Diagnostic utility of waveform analysis of compound muscle action potentials for carpal tunnel syndrome

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ABSTRACT

Purpose. To determine the diagnostic utility of waveform analysis of compound muscle action potentials (CMAP) for carpal tunnel syndrome (CTS).

Methods. A total of 131 hands in 71 patients diagnosed with CTS (grouped according to severity) and 80 hands in 44 normal subjects were evaluated using nerve conduction test through the carpal tunnel combined with waveform analysis of CMAP.

Results. Compared to normal subjects, the sensory nerve conduction velocity and mean frequency of the CMAP waveform were significantly reduced in patients with CTS. Compared with distal motor latency and sensory nerve conduction velocity, the mean frequency of the CMAP decreased significantly with increasing clinical severity.

Conclusion. This study suggests that waveform analysis of CMAP is of diagnostic value in CTS, and is also of value in objective evaluation of postoperative recovery of carpal median nerve dysfunction.

Key words: carpal tunnel syndrome; neural conduction

INTRODUCTION

Carpal tunnel syndrome (CTS) is an entrapment neuropathy caused by compression of the median nerve in the carpal tunnel. Both clinical findings and symptoms reported by patients are important for the diagnosis. Electrophysiological test of nerve conduction is frequently performed to objectively assess the neurological function. However, conventional electrophysiological testing is unable to detect abnormalities in patients of early CTS. Furthermore, discrepancy between electro-
physiological findings and the severity indicated by clinical findings (clinical severity) has been reported in as many as 70% of patients with mild CTS, 64% with moderate CTS, and 30% with severe CTS. Therefore, an electrophysiological parameter that can identify abnormal findings in early CTS and more precisely reflect clinical severity is needed.

Motor nerve conduction test is used to assist in treatment planning and in evaluating the efficacy of treatment for CTS. Conventionally, distal motor latency (DML) has been the parameter measured in the test. This method assesses only the effects on nerve fibres with the fastest conduction velocity, but not the slower nerve fibres. In contrast, the compound muscle action potential (CMAP) is the sum of action potentials of all muscle fibres controlled by nerve fibres of varying conduction velocities. Therefore, by analysing the CMAP waveform, it is theoretically possible to evaluate the changes in nerve fibres with both fast and slow conduction velocities. This study aimed to examine the diagnostic utility of CMAP waveform analysis for patients with carpal median nerve dysfunction.

PATIENTS AND METHODS

Patients

Between April 1993 and January 1997, 71 patients (131 hands) with a clinical diagnosis of CTS (11 men and 60 women) were enrolled in the study. A further 44 normal subjects (80 hands) with no known neurologic manifestations served as controls. Patients with CTS who had associated diseases, such as metabolic peripheral neuropathy (e.g. due to diabetes mellitus, haemodialysis) and/or cervical radiculomyelopathy were excluded from the study.

Table 1 provides a summary of patient characteristics according to the severity of CTS. A total of 13 patients (20 hands; one man and 12 women) underwent surgery (carpal tunnel release). Nerve conduction tests were performed before surgery and at one, 4, and 24 weeks after surgery for this group of patients.

Clinical findings

Diagnostic criteria of CTS included symptoms such as tingling and numbness along the median nerve in the hand; and clinical findings, including radiating pain in response to tapping on the wrist, a positive Phalen’s test, decreased two-point discrimination, and diminished light touch sensation on the Semmes-Weinstein test. Patients were grouped according to MacKinnon’s clinical severity classification, and were assigned to one of the following groups:

1. Mild: intermittent CTS symptoms, a positive Phalen’s test, radiating pain when tapping at the wrist, and hypersensitivity to vibratory stimulation at 256 Hz;
2. Moderate: diminished vibration sense in the median nerve territory, a positive Phalen’s test, radiating pain when tapping on the carpal tunnel, no thenar muscle atrophy or muscle weakness; and
3. Severe: muscle atrophy, paraesthesia, and abnormalities on the static or moving two-point discrimination test.

Patients in the mild group who had a DML of less than 5 ms were classified as having early CTS.

