

Segmental study of the median nerve versus comparative tests in the diagnosis of mild carpal tunnel syndrome

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Accepted 4 February 2006

Available online 4 April 2006

Abstract

Objective: The aims of this study were to analyze normative data of nerve conduction studies (NCS) by optimal transformations, and compare the utility of electrodiagnostic tests in detecting mild carpal tunnel syndrome (CTS).

Methods: In 131 hands of patients with mild CTS and 136 hands of controls, the segmental study of the median nerve between the digit–palm and palm–wrist segments, and the median-to-ulnar and median-to-radial comparative tests were performed. Normal limits were derived by calculating the mean \pm 2 standard deviations of the optimally transformed data of the controls. The specificity, sensitivity, and misclassification rate were calculated to evaluate the utility of each test.

Results: All tests had high specificities, ranging from 98.5 to 100%. The distoproximal latency ratio (DPLR) of the median nerve showed the highest sensitivity and the difference between the median and radial sensory latencies (DIM–DIR) the second highest, but there was no statistical difference between them. The difference between the median and ulnar mixed nerve latencies in the palm-to-wrist segment (PM–PU) showed the lowest sensitivity. Misclassification rates of the DPLR, DIM–DIR, and PM–PU were 6.9, 3.8, and 6.1%, respectively.

Conclusions: Optimal transformation of NCS data is mandatory to diminish the effect of skewness and enhance the diagnostic accuracy. As compared to the comparative tests, the segmental study of the median nerve is more easily applied and yields higher sensitivity in detecting mild CTS.

Significance: With a high diagnostic yield and easy application, the segmental study of the median nerve may routinely be used to evaluate patients with mild CTS.

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Keywords: Carpal tunnel syndrome; Median nerve; Electrodiagnosis; Segmental study; Comparative test; Transformation

1. Introduction

The diagnosis of carpal tunnel syndrome (CTS) requires confirmation of the symptoms and signs with objective electrodiagnostic tests which identify and localize dysfunction of the median nerve in the carpal tunnel (Johnson, 1993). With increased knowledge of CTS, many patients with typical CTS symptoms are referred earlier and fail to show abnormalities using diagnostic criteria created by

conventional electrodiagnostic methods (Jablecki et al., 1993; Jackson and Clifford, 1989). In order to improve the electrodiagnostic yield, a number of nerve conduction studies (NCS) have been developed, which include: (1) segmental study of the median nerve with stimulation proximal and distal to the carpal tunnel (Andary et al., 1996; Buchthal and Rosenfalck, 1971; Cruz Martinez et al., 1978; Kimura, 1978, 1979; Kuntzer, 1994; Lew et al., 2005; Monga et al., 1985; Padua et al., 1996; Sharma et al., 2001; Wongsam et al., 1983); (2) sensory latency or conduction velocity (CV) difference between the median and ulnar nerves (Charles et al., 1990; Foresti et al., 1996; Jackson and Clifford, 1989; Johnson et al., 1981; Lauritzen et al., 1991; Uncini et al., 1989, 1993); (3) sensory latency or CV

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difference between the median and radial nerves (Carroll, 1987; Cassvan et al., 1988; Ghavanini et al., 1996; Jackson and Clifford, 1989; Johnson et al., 1987; Pease et al., 1989); and (4) median and ulnar latency difference after palmar stimulation (Jackson and Clifford, 1989; Mills, 1985; Sander et al., 1999). There are few studies of comparisons of the segmental study of the median nerve with comparative tests of the median and ulnar or radial nerves, and there is no agreement on which of these tests is more sensitive or specific in diagnosis of mild CTS (Andary et al., 1996; Demirci and Sonel, 2004; Kuntzer, 1994; Padua et al., 1996; Pease et al., 1989).

