%, cutoff 0.6 ms). Cassvan et al. evaluated D1SLD and D4SLD and they also found D1SLD to be more sensitive. Cifu et al. evaluated patients with demyelinating peripheral neuropathy and reported that D1SLD may serve as a sensitive screening technique for CTS because superficial radial nerve involvement in demyelinating peripheral neuropathy occurs later than demyelination of other sensory nerves. Other studies have also shown D1SLD to be a sensitive technique for diagnosing CTS. Similar to previous reports we also found D1SLD to be a sensitive test for diagnosing CTS, however, when compared with other techniques it was not found to be the most sensitive test. In most previous studies, the authors did not compare D1SLD with other techniques and/or did not evaluate the diagnostic accuracy of D1SLD for different electrophysiological stages, which may explain why we found different results for the diagnostic accuracy of D1SLD.

Results also differ in the diagnostic accuracy of the motor comparative techniques in the literature. Although many studies evaluated 2LI-DMLD in diagnosing CTS, studies evaluating THLD and TTLD are limited. Sander et al. evaluated TTLD and THLD in clinically diagnosed CTS patients and the cutoffs were 0.8 ms and 1.2 ms, respectively. The diagnostic sensitivities were 95% for TTLD and 85% for THLD while the specificities were 100% for both. In our study the cutoffs were lower. Specifically, the cutoffs were 0.3 ms for TTLD and 0.75 ms for THLD and THLD showed greater sensitivity. In another study CTS patients were categorized according to the different electrophysiological stages, and the authors evaluated 2LI-DMLD, TTLD and D4SLD. Similar to our findings, this study reported greater sensitivity for D4SLD in mild and moderate cases and greater sensitivity for 2LI-DMLD and TTLD in severe cases. In other studies, the cutoff for THLD ranged from 1 to 1.8 ms. For both the THLD and THLD comparative techniques, the cutoffs were reported to be higher than our values. These varying results among studies may be explained by the differential inclusion criteria and the number of patients in different electrophysiological stages. Similar to our study, previous studies reported cutoff values ranging from 0.4 to 1 ms for 2LI-DMLD, and 2LI-DMLD has shown greater sensitivity in diagnosing CTS. As reported by Meena et al., the difference between cutoff values may be explained by physical and biological factors, such as the placement of
the active electrode and the measurement of latency. One study also evaluated diagnostic accuracy according to the electrophysiological stages, and 2LI-DMLD was found to have a greater sensitivity in moderate and severe stages of CTS\(^{14}\). In our study, we found that D4SLD was the most sensitive technique for diagnosing CTS. However, 2LI-DMLD and THLD were also found to be highly sensitive in mild cases. As reported by Meena et al., this observation is contrary to the belief that motor fibers are protected from compression in mild cases\(^{14}\).

The evaluation of various comparative techniques, specifically according to the electrophysiological stages of CTS, is the primary advantage of our study. However, the unblinded nature of the study, and the lack of patients with extreme CTS are the limitations.

Comparative techniques are easily performed and may be valuable tests for diagnosing CTS in some patients, especially those with very mild CTS, with severe CTS and CTS associated with polyneuropathy. In particular, D4SLD in mild cases, D4SLD and THLD in moderate cases, and THLD and 2LI-DMLD in severe cases, may be useful complementary tests to routine nerve conduction tests in such situations where there is a problem in diagnosing CTS.

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**Correspondence to:**
Ayşe Oytun Bayrak
E-mail: oytun.bayrak@gmail.com

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**REFERENCES**