Electrophysiological testing

Testing of nerve conduction through the carpal tunnel was completed in a shielded room using an electromyograph (MEB-5504; Nihonkohden, Tokyo, Japan), with subjects lying on a couch. Using patch-type skin thermography, the patient’s skin temperature was confirmed as not lower than 32°C at the time of measurement.

Motor nerve conduction tests were performed on the median nerve, and DML and CMAP amplitudes were measured. A silver-silver chloride–recording electrode was placed on the centre of the muscle belly of abductor pollicis brevis. The median nerve was stimulated at the wrist, 7 cm proximal to the recording electrode. The onset latency of the CMAP was recorded as the DML, and the electrical potential difference between the lowest and the highest points was recorded as the amplitude. The sensory nerve conduction velocity (SCV) was measured first by placing a recording ring-electrode on the base of the ring finger. Then, the median nerve was stimulated at the wrist, 13 cm proximal to the recording electrode, and the antidromic sensory nerve action potential (SNAP) was measured. The analogue quantity was converted to a digital value by a standardised quantity, and the data were then converted at 5 kHz to become the CMAP waveform.

The data were transferred to a personal computer using data management software (data analyzer model QP-422B; Nihonkohden, Tokyo, Japan), and then integral values and mean frequency were calculated using waveform analysis software (Bimutas and HyperWave; Kissei Comtech, Tokyo, Japan). The integral value was obtained by adding the positive and
the negative areas. The mean CMAP frequency was obtained by computing the fast Fourier transformation of the CMAP waveforms and then calculating the mean of the power spectrum (Fig. 1).

**Statistical analysis**

All values were reported as means and standard deviations, and p<0.05 was considered statistically significant. The nerve conduction test measurements and CMAP waveform analysis—DML, SCV, CMAP amplitude, integral values, and the mean CMAP frequency—obtained from the control and patient groups were compared. One-way analysis of variance was performed, and the mean differences were evaluated using Scheffe’s F test, if significant differences were detected. The same analytical method was conducted separately for the patient groups.

**RESULTS**

**Clinical results**

Of the 71 patients with CTS, 28 patients (43 hands) had early CTS. In total, 31 patients (58 hands) had mild

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Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of hands (patients)</th>
<th>Male:female</th>
<th>Mean age (range) [years]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects</td>
<td>80 (44)</td>
<td>24:20</td>
<td>38 (19–84)</td>
</tr>
<tr>
<td>Patients with CTS</td>
<td>131 (71)</td>
<td>11:60</td>
<td>53 (21–87)</td>
</tr>
<tr>
<td>Mild</td>
<td>58 (31)</td>
<td>11:20</td>
<td>50 (19–87)</td>
</tr>
<tr>
<td>Moderate</td>
<td>40 (23)</td>
<td>5:18</td>
<td>58 (19–84)</td>
</tr>
<tr>
<td>Severe</td>
<td>33 (17)</td>
<td>5:12</td>
<td>54 (21–80)</td>
</tr>
<tr>
<td>Patients with early CTS</td>
<td>43 (28)</td>
<td>11:17</td>
<td>45 (19–84)</td>
</tr>
<tr>
<td>Patients who underwent surgery*</td>
<td>20 (13)</td>
<td>1:12</td>
<td>63 (42–81)</td>
</tr>
</tbody>
</table>

* Operation for carpal tunnel release

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Figure 1  (a) Integral value of CMAP waveform (shaded area), and (b) frequency of CMAP. The mean value of the power spectrum was obtained by fast Fourier transformation of the compound muscle action potential waveform.
CTS, 23 patients (40 hands) had moderate CTS, and 17 patients (33 hands) had severe CTS. Of the 13 patients (20 hands) who underwent surgery, 9 patients (14 hands) had moderate CTS and 4 patients (6 hands) had severe CTS. None of the patients with mild CTS underwent surgery (Table 1).

