The relationship between median nerve axon count and clinical findings and electrophysiological parameters in patients with carpal tunnel syndrome

Ejder Berk, Vedat Nacitarhan

Sutcu Imam University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Kahramanmaras, Turkey

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Abstract

Aim: To determine the association of clinical and electrophysiological findings in cases of carpal tunnel syndrome (CTS) using motor unit (axon) number estimation (MUNE) of the median nerve and to evaluate how these findings can contribute to treatment planning.

Material and Methods: Evaluation was made of 43 hands of 25 patients (22 females, 3 males, mean age 45.63±9.89 years) with clinical and electrophysiological diagnosis proven CTS and a healthy control group of 50 hands of 25 subjects (21 females, 4 males, mean age 44.72±8.89 years). Electrophysiological nerve transmission measurements and CTS grading were applied. MUNE measurement was made from the abductor pollicis brevis (APB) muscle with the incremental method.

Results: According to the electrophysiological grading, the mean MUNE values were at Grade-0: 134.66±41.00, Grade-1: 78.83±33.51, Grade-2: 71.72±32.15 and Grade-3: 50.25±27.45. A positive correlation was determined between electrophysiological grading and APB muscle atrophy, and median nerve latency. A negative correlation was determined with MUNE, muscle strength, median nerve amplitude and conduction velocity. Between MUNE and muscle strength, median nerve amplitude and conduction velocity there was a positive correlation, between MUNE and median nerve latency, a negative correlation was found. According to regression analysis, median nerve wrist segment sensory velocity and median nerve distal motor action potential amplitude were predictive parameters for MUNE.

Conclusion: Together with the clinical evaluation, patients with grade 3 and/or MUNE value below 2 standard deviations of normal according to the electrophysiological evaluation, should be considered for surgery, while in milder cases, it can be recommended that clinical and electrophysiological follow-up is added to conservative treatment.

Keywords: Carpal tunnel syndrome; electromyography; motor endplate; axons.

INTRODUCTION

Carpal Tunnel Syndrome (CTS), which occurs with entrapment of the median nerve at the level of the wrist, is the most common and well-defined entrapment neuropathy (1-3). CTS affects approximately 2% of the adult population and its prevalence has been reported as 3%-3.4% in females and 0.6%-2.7% in males (4-5). CTS diagnosis is based on medical history, clinical symptoms, physical examination, and electrophysiological examinations. In the CTS diagnosis, electrophysiological examinations have high sensitivity and specificity in objectively showing the median nerve neuropathy and determining the level and severity of entrapment (6-8).

Motor Unit Number Estimation (MUNE) is an important electrophysiological measurement method that estimates the number of surviving axons in patients with motor neuron or motor axon loss (9). This method is based on the electrophysiological evaluations of motor unit characteristics that could represent the number of all motor units innervating a muscle or muscle group. Although several MUNE methods (Incremental MUNE, Multiple Point Stimulation, Spike-Triggered Averaging, Decomposition STA, F-wave and statistical methods) have been described, the most preferred is the McComas incremental method (10). The aim of this study was to investigate the relationship between estimated median nerve motor unit (axon) count and clinical and electrophysiological findings in patients...
with CTS and to examine how this relationship could contribute to treatment management of CTS.

**MATERIAL and METHODS**

The study was conducted on the Physical Medicine and Rehabilitation (PMR) Department. This study was approved by the Institutional Ethics Committee. The study was carried out according to the Declaration of Helsinki and informed consent was obtained from all the study participants before the study.

The study group consisted of 43 hands of 25 patients who presented to the PMR Polyclinic with complaints of numbness, burning, paresthesia, pain and/or weakness of the hand and had the diagnosis of CTS confirming electrophysiologically. The control group was formed of 50 hands of volunteer hospital personnel with no complaints of the hands.

Patients were excluded if they had CTS together with cervical disc disease, systemic disease which could cause polyneuropathy such as diabetes mellitus, thyroid dysfunction, previous CTS surgery, rheumatismal disease involving the wrist, a history of fracture in the ipsilateral upper extremity, a mass within the carpal tunnel, were determined with Martin-Gruber anastomosis, cognitive function disorder or a cardiac pacemaker.

Symptom duration, paresthesia and loss of strength, the Tinel and Phalen compression tests results, and muscle atrophy status were recorded. Visual Analog Scale (VAS) was used to evaluate the severity of pain. The Boston Questionnaire (BQ) was performed to determine the severity of the CTS symptoms and the functional status of the patients (11).

**Electrophysiological Evaluation**

For the electrophysiological evaluation, a Neuro-MEP-Micro Electromyography (EMG) device (Neurosoft Medical diagnostic equipment, Ivanovo, Russia) was used. In all the electrophysiological measurements, the sampling frequency was selected as 25,000 Hz. Latency and amplitude values were measured after supramaximal stimulus. An earthed electrode was placed on the back of the hand in all the measurements (12,13).

