What Is the Most Sensitive Test for Diagnosing Carpal Tunnel Syndrome?

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Objective: To compare sensitivities between 7 principal nerve conduction studies (NCS) for diagnosing carpal tunnel syndrome (CTS).
Method: In 104 CTS and 64 control hands, following "Standard" NCSs were examined simultaneously: (1) Median sensory NCS; (2) segmental wrist-palm sensory NCS; (3) 4th digit latency difference; (4) 1st digit latency difference and (5) palmar mixed nerve latency difference. As "Guideline" and "Option" NCSs, we also examined: (6) Median motor distal latency and (7) second lumbrical-interossei latency difference (2LILD). Forty-nine CTS hands were divided into a milder subgroup only if action potentials could be recorded using all tests applied; that is, those with any absent potentials were excluded from the subgroup. Sensitivities and specificities were compared to each other.
Results: In all CTS hands, the sensitivity of test (1), (2), (3), (4), (5), (6) and (7) was 83, 87, 92, 90, 90, 70 and 92%, respectively. In the milder subgroup, it was 67, 78, 84, 82, 84, 43, and 84% in the same order. There was no statistical difference between Standard tests and 2LILD. Specificities of all tests were over 95%.
Conclusions: All "Standard" tests and 2LILD have high comparable sensitivities. Therefore, 2LILD should be recommended as "Standard" NCS detecting CTS.

Key words: Carpal tunnel syndrome; Median nerve; Sensitivity; Nerve conduction study; Second lumbrical interossei study

INTRODUCTION

Electrodiagnostic (EDX) tests supply useful information for an assessment of neurophysiological severity and a decision of therapeutic strategy in patients with carpal tunnel syndrome (CTS). These tests must have high sensitivity and specificity for diagnosis. In the past four decades, a number of EDX tests have been performed: segmental sensory latency from wrist to palm (SLWP) [1–3], median-ulnar sensory latency difference to 4th digit (LD4) [4–7], median-radial sensory latency difference to 1st digit (LD1) [8–10], and median-ulnar mixed nerve palm latency difference from palm to wrist (MNLD) [5, 11], have been developed and investigated for their sensitivity limits. Hence, these four tests have been encouraged in patients suspected of CTS, as "Standard" EDX test (Standard Test) recommended by American Association of Electrodiagnostic Medicine (AAEM), American Academy of Neurology and the American Academy of Physical Medicine and Rehabilitation [12, 13]. In the recommendation, pooled sensitivities were analyzed from results of previous literatures [13]. However, some inconsistencies were described and questions remain. Firstly, are there any differences in sensitivity (i.e., an order of priority) between these Standard Tests? Next, the median motor nerve conduction study (NCS) is commonly less sensitive compared with sensory NCS in CTS. However, the pooled sensitivity of median sensory nerve conduction velocity between wrist and digit (MSCV) and median motor distal latency (MDL) was almost same (0.65 vs. 0.63). Significant difference between these values was not confirmed. However whereas MSCV was recommended as "Standard", MDL was suggested as "Guideline". Finally, we questioned whether the sensitivity of a second lumbrical interossei latency difference (2LILD), which is the test to compare the latency between median and ulnar nerve motor conduction [14, 15], was as high as Standard Tests or not? It has been well known for being useful in detecting mild CTS hands [16–18] as well as severe ones [17, 19–21]. In contrast, some studies had reported a low sensitivity of detecting mild hand CTS [22, 23]. Therefore, controversy remains. To resolve this issue, the "Option" EDX test (Option Test) has been recommended [12, 13]. These uncertainties were due to researches not comparing sensitivities and specificities between all of the EDX tests in patients with CTS simultaneously. Thus, the goal of the present study was to compare sensitivities of principal EDX tests, which are well recognized for electromyographers.

MATERIALS AND METHODS

Between November 2008 and December 2011, we studied healthy subjects prospectively (i. e., a control group) and patients with symptoms and signs suggestive of CTS (described as follows). Patients were suspected clinically as CTS by experienced hand surgeons, neurologists, and physiatrists. They were then referred to the electromyography laboratory at Tokai

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The present study was approved by the Clinical Research Review Committee of the Tokai University School of Medicine and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all subjects before the EDX studies were initiated.