Normal limits for NCS parameters are usually calculated as the mean ± 2 standard deviations (SD) of controls assuming the data are normally distributed. However, many variables in electrodiagnostic medicine are skewed in one direction, and do not follow a normal distribution in the normal population. Optimal transformation is applied to reduce the degree of skewness and to convert data into a distribution more closely approximating a Gaussian curve. Hence, normative data are best derived from the mean ± 2 SD of the optimally transformed data (Campbell and Robinson, 1993; Dorfman and Robinson, 1997; Robinson et al., 1991). To the best of our knowledge, there is no study of comparisons of different electrodiagnostic tests of CTS, which apply transformation methods for normal limits. The aims of this study were to analyze normative data of NCS by optimal transformations of the control data, and compare the utility of the segmental study of the median nerve with the median-to-ulnar and median-to-radial comparative tests in detecting mild CTS.

2. Patients and methods

2.1. Control subjects

One hundred and thirty-six healthy subjects (mean age 49.67 years; range 21–79 years; 82.4% females) were evaluated with unilateral NCS. A screening history and physical examination were carried out for all subjects to exclude any obvious peripheral neuropathy, neuromuscular disease, as well as relevant systemic conditions such as diabetes, uremia, excessive alcohol intake, or toxin exposure.

2.2. Patients

Patients referred to the electrodiagnostic laboratory were prospectively evaluated. The diagnosis of CTS was made clinically based upon paresthesia in the median nerve territory with histories and physical examination suggestive of CTS, including at least one of the following: (1) nocturnal paresthesia exacerbation; (2) symptoms precipitated by manual activities such as using hand tools or driving a car; (3) a positive Phalen's sign or Tinel's sign; (4) weakness or

atrophy of the thenar muscles. Subjects with a history or physical examination suggestive of a neuromuscular disorder other than CTS or with abnormal ulnar distal motor latency (DML) or sensory latency were excluded. Totally, 235 hands in 153 patients were included. Eighty-five percent of the hands showed nocturnal exacerbation of paresthesia. In 70% of the hands, symptoms were precipitated by manual activities. A positive Phalen's sign or Tinel's sign was present in 65% of the hands. Weakness or atrophy of the thenar muscles was only present in 10% of the hands. One hundred and four symptomatic hands had abnormal median DML or sensory latency (see results for the criteria of abnormality) making obvious the electrodiagnosis of CTS. Of these 104 hands, 13 had an absent median sensory response and 3 had an absent median motor response. One hundred and thirty-one mild CTS hands of 104 patients (mean age 49.25 years; range 28–74 years; 84.6% female) had normal median DML and sensory latency.

2.3. Electrodiagnostic methods

A Medelec Synergy electromyograph (Medelec, Surrey, England) was used in the study. Filters were set at 2 Hz and 10 kHz for motor studies and at 20 Hz and 2 kHz for sensory studies. The sweep speed was set at 1 ms/division. One centimeter disc recording electrodes were used for motor studies and the median and ulnar mixed nerve studies, and ring recording electrodes were used for sensory studies. Supramaximal stimuli of 0.05–0.1 ms were delivered by a hand-held bipolar stimulator. For sensory studies, the potentials were recorded by averaging 16 responses, and a gain setting of 10 μ V/division was used to determine latencies measured from the stimulus artifact to the negative peak. Latencies were measured to the nearest 0.05 ms using a cursor and digital display. Hand skin temperatures were continuously monitored and maintained at 32–34 °C during the procedures.

2.3.1. Segmental study of the median nerve

The segmental study of the median nerve was performed in control and CTS hands. The antidromic sensory latency of the median nerve was recorded from digit 3 with the active recording electrode placed at the proximal interphalangeal (PIP) joint. The reference electrode was placed 4 cm distal to the active electrode or placed distally with a maximal possible interelectrode spacing (of at least 3 cm) in the small hands (2 of 136 control hands and 5 of 235 CTS hands). The median nerve was stimulated 7 cm proximally in the palm and 14 cm proximally at the wrist by a bipolar stimulator. Distances were measured in fully extended hands with a flexible tape measure. The sensory conduction time across the carpal tunnel (palm–wrist latency, PWL) was determined by subtracting the latency obtained in the palm (digit–palm latency, DPL) from the latency at the wrist (digit–wrist latency, DWL). Two indices, for segmental