Nerve transmission measurements were made based on antidromic and initial latency. The median nerve and ulnar nerve functions were evaluated using the sensory transmission rates and sensory nerve action potentials. Motor function was evaluated using distal motor delays and compound muscle movement potential amplitudes. Sensory and motor impairments were interpreted using the threshold values for each measurement defined in the American Association of Neuromuscular and Electrodiagnostic Medicine standards (14).

Patients were grouped as mild, moderate and severe CTS according to the electrophysiological evaluations (15-17). The control group was evaluated as normal (Grade 0).

The median nerve estimated axon count was made on the Abductor Pollicis Brevis (APB) muscle using the McComas incremental method of the quantitative MUNE techniques (10) (Figure 1).

![Figure 1. Amplitude increase technique](image)

Maximum CMAP=10.1 mV, 2. Mean increase=110 µV, Motor unit number estimation count=91

The active disc electrode was placed on the APB muscle at the midpoint of a line between the metacarpophalangeal joint of the thumb and the distal wrist and the reference electrode was placed over the distal interphalangeal joint. Maximal compound muscle action potential (mCMAP) was obtained from the APB muscle by first giving a supramaximal stimulus of 0.2 ms duration. In the continuation, the stimulus duration was reduced to 0.05 ms and the current to below the threshold value. Then by increasing the current in steps of 0.1 mA, the first potential was obtained at the threshold value. The stimulus severity was automatically increased by the incremental MUNE program on the EMG unit and a total of 11 potential steps were formed. The mean amplitude increase amount in each step was determined by dividing the total amplitude increases obtained through the MUNE program by the number of increases (11 steps) and the motor unit count (MUC) was found by dividing the mCMAP value by the mean amplitude increase amount. With 3 repetitions, the mean MUC was taken for evaluation. Throughout the study, the placement of the stimulus and recording electrodes was not changed.

**Statistical Analysis**

Statistical analysis were performed using the Statistical Package for the Social Sciences (SPSS) for Windows vn. 13.0. In the comparison of continuous variables conforming to normal distribution, the independent t-test was used, and for non-parametric data, the Chi-square and Mann Whitney U-tests were used. To determine the relationships between data, Spearman correlation
analysis was applied and multiple stepwise regression analysis was used to determine parameters affecting axon count. In the comparison of parameters according to the electrophysiological evaluation, the One-Way ANOVA test was used. Data were expressed as mean ± standard deviation (SD) or number (n) and percentage (%). P < 0.05 was accepted as statistically significant.

RESULTS

The 25 patients with CTS comprised 22 (88%) females and 3 (12%) males with a mean age of 45.63 ± 9.89 years (range, 20 - 62 years). The control group comprised 21 (84%) females and 4 (14%) males with a mean age of 44.72 ± 8.89 years (range, 27 - 61 years). No statistically significant difference was determined between the groups in terms of age or gender (p=0.642, p=0.684) (Table 1).

The mean duration of symptoms was determined as 40.88 ± 27.73 months. The dominant hand was the right hand in 23 (92%) cases in both groups. No significant difference was determined between the groups in terms of the dominant hand (p=1.00). In the patient group, 7 (28%) patients were affected unilaterally and 18 (72%) were affected bilaterally. Tinel test positivity was determined in 30 (69.76%) hands, Phalen test positivity in 31 (72.09%) hands, compression test positivity in 28 (65.11%) hands, atrophy in 14 (32.55%) hands and loss of strength in 14 (32.55%) hands (Table 1).

A statistically significant difference was determined between the patient and control groups in all electrophysiological measurements of the median nerve motor and sensory parameters (p < 0.001) and in respect of the MUNE values (p < 0.001) (Table 2,3).

In the Spearman correlation analysis, a positive correlation was determined between the electrophysiological evaluation and symptom duration (r= 0.912), VAS (r= 0.883), Boston symptom severity score (SSS) (r= 0.868), functional status score (FSS) (r= 0.884), nocturnal pain (r= 0.823), paresthesia(r= 0.874), Tinel test positivity (r= 0.593), Phalen test positivity (r= 0.590), compression test positivity (r= 0.571) and APB muscle atrophy (r= 0.533) values (Table 4).