Control group

A control group consisted of healthy volunteers. They received a screening history and physical examination to eliminate nerve injuries, or the other neuromuscular diseases. In 64 hands from 38 healthy subjects (age 52 ± 15 years, 38 hands in 24 females, and 37 right hands), all of the EDX tests (mentioned as follows) were carried out in the same manner as the CTS patients.

Patients group

A total of 129 hands of 99 patients were studied consecutively based on the following criteria: 1) paresthesias in the hand; 2) hypesthesias in the median distribution of hand; 3) intermittent wrist and palm pain; 4) isolated weakness and atrophy of the abductor pollicis brevis muscle (APB); 5) Tinel's or Phalen's signs. Before the EDX studies, we confirmed a clinical diagnosis of CTS and patients were enrolled in this study if they had two or more of these findings. From the results of EDX tests, 25 hands in 18 patients were excluded because of the presence of concomitant diseases (14 hands in 9 patients with concomitant polyneuropathy, 10 hands in 8 patients with cervical radiculopathy and 1 hand with a history of trauma in the thenar eminence). Hence, 104 hands in 81 patients (age 55 ± 15 years, 58 females and 61 right hands) were definitively diagnosed as CTS. Alternatively, these overall CTS hands were divided into a subgroup with relatively mild CTS, if action potentials could be evoked in all EDX tests. That is, those with absent action potentials in any EDX tests were excluded.

Electrodiagnostic tests

EDX tests were conducted in a quiet laboratory room at a controlled temperature of 24−26ºC. The patients lay comfortably on a bed while all of the examinations were performed (described as follows). An infrared heater was used to maintain hand and forearm skin temperatures at > 32ºC. Neuropack MEB 2200 (Nihon-Koden, Tokyo, Japan) was used with a bandpass filter of 10−5000 HZ for motor NCSs and 20−2000 HZ for sensory and mixed NCSs. Compound muscle action potentials (CMAPs), sensory nerve action potentials (SNAPs) and mixed nerve action potentials (MNAPs) were recorded using 10 mm Ag/AgCl surface electrodes (NE-132B, Nihon-Koden, Tokyo, Japan) or ring electrodes (NM-450S, Nihon-Koden, Tokyo, Japan). Sweep time was established between 1 and 2 ms/div. The sensitivity was changed from 100 μV/div to 5 mV/div for the motor NCSs and from 10 to 50 μV/div for the sensory and mixed NCSs. The ground electrode was attached between the recording site and the stimulation site. Electrical stimulation was performed using a bipolar electrical stimulator with 0.2 ms duration for the NCSs. Latency was measured from the stimulus onset to the negative onset of each action potential. An averaging of the signal (maximum of 20) was used when the SNAPs or the MNAPs were too small to be obtained with a single stimulus.

Standard tests and measurements

a) MSCV: was calculated using an onset latency of a median antidromic SNAP from wrist to 2nd digit at 14 cm.

b) SLWP: was calculated as the onset latency of the median 2nd digit antidromic SNAP from wrist to 2nd digit at 14 cm minus an onset latency of a median 2nd digit antidromic SNAP from the palm to the 2nd digit at 7 cm. [2]

c) LD4: was calculated as a median minus an ulnar onset latency of antidromic SNAP between wrist and 4th digit at 14 cm. [5]

d) LD1: was calculated as a median minus a radial onset latency of antidromic SNAP between wrist and 1st digit at 10 cm. [5]

e) MNLD: was calculated as a median minus an ulnar onset latency of orthodromic MNAP between palm and wrist at 8 cm. [5]

Guideline test and Option test and measurements

a) MDL: routine MDL was recorded wrist to APB at 7 cm.

b) 2LILD: was calculated as a latency of 2nd lumbrical (2L) CMAP minus a latency of interossei (INT) CMAP following respective stimulation from the wrist at 10 cm [14]. Decisions of CMAP latencies were usually performed at 1 mV/div except at the 2LILD. However, in this test, decisions in latencies of 2L and INT CMAP were performed at a high sensitivity of 100 μV/div. A premotor potential, derived from median digital sensory fibers on the palm [24], is often recorded preceding 2L-CMAP. Therefore, the latency of 2L-CMAP should be decided strictly at an initial negative deflection of those after the premotor potentials [25].