Electrophysiological results

Table 2 reports the results of nerve conduction testing and analysis of CMAP. The CMAP was obtained from all patients with early CTS and the mean DML was $3.8 \pm 0.6$ ms in this group. In the mild, moderate, and severe groups, the DML was obtained from $58$ (100%), $38$ (95.0%), and $26$ (78.8%) hands, respectively. The mean DML was $4.3 \pm 1.1$ ms, $6.0 \pm 2.0$ ms, and $5.4 \pm 2.9$ ms for the mild, moderate, and severe groups, respectively (Table 2). There were significant differences between normal subjects and all patient groups (except early CTS group), as well as between the mild and moderate CTS groups ($p<0.01$), and between the mild and severe CTS groups ($p<0.05$) [Fig. 2a].

Of the 13 patients who underwent surgery, the CMAP was obtained from 16 (80%) hands before and
after surgery. The DML was 7.3±1.7 ms before surgery, and was 6.6±1.7 ms, 6.4±1.1 ms, and 6.5±1.3 ms at one, 4, and 24 weeks after surgery, respectively (Fig. 2b).

The mean CMAP amplitude of the patients with CTS was 6.2±3.5 mV. The mean CMAP amplitude was 7.8±2.7 mV for those with early CTS, 6.6±2.9 mV for those with mild CTS, 5.7±3.3 mV for those with moderate CTS, and 2.1±2.5 mV for those with severe CTS (Table 2). There was significant difference in the mean CMAP amplitude between the groups of normal subjects and moderate CTS, and between the moderate and severe CTS groups (p<0.05). The differences between normal subjects and those with severe CTS, and that between the mild and severe CTS groups, were statistically significant (p<0.01) [Fig. 3].

For those patients who underwent surgery, the mean CMAP amplitude was 4.7±4.0 mV before surgery, and 4.8±3.3 mV, 4.2±2.5 mV, and 4.5±2.3 mV at one, 4, and 24 weeks after surgery, respectively.

The SNAP data were obtained from 93 (71.0%) hands, and the mean was 48.2±10.8 m/s. In the group with early CTS, the mean SNAP was 48.7±8.6 m/s as measured from 37 (86.0%) hands. The mean SNAP for the groups with mild, moderate, and severe CTS were 46.1±10.1 m/s, 37.3±12.7 m/s, and 50.9±11.9 m/s when 48 (82.8%) hands, 25 (62.5%) hands, and 20 (60.6%) hands were measured, respectively (Table 2). There were significant differences between normal subjects and those with early CTS (p<0.05), between normal subjects and mild CTS group, between normal subjects and moderate CTS group, between mild and moderate CTS groups, and between moderate and severe CTS groups (p<0.01) [Fig. 4].

Among the 20 hands that underwent surgery, the SNAP could be obtained before and after surgery from 4 (20%) hands only.

The integrated value for the CMAP was 48.7±31.4 mV•ms in patients with CTS—57.8±31.6 mV•ms in the early CTS group, 47.5±37.3 mV•ms in the mild CTS group, 46.5±30.8 mV•ms in the moderate CTS group, and 38.8±24.1 mV•ms in the severe CTS group (Table 2). There were no significant differences between the normal subjects and any of the patient groups. For those patients who underwent surgery, the integrated value of the CMAP was 42.7±25.0 mV•ms before surgery, and 38.8±27.5 mV•ms, 46.5±22.1 mV•ms, and 47.0±24.1 mV•ms at one, 4, and 24 weeks after surgery, respectively. There were no significant differences between these values.

The overall mean frequency of the CMAP was 112.2±29.5 Hz in patients with CTS. It was 119.0±20.9 Hz in the early CTS group, 120.6±33.6 Hz in the mild CTS group, 111.4±14.4 Hz in the moderate CTS group, and 98.3±28.2 Hz in the severe CTS group (Table 2). Compared to normal subjects, the mean frequency of the CMAP was significantly reduced in the early CTS group (p<0.05; Fig. 5a). There were
significant differences seen between normal subjects and all CTS groups, and between mild and severe CTS groups (p<0.01). There were also significant differences between the mild and moderate CTS groups, and between moderate and severe CTS groups (p<0.05).