comparison of conduction between digit 3 and the palm and between the palm and the wrist, were calculated as follows:

$$\text{Distoproximal latency ratio (DPLR)} = \text{DPL}/\text{PWL},$$

and

$$\text{Distoproximal latency difference (DPLD)} = \text{DPL} - \text{PWL}.$$

2.3.2. Comparative tests

We performed three comparative tests in control and mild CTS hands. The first comparative test compared the median and ulnar antidromic sensory latencies at digit 4. The active recording electrode was placed at the PIP joint, and the reference electrode was placed 4 cm distally or placed distally with a maximal possible interelectrode spacing (of at least 3 cm) in the small hands. Stimulation was delivered at a distance of 14 cm over the median and ulnar nerves at the wrist. The difference between the median and ulnar latencies was calculated as D4M–D4U.

The second test compared the median and radial antidromic sensory latencies at the thumb. The active recording electrode was placed at the metacarpophalangeal joint, and the reference electrode was placed distally with a maximal possible interelectrode spacing (of at least 3 cm). Stimulation was delivered at a distance of 10 cm over the median nerve at the wrist and the radial nerve on the dorsolateral surface of the wrist. The difference between the median and radial latencies was calculated as D1M–D1R.

The third test compared the median and ulnar mixed nerve latencies in the palm-to-wrist segment. The median nerve was stimulated in the palm, between the second and third metacarpal bones, at a distance of 8 cm distal to the median recording site at the wrist. The ulnar palmar latency was made similarly, but with the recording over the ulnar nerve at the wrist and the stimulation between the fourth and fifth metacarpal bones. The difference between the median and ulnar palmar latencies was calculated as PM–PU.

2.4. Statistical analysis

For the NCS parameters of the controls, transformations were performed to bring the coefficient of skewness closer to zero, and to convert data to a normal distribution. The ideal normal limits of the controls were derived from the mean ± 2 SD of the optimally transformed data and by converting these endpoints back to original units, or the mean ± 2 SD of the raw data if they followed a normal distribution.

The specificity of each test was calculated as: (number of control hands with a normal test result/number of control hands) $\times 100$. The sensitivity of each test was calculated as: (number of mild CTS hands with an abnormal test result/number of mild CTS hands) $\times 100$. The misclassification rate was determined by counting the percentage of mild CTS hands that were called normal by the criteria of abnormality using the raw data, but would have been abnormal using that of the optimally transformed data, or the percentage of mild CTS hands that were called abnormal by the criteria of abnormality using the raw data, but would have been normal using that of the optimally transformed data. The McNemar chi-square statistic was used to test the statistical significance of comparisons between the sensitivities of the segmental study of the median nerve and the comparative tests. A *P*-value of <0.05 was considered statistically significant.

3. Results

3.1. Control subjects

The results of electrodiagnosis in the controls are summarized in Table 1. The raw data of the DPLD and D4M–D4U closely followed a normal distribution and no method of transformation brought the coefficient of skewness closer to zero. The lower normal limit of

Table 1
Summary of normal values in 136 control hands

Variable	Mean \pm SD	Range	Uncorrected coefficient of skewness	Criteria of abnormality by raw data	Best transformation method	Corrected coefficient of skewness	Criteria of abnormality by transformed data
Median DML (ms)	3.22 \pm 0.30	2.60–3.85	0.26	> 3.85	Log	0.07	> 3.90
DWL (ms)	3.19 \pm 0.24	2.70–3.75	0.23	> 3.70	Log	0.06	> 3.70
DPLR	1.33 \pm 0.15	1.03–1.83	0.27	< 1.02	Log	–0.02	< 1.05
DPLD (ms)	0.44 \pm 0.18	0.05–0.95	–0.06	< 0.05	None		
D4M–D4U (ms)	0.09 \pm 0.15	–0.25–0.40	0.05	> 0.40	None		
D1M–D1R ^a (ms)	0.21 \pm 0.13	–0.10–0.45	–0.23	> 0.50	Square	0.01	> 0.45
PM–PU ^a (ms)	0.08 \pm 0.13	–0.20–0.40	0.10	> 0.35	Square root	0.00	> 0.40