To exclude median nerve involvement at a level proximal to the wrist, the median motor nerve conduction velocity (MCV) between wrist and elbow was evaluated routinely. Likewise, the ulnar motor distal latency (wrist to abductor digiti minimi muscle at 7 cm), the ulnar MCV between wrist and elbow, and the ulnar sensory NCS between the wrist and digit 5 (at 14 cm) were performed in each subject to exclude the presence of ulnar nerve involvement, polyneuropathy, or both. If a patient did not have neurophysiological symptoms, or had CTS with borderline parameters on the ulnar NCS, their sural nerve sensory NCS were performed either. In patients with a history of cervical radiculopathies, especially lesions of the C6 or C7 roots, which may cause both paresthesias and pain around the wrist and palm, we performed needle electromyography of their hand and arm muscles to exclude concomitant radiculopathy.

After all tests, the patients were divided into 6 classes, based on a standard neurophysiological classification [3]: negative, normal findings in all tests; minimal, normal MSCV and MDL with abnormal segmental or comparative tests; mild, decreased MSCV and normal MDL; moderate, decreased MSCV and

delayed MDL; severe, absence of median 2nd digit SNAP and delayed MDL; extreme, absence of thenar motor and routine median 2nd digit SNAP, to assess a distribution of severity in hands with CTS. In the original classification, median 1st and 3rd digit sensory NCSs were performed as routine NCSs, but we modified this using median 2nd digit sensory NCS as the routine one. Also, orthodromic median 3rd digit segmental (palm to wrist) sensory conduction studies were used to classify a patient as having minimal CTS, whereas we modified this using all of the comparative or segmental EDX tests that were performed.

Data analysis

The mean ± 2 standard deviations of the measurements obtained from the control group were calculated as normal limits. Differences in the measurements between the control group and the patient group were assessed using the unpaired Student's *t*-test when normality (checked by a Komolgorov-Smirnov one-sample test combined with a histogram) and homogeneity assumptions were satisfied. Otherwise the Mann-Whitney *U* test was conducted. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were analyzed. The sensitivity of each EDX test was calculated as: (number of CTS hands with an abnormal study result/number of CTS hands) × 100. We presented sensitivities in overall CTS and a subgroup with relatively mild CTS, respectively. The specificity was calculated as; (number of control hands with a normal test result/number of control hands) × 100. The PPV of each test was calculated as: (number of CTS hands/number of hands with an abnormal study result) × 100. The NPV was calculated as: (number of control hands with a normal study result/number of hands with a normal study result) × 100. In overall CTS, a percentage of absent median sensory or motor responses was investigated in each median NCS (i.e., median 2nd, 4th, 1st digit SNAP, median MNAP, APB-CMAP, and 2L-CMAP). The following values were compared by use of the Fisher's exact test: Age, gender, and laterality of examined hand between the control group and patient group, sensitivity, PPV, NPV and percentages of absent median sensory or motor responses between EDX studies. All analyses were performed by use of the IBM SPSS statistics Version 21 (IBM Corp., New York, USA) with statistical significance set at $P < 0.05$.

RESULTS

Control group

All of the EDX tests were examined in 64 control hands and measurements of those could be obtained completely. Age, gender and laterality of examined hand were not different significantly between the control group and the patient group ($p > 0.05$, respectively), or between the control group and the subgroup ($p > 0.05$, respectively). In the control group, measurements in all EDX tests were confirmed normal distributions ($p > 0.05$). The mean ± 2SD of EDX measurements in the control group are shown in Table 1. Normal limits of those are summarized in Table 2.

Patient groups

Of overall 104 CTS hands in patient group, 49 were enrolled for the subgroup with relatively-mild CTS. The mean ± 2SD of EDX measurements in each overall CTS and its subgroup are shown in Table 1. In every EDX measurement, significant differences between the control group and overall CTS, as well as the subgroup, were found ($p < 0.001$ in every comparison).