A negative correlation was found between the electrophysiological evaluation and MUNE (r= -0.717), and muscle strength (r = -0.533) values. No correlation was determined between electrophysiological evaluation and age (r= 0.115) (Table 4).
Table 4. VAS, BQ and median nerve parameters according to the electrophysiological evaluation grading

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Electrophysiological evaluation</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Case (hand) n</td>
<td>Stage 0</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>6</td>
</tr>
<tr>
<td>Age</td>
<td>44.72 ± 8.89</td>
<td>46.33 ± 10.69</td>
</tr>
<tr>
<td>Symptom Duration</td>
<td>0.24 ± 1.19</td>
<td>18.50 ± 11.76</td>
</tr>
<tr>
<td>VAS</td>
<td>1.06 ± 0.24</td>
<td>5.67 ± 1.51</td>
</tr>
<tr>
<td>SSS</td>
<td>1.03 ± 0.07</td>
<td>2.34 ± 0.64</td>
</tr>
<tr>
<td>FSS</td>
<td>1.03 ± 0.07</td>
<td>2.29 ± 0.88</td>
</tr>
<tr>
<td>MUNE</td>
<td>134.66 ± 41.00</td>
<td>78.83 ± 33.51</td>
</tr>
<tr>
<td>MMDL</td>
<td>3.21 ± 0.34</td>
<td>3.89 ± 0.41</td>
</tr>
<tr>
<td>MMDA</td>
<td>10.73 ± 2.47</td>
<td>8.17 ± 2.00</td>
</tr>
<tr>
<td>MMDArea</td>
<td>35.38 ± 9.20</td>
<td>24.91 ± 5.85</td>
</tr>
<tr>
<td>MMDVelocity</td>
<td>57.41 ± 3.53</td>
<td>52.63 ± 1.56</td>
</tr>
<tr>
<td>MSPL</td>
<td>1.09 ± 0.08</td>
<td>1.05 ± 0.07</td>
</tr>
<tr>
<td>MSPA</td>
<td>37.83 ± 12.69</td>
<td>22.85 ± 10.60</td>
</tr>
<tr>
<td>MSP2Lev</td>
<td>64.78 ± 4.32</td>
<td>66.71 ± 4.30</td>
</tr>
<tr>
<td>MSWL</td>
<td>2.34 ± 0.16</td>
<td>3.00 ± 0.16</td>
</tr>
<tr>
<td>MSWA</td>
<td>34.41 ± 11.20</td>
<td>16.30 ± 7.69</td>
</tr>
<tr>
<td>MSW2Lev</td>
<td>60.08 ± 3.93</td>
<td>46.78 ± 2.47</td>
</tr>
<tr>
<td>MSWSegLat</td>
<td>1.25 ± 0.10</td>
<td>1.95 ± 0.13</td>
</tr>
<tr>
<td>MSWSegLev</td>
<td>56.16 ± 4.52</td>
<td>36.09 ± 2.35</td>
</tr>
<tr>
<td>MTLI</td>
<td>0.44 ± 0.05</td>
<td>0.39 ± 0.05</td>
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<tr>
<td>MSDPindex</td>
<td>1.16 ± 0.09</td>
<td>1.84 ± 0.17</td>
</tr>
<tr>
<td>MUSLatDiff</td>
<td>0.07 ± 0.12</td>
<td>0.76 ± 0.14</td>
</tr>
</tbody>
</table>

Data are expressed as the mean ±SD unless otherwise noted. One-Way ANOVA (with Tukey HSD)

A positive correlation was determined between MUNE values and muscle strength (r= 0.580). A negative correlation was determined between MUNE values and age (r= -0.223), symptom duration (r= -0.688), VAS (r= -0.657), SSS (r= -0.704), FSS (r= -0.731), nocturnal pain (r= -0.625), paresthesia (r= -0.712), Tinel test positivity (r= -0.543), Phalen test positivity (r= -0.513), compression test positivity (r= -0.440) and APB muscle atrophy (r= -0.580) values. A statistically significant difference was determined in all the parameters measured of the median nerve with VAS, SSS and FSS according to the electrophysiological evaluation (p<0.001, Anova test) (Table 4).

Post hoc analysis (Dunnett C, when variances were not equal) was performed if it was seen that the statistical differences in symptom duration were between electrophysiological evaluation Grade 0 and Grades 1, 2 and 3 and between Grade 1 and Grade 2.

In median motor distal latency (MMDL) statistically significant differences were determined between Grade 0 and Grades 1, 2 and 3, and between Grade 1 and Grade 2.

In median motor distal amplitude (MMDA), statistically significant differences were determined between Grade 0 and Grades 2 and 3, and between Grade 2 and Grade 3.

When multiple regression analysis was applied with MUNE-dependent variables and parameters with a high correlation with MUNE as independent variables, 2 regression thresholds were obtained. According to these regression thresholds, it is possible to calculate the MUNE values with 2 different formulae:

1st regression threshold

MUNE = (2.303 x MSWSegLev) + 0.876

According to this threshold, the estimated MUNE number can be obtained by multiplying the MSWSegLev value by the coefficient of 2.303, then adding 0.876. According to this, a fall in the MSWSegLev value will cause a fall in MUNE count.

2nd regression threshold

MUNE = (MSWSegLev x 1.608 + MMDA x 6.229) - 25.439
According to this threshold, the estimated MUNE number can be obtained by multiplying the MSWSegLev value