Median DML, median distal motor latency from wrist to abductor pollicis brevis; DWL, median sensory latency from wrist to digit 3; DPLR, distoproximal latency ratio; DPLD, distoproximal latency difference; D4M–D4U, difference between median and ulnar sensory latencies at digit 4; D1M–D1R, difference between median and radial sensory latencies at thumb; PM–PU, difference between median and ulnar mixed nerve latencies from palmar stimulation; SD, standard deviation.

^a Transformation of (raw value + 1) due to the presence of negative values, such as square root of (raw value of PM–PU + 1).

Table 2
Sensitivities, specificities, and misclassification rates of electrodiagnostic tests

Test	Criteria of abnormality by raw data		Criteria of abnormality by ideal normal limits ^a		
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Misclassification rate (%)
DPLR	71.0	100	77.9	98.5	6.9
DPLD	71.8	100	71.8	100	
D4M–D4U	70.2	100	70.2	100	
D1M–D1R	70.2	100	74.0	100	3.8
PM–PU	59.5	99.3	53.4	100	6.1

^a Ideal normal limits: derived from mean \pm 2 SD of the raw data of DPLD and D4M–D4U, and from mean \pm 2 SD of the optimally transformed data of DPLR, D1M–D1R, and PM–PU. All abbreviations as in Table 1.

the DPLD was 0.05 ms and the upper normal limit of the D4M–D4U was 0.40 ms.

The median DML, DWL, DPLR and PM–PU values showed a positive skew, and log or square root transformations brought the coefficient of skewness closer to zero. The D1M–D1R showed a negative skew, and square transformation brought the coefficient of skewness closer to zero. After an optimal transformation, the upper normal limit of the median DML was 3.90 ms and the upper normal limit of the DWL was 3.70 ms. The lower normal limit of the DPLR was 1.05, the upper normal limit of the D1M–D1R were 0.45 ms, and the upper normal limit of the PM–PU was 0.40 ms.

3.2. Specificities, sensitivities, and misclassification rates of the segmental study and comparative tests

The specificities, sensitivities, and misclassification rates of the segmental study of the median nerve and the median-to-ulnar and median-to-radial comparative tests are shown in Table 2. All tests had high specificities, ranging from 98.5 to 100%, whether raw data or transformed data were used. The highest diagnostic yield was obtained when all tests were combined, and the combined sensitivity was 84.7% using the criteria of abnormality with an ideal normal limit. Using the criteria of abnormality with an ideal normal limit, the DPLR showed the highest sensitivity being <1.05 in 77.9% of

mild CTS hands, and the D1M–D1R showed the second highest sensitivity being >0.45 ms in 74.0% of hands. The DPLD was <0.05 ms in 71.8% of hands, and the D4M–D4U was >0.40 ms in 70.2% of hands. The PM–PU showed the lowest sensitivity being >0.40 ms in only 53.4% of hands.

Using the mean -2 SD of the raw data of the DPLR as a normal limit misclassified 6.9% of mild CTS hands as normal, when compared with the mean -2 SD of the log-transformed data. Using the mean $+2$ SD of the raw data of the D1M–D1R as a normal limit misclassified 3.8% of mild CTS hands as normal, when compared with the mean $+2$ SD of the square-transformed data. Using the mean $+2$ SD of the raw data of the PM–PU as a normal limit misclassified 6.1% of mild CTS hands as abnormal, when compared with the mean $+2$ SD of the square root-transformed data.

3.3. Comparisons of sensitivities of the segmental study and comparative tests

The results of comparisons between the sensitivities of the segmental study of the median nerve and the comparative tests are shown in Table 3. Both DPLR and DPLD had much greater sensitivity compared with the PM–PU ($P=0.00$). Although the DPLR had the highest sensitivity, there were no significant differences compared to the D4M–D4U or D1M–D1R.