Three, 13, 15, 44, 22, and 7 of overall CTS hands were classified as negative, minimal, mild, moderate, severe and extreme CTS, respectively. Also, 3, 13, 12, and 22 hands of the subgroup were divided for negative, minimal, mild and moderate CTS, respectively.

Sensitivities and specificities

The overall sensitivity of MSCV, SLWP, LD4, LD1, MNLD, MDL and 2LILD was 83%, 87%, 92%, 90%, 90%, 70%, and 92%, respectively (Table 3). The specificity was 97%, 95%, 98%, 98%, 98%, 97% and 97% in the same order. One hundred and one CTS hands had at least one abnormality across all of the EDX studies (97%). Every Standard Test and 2LILD had significantly higher sensitivity than MDL (Fisher's exact test, $p < 0.05$ in all six comparison). MSCV was less sensitive than SLWP, LD4, LD1, MNLD and 2LILD, but was not significant. There were no differences in sensitivity for SLWP, LD4, LD1, MNLD and 2LILD. In the subgroup with relatively mild CTS, the sensitivity of MSCV, SLWP, LD4, LD1, MNLD, MDL and 2LILD was 67%, 78%, 84%, 82%, 84%, 43% and 84%, respectively (Table 3). Similarly, in the subgroup, significant differences were shown in sensitivity between the MDL and every Standard Test and 2LILD (Fisher's exact test, $p < 0.05$ in all six comparison). No significant differences were confirmed in the comparison between each Standard Test and 2LILD each other.

Positive and negative predictive values

PPV and NPV were shown in Table 3. The PPVs in every EDX test were indicated over 95%. There were no differences in PPV of MSCV, SLWP, 4DL, 1DL, MNDL and 2LILD to each other. The NPV in MDL was 65% and was significantly lower than that of every Standard Test and 2LILD (Fisher's exact test, $p < 0.05$ in all of comparison). No significant differences of NPV were obtained between all of Standard Tests and 2LILD to each other.

Percentage of absent sensory or motor response in median NCSs

The percentage of absent 2nd digit SNAP, 4th digit SNAP, 1st digit SNAP, MNAP, APB-CMAP and 2L-CMAP was 28%, 45%, 25%, 27%, 7% and 0%, respectively. 2L-CMAP could be obtained in all of CTS hands. On the other hand, the percentage of absent 4th digit SNAP was the highest and significant differences were obtained, compared with every other potential (Fisher's exact test, $p < 0.05$).

DISCUSSION

This prospective study was designed to conform to the recommendations by AAEM in 2002 for future research with regard to CTS and had unprecedented

Table 1 Summary of EDX measurements in control and patient groups.

Group	Control group	Patient group	
		Subgroup (relatively-mild)	Overall CTS hands
No. of hand	64	49	104
male / female	26 / 38	15 / 34	28 / 76
Age	52 ± 15	52 ± 15	55 ± 15
right / left	37 / 27	26 / 23	61 / 43
"*Standard*"			
MSCV	53.1 ± 3.9	42.3 ± 8.7	40.1 ± 8.3
SLWP	1.28 ± 0.19	2.10 ± 0.60	2.19 ± 0.60
LD4	0.11 ± 0.19	1.39 ± 0.95	1.45 ± 0.92
LD1	0.18 ± 0.20	1.21 ± 0.70	1.41 ± 0.80
MNLD	0.08 ± 0.18	0.95 ± 0.63	1.15 ± 0.78
"*Guideline*"			
MDL	3.50 ± 0.38	4.44 ± 1.02	5.42 ± 1.68
"*Option*"			
2LILD	0.30 ± 0.21	1.62 ± 0.99	2.51 ± 1.60

Mean ± SD values were presented in age and each EDX measurement. A subgroup was included only if action potentials could be recorded using all EDX tests and was divided from overall CTS hands. $p < 0.001$ control group vs. overall hand CTS cases on all seven measurements; $p < 0.001$ control group vs. subgroup on all seven measurements

MSCV, median digit 2 sensory nerve conduction velocity; SLWP, Median segmental sensory wrist to palm latency; LD4, Median-ulnar 4th digit sensory latency difference; LD1, Median-radial 1st digit sensory latency difference; MNLD, Median-ulnar mixed nerve latency difference; MDL, Median motor distal latency; 2LILD, Median-ulnar 2nd lumbrical-interossei latency difference. *Hands with absent responses were excluded.