For the patients who underwent surgery, the values were 68.0±20.9 Hz pre-operatively and 80.5±17.0 Hz, 81.2±22.1 Hz, and 89.6±19.0 Hz at one, 4, and 24 weeks postoperatively, respectively. Compared to the pre-surgical value, the values were significantly different suggesting improvement at one and 4 weeks (p<0.05), as well as at 24 weeks (p<0.01) after surgery (Fig. 5b).

DISCUSSION

The integral value and mean CMAP frequency were selected as the parameters for analysing the CMAP waveform. The integral value provides information regarding the total muscle discharge. In contrast, the mean frequency indicates the relative activity of type I and type II muscle fibres.14,15 Muscle fibres differ according to their physiological characteristics. Type I muscle fibres correspond to the low-frequency components of the CMAP. They are fatigue-resistant, slow-twitch muscle fibres, with relatively small axon diameters (4.5–7.2 µm). They are under the control of slow-conducting nerve fibres. In contrast, type II muscle fibres are fatigue-susceptible, fast-twitch muscle fibres for quick movements. They correspond to the high-frequency component of the CMAP, and are under the control of fast-conducting nerve fibres, with large axon diameters (>11.4 µm).4,13 Thus, the mean frequency decreases when type II muscle fibre activity decreases.19–23 In the early stage of entrapment neuropathy, myelinated nerves with large diameters frequently sustain damage. Many investigators have suggested that changes in the conduction velocity of thick sensory nerves with large diameters, not motor nerves, are diagnostic for early CTS.4,13,24 In this study, SCV was significantly lower in the group with early CTS compared with normal subjects (Fig. 4), although the mean age in the control group was slightly (6.1 years) younger. The mean CMAP frequency was also significantly decreased between normal and early CTS groups (Fig. 5a). These results suggest that the motor nerves controlling type II muscle fibres were injured early in patients with CTS.

Currently there are several methods available to evaluate the clinical severity using electrophysiological tests.11,25–28 Segmental demyelination is frequently observed in early CTS, and it progresses to axonal degeneration as the clinical severity increases. In axonal degeneration, conduction velocity significantly decreases to 60% to 70% of the normal value.
However, the occurrence of axonal degeneration does not directly correlate with further conduction disorders.\textsuperscript{4,13} In this study, the DML and SCV were shown to have already decreased in the group with early CTS, and did not further decrease with progression in clinical severity (Fig. 4). With regard to entrapment neuropathy, a significant reduction in conduction velocity was observed at a relatively early stage, and thus changes in conduction velocity were considered not to adequately reflect the clinical severity. The CMAP amplitude and its integral value are reduced when axonal degeneration develops. The CMAP amplitude reflected clinical severity better than conduction velocity, although a dramatic change was not recognised in a mild group in transition of amplitude.

Conversely, the mean frequency of the CMAP was the only measurement that decreased as the clinical severity progressed (Fig. 5a). A possible explanation for this is that during the early stages of the disease, dysfunction of type II muscle fibres occurs, leading to a relative increase in type I muscle fibre activity. In addition, the number of dysfunctional type II muscle fibres increases as the disease progresses.

Weakness in the thenar muscles, muscle atrophy, and perceptual disorders were observed in all surgery cases. Changes in CMAP were an effective parameter for the evaluation of nerve function, replacing the sensory nerve conduction test using SNAP, which detected only 60.6\% of the severe CTS group. Unlike DML, increase in the mean frequency of the CMAP occurred at an earlier stage, and it recovered with time after surgery (Fig. 5b). After carpal tunnel release, the temporarily immobilised type II muscle fibres rapidly resume their activity.\textsuperscript{3,4,13,16} We also found that recovery from segmental demyelination and axonal degeneration led to increase in the mean CMAP frequency.

In conclusion, the mean frequency of the CMAP was found to be a useful electrophysiologic parameter for the diagnosis of CTS and its clinical severity, and for objective evaluation of postoperative recovery of median nerve dysfunction.

REFERENCES