Table 3
Comparisons of sensitivities^a of segmental study and comparative tests in 131 mild CTS hands

Test	D4M–D4U			D1M–D1R			PM–PU		
	Positive hands ^b	Negative hands ^c	<i>P</i> -value	Positive hands	Negative hands	<i>P</i> -value	Positive hands	Negative hands	<i>P</i> -value
<i>DPLR</i>									
Positive hands	84	18	0.08	90	12	0.36	69	33	0.00
Negative hands	8	21		7	22		1	28	
<i>DPLD</i>									
Positive hands	80	14	0.85	84	10	0.68	64	30	0.00
Negative hands	12	25		13	24		6	31	

^a Sensitivity using criteria of abnormality by ideal normal limits.

^b Positive hands: hands with an abnormal test result.

^c Negative hands: hands with a normal test result. All abbreviations as in Table 1.

4. Discussion

This prospective study meets all 6 criteria recommended by the American Association of Electrodiagnostic Medicine (AAEM) Quality Assurance Committee, and our results are in accordance with the AAEM's statement that the segmental study of the median nerve is the most sensitive test in the electrodiagnosis of mild CTS (Jablecki et al., 2002). Our results are also in agreement with those of Andary et al. (1996) and Uncini et al. (1993) that the difference between median and ulnar nerve latencies from palmar stimulation has relatively low sensitivity because both sensory and motor fibers rather than only sensory fibers are tested. Although there was no significant difference between the sensitivity of the segmental study of the median nerve and that of the DIM–D1R, there were 12 cases with an abnormal test result of the DPLR but a normal test result of the DIM–D1R, and another 7 cases with an abnormal test result of the DIM–D1R but a normal test result of the DPLR (Table 3). These electrophysiologic findings suggest that the effect of compression of branches of the median nerve under the carpal tunnel is not uniform but affects certain branches more than others among different patients.

The sensitivities of the tests in our study were lower than those of Demirci and Sonel (2004), Padua et al. (1996) and Pease et al. (1989). The difference is primarily due to various degrees of severity of CTS among these studies. First, CTS patients studied by Padua et al. (1996) were not limited to those with mild disease, and hence higher sensitivities were reported. Second, the upper normal limit of the median sensory latency of the controls in our study (3.7 ms) was lower than the criterion used by Pease et al. (4.0 ms) (1989). Demirci and Sonel (2004) also reported a higher median sensory latency among the CTS group. Our lower normal limit for the median sensory latency results in more cases of mild CTS with the normal comparative tests and segmental study of the median nerve. Pease et al. (1989) reported that the sensitivity of the ratio of sensory conduction of the median nerve between the wrist–palm segment and wrist–digit segment was lower than that of the median-to-ulnar or median-to-radial comparative tests in detecting mild CTS. Andary et al. (1996) had similar observations and concluded that the ratio of median sensory latency across the wrist to the latency from the wrist to the digit added no more yield to the diagnosis of CTS. In contrast, Demirci and Sonel (2004) and Padua et al. (1996) reported a higher sensitivity of the segmental study of the median nerve than that of the comparative tests. Our results showed that the DPLR had the highest sensitivity and the DIM–D1R the second highest sensitivity, but no significant difference existed between them. The disparity in the sensitivities among different studies is probably a consequence of selection biases in the choice of the study population, differences in methodology, the use of different cutoff points to define an abnormal value (AAEM, 2002),

and different statistical methodologies (Robinson et al., 1991).