Table 2 Normal limits of the EDX tests

	normal limits
"*Standard*"	
MSCV	45 m/s
SLWP	1.65 ms
LD4	0.5 ms
LD1	0.6 ms
MNLD	0.45 ms
"*Guideline*"	
MDL	4.3 ms
"*Option*"	
2LILD	0.7 ms

Normal limits: determined from mean ± 2SD of the raw data.
All abbreviations as in Table 1.

significance in terms of investigating diagnostic comparisons between the largest numbers of EDX tests in patients with CTS simultaneously. As a result, two main findings were obtained in this study: First, each of comparative or segmental EDX tests, recommended as "Standard", had almost the same sensitivity, that is, there is no test with a special advantage. Second, 2LILD had high sensitivity, specificity, PPV and NPV as much as any other Standard Test in overall CTS severities.

Our normal limits of latency values were relatively longer than previous literature. For example, in a study reported by Andary *et al.*, both of LD1 and MNLD was 0.4 ms (mean age: 39 y/o) [26]. Preston *et al.*, reported that the normal limit of MNLD and 2LILD was 0.3 ms and 0.4 ms, respectively (mean age: 31y/o) [14]. Uncini *et al.* reported that the normal limit of LD4, MNLD and 2LILD was 0.4 ms, 0.4 ms, and 0.5 ms, respectively (mean age: 44.7 y/o) [22]. Our normal values in this study were approximately 0.1 ms longer than theirs. Differences might be due to the reason that our participants in the control group were older than subjects in these studies. Thus, our mean values or standard deviations of most measurements were slightly larger than the other literatures as mentioned above. Even so, the differences could be considered acceptable for further analysis, because no significant differences were confirmed between distributions of age in the control group and in overall CTS as well as the subgroup.

In prior studies, LD4 was reported as one of the highest in sensitivity for EDX tests. Because the 4th digit cutaneous sensory fibers run at the most anteromedial side in a distal portion of the carpal tunnel [22], where the compression is severe, they may be impaired earlier (i.e., mild CTS) than the other fibers running at more central portion of the median nerve. Therefore LD4 had the highest sensitivity, in addition the percentage of absent 4th digit SNAP was also the highest, in this study. These results supported those anatomical features, i.e., susceptible 4th digit sensory fibers.

All Standard Tests are thought to be logical techniques anatomically or neurophysiologically. Several studies reported the comparison of the sensitivity between two, three, or four kinds of Standard Tests, which were performed in this study, in mild CTS. A study in mild CTS by Jackson, *et. al.*, reported that the sensitivity of LD4, LD1 and MNLD was 44%, 44%, 30%, respectively5. A study by Uncini, *et. al.*, indicated that the sensitivity of LD4 (77%) was significantly

Table 3 Sensitivity, specificity, positive and negative predictive value of the EDX tests

Tests	Sensitivity		Specificity	PPV	NPV
	Subgroup	Overall CTS hands			
"*Standard*"					
MSCV	67	83	97	98	78
SLWP	78	87	95	97	82
LD4	84	92	98	99	89
LD1	84	90	98	99	88
MNLD	82	90	98	99	86
"*Guideline*"					
MDL	43[a]	70[b]	97	97	65[c]
"*Option*"					
2LILD	84	92	97	98	89

a, b, c $p < 0.05$ MDL vs. All five Standard Tests and 2LILD on sensitivities in both Overall CTS hands and Subgroup, and on NPV
PPV, positive predictive value; NPV, negative predictive value
Abbreviations in Table 1.

higher than MNLD (56%) [22]. Andary, *et. al.*, also investigated the sensitivity of LD1, MNLD and SLWP, which was 90%, 61% and 41%, respectively [26]. Robinson, *et al.*, compared relatively mild CTS, which could be obtained all 3 EDX measurements. They reported that the sensitivity of LD4, LD1 and MNLD was 74.2%, 75.8% and 69.7%, respectively [27]. Sheu, *et al.*, investigated the use of four Standard Tests and reported that median segmental latency ratio (palm-digit/wrist-palm), LD4, LD1 and MNLD was 77.9%, 70.2%, 74.0%, and 53.4%, respectively [28]. MNLD might have relatively lower sensitivities than LD4 and LD1 within mild CTS from this evidence. However, the present study provides contrasting data on the issue. Four Standard Tests (i.e., SLWP, LD4, MNLD and LD1) have similarly high sensitivity. Our inclusion criteria for the mild subgroup were same as the Robinson, *et al.*, study [27]. These controversial results might be caused by the difference in mean age in control groups as described above. 2LILD was recommended as Option Test in the practice parameter [12, 13]. Despite MDL being recommended as a Guideline Test, while 2LILD is placed as a lower recommendation in EDX, the sensitivity of 2LILD has been investigated and it was as high as MNLD in comparison to CTS severity [14, 18] and LD4 in mild CTS [15]. Meena, *et al.*, reported that 2LILD was as sensitive as MNLD in mild. Also, it was more sensitive than MNLD in overall CTS severity [21]. Löscher, *et al.*, suggested that the sensitivity of 2LILD was 97.5% and it was more sensitive than a median-radial 1st digit SCV difference and the median palm to wrist SCV difference in overall CTS severity [17]. Conversely, Uncini, *et al.*, reported a low sensitivity of 2LILD (10%) in mild CTS. This was significantly lower than LD4 (77%) and MNLD (56%) in the mildest CTS [22]. The reasons are not yet clear. However, it seems that there might be a difference associated with decision between the latencies in 2LILD. These authors decided on a latency limit at a sensitivity of 1 mV/div. On the other hand, our study set latencies at higher sensitivity of 100 μV/div, for reasons mentioned above. In spite of our normal limit of 2LILD, this was relatively longer compared with other researches. However, in this study 2LILD was still sensitive, having a high specificity, PPV and NPV. We believe that our results were reasonable with previous evidence on the following points: firstly, the sensitivity of 2LILD is definitely higher than MDL. Next, 2LILD has the same sensitivity compared with MSCV. Finally, it may be as sensitive as the other Standard Tests in mild CTS.

Meanwhile, 2LILD has been well-known for the advantage of lesion localization at the wrist in severe CTS [17, 19–21, 29]. In extremely severe CTS with absent median APB-CMAP and 2nd digit SNAP, the 2L-CMAP could be still obtained. Because motor fibers innervating to the 2L run central portion of the median nerve in carpal tunnel, where is not adjacent to the site of compression, the fibers could be spare more than other fibers. Indeed, in the present study, all hands were observed with 2L-CMAP. This result is similar with a study by Boonyapisit, *et al.* [19], (92.8%) and a study by Löscher, *et al.* [17], (86.1%).

The present study had a few limitations. It was a relatively small in sample size in mild CTS that participated in the study. A larger number of mild CTS hands might produce more detailed results and sensitivity differences especially, between Standard Tests and 2LILD might be detected. We also considered that a combination of several Standard Tests might be necessary for further improvement of the sensitivity of EDX [5, 27]. To clarify the best combination, lager sample size in the mildest CTS, which has the normal conventional NCSs (i.e., MSCV and MDL) with abnormal comparative or segmental tests, is needed. Therefore, we have to plan for further research to confirm about these issues.

In conclusion, all of the Standard Tests and 2LILD have the same level of high sensitivity for diagnosing CTS. In particular, we conclude that the 2LILD should be included for Standard Tests and must be performed routinely for electrodiagnostic evaluation in not only severe CTS but also mild conditions. Finally, according to these results, we should recommend that the practice parameter for EDX studies for diagnosing CTS should be reconsidered.

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