Our results are in accordance with those of Robinson et al. (1991) that motor and sensory latencies were positively skewed. We also demonstrated that sensory latency ratio of the median nerve was positively skewed, but latency differences of the segmental study and comparative tests may follow a normal distribution, or be positively or negatively skewed. A boundary to the left (on the side of shorter latency) is a possible explanation for positive skews of latency measurements (Robinson et al., 1991). However, the reasons for positive skews of latency ratio of the median nerve and positive or negative skews in latency differences of the comparative tests are not known, and further studies based on a larger number of subjects may be needed. Although transformation seemed to produce only a small absolute change in the normal limits (0.03 for the DPLR, and 0.05 ms for the DIM–D1R and PM–PU), this is meaningful in terms of the percentage of hands misclassified. For example, the distribution of the DPLR was positively skewed in the controls, and 6.9% of mild CTS hands would be misclassified as normal if the abnormal cutoff value was based on the mean–2 SD of the raw data, leading to diagnostic underestimation (Table 2). Thus, application of optimal transformations to generate normative values in the segmental study of the median nerve and the comparative tests is important for diminishing the effect of skewness and enhancing diagnostic accuracy.

The rationale for the segmental study of the median nerve is that the slow-conducting segment of the nerve within the carpal tunnel is quite short, and the segment of the nerve distal to the carpal tunnel is little impaired in early CTS. If this normally conducting segment distal to the carpal tunnel is included in latency measurements as in the conventional techniques, the abnormality may be diluted and the overall conduction time may remain within normal limits (Jackson and Clifford, 1989). The shorter the nerve segment enclosing the abnormality, the more prominent the slowing of conduction will be. The disadvantages of the orthodromic sensory conduction study performed by Padua et al. (1996) include the small amplitude of the sensory nerve action potential (SNAP), interference by the stimulus artifact, and hence difficulty in accurately identifying the onset latency for velocity calculation, especially when testing the short nerve segment (Wilbourn, 1994). Thus, Padua et al. (1996) mentioned that all measurements used to calculate the distoproximal ratio of the CV must be made with extreme care because of the relatively short distances of the digit to the palm and the palm to the wrist. To tackling such problems, we performed antidromic stimulation over the already premeasured, marked points in the palm and at the wrist, and measured peak latencies rather than onset latencies for both DPLR and DPLD calculations. In most of the hands, the distance between the PIP joint and the tip of the finger exceeded 4 cm, and we placed the reference electrode 4 cm distal to the active electrode. In extremely

small hands (2 of 136 control hands and 5 of 235 CTS hands), we placed the reference electrode distally with a maximal possible interelectrode spacing (of at least 3 cm) as done at the thumb. An interelectrode spacing of the recording electrodes exceeding 3 cm can avoid distortion of the SNAP waveform (Wilbourn, 1994). The amplitude of the SNAP obtained by this method is larger than that by orthodromic stimulation, and measurement of the peak latency is easier and more accurate than that of the onset latency. The formulas of the DPLR and DPLD are simpler than that of the distoproximal ratio of the CV (digit-to-palm CV, palm-to-wrist CV, and their ratio), and hence diminish the inherent error of calculation (Sharma et al., 2001). In addition, similar formulas for calculation, and the agreement of the antidromic techniques and the peak latency measurements in our study increase the comparability among the DPLD, and median-to-ulnar and median-to-radial comparative tests. The DPLR and DPLD also take advantage of the comparative approach in which each patient serves as his own control, and intersubject variability in the electrodiagnosis is eliminated (Carroll, 1987; Padua et al., 1996; Uncini et al., 1993).

The AAEM recommended comparison of median sensory or mixed nerve conduction through the carpal tunnel to NCS of proximal or distal segments of the median nerve if normal median sensory NCS across the wrist with a distance of 13–14 cm. (AAEM, 2002; Jablecki et al., 2002). Our study shows that the segmental study of the median nerve, requiring only an additional stimulus in the palm, is easily applied in electrodiagnostic laboratories. As compared to the median-to-ulnar and median-to-radial comparative tests, the segmental study of the median nerve is simple and timesaving, and produces lesser discomfort to patients. In addition, the DPLR had the highest diagnostic yield. We recommend that the segmental study of the median nerve may routinely be used in the evaluation of patients with mild CTS. Optimal transformation of NCS data is mandatory to diminish the effect of skewness and to enhance the diagnostic accuracy. Each laboratory should establish its own normal limits of NCS parameters in the electrodiagnosis of CTS based on optimally transformed data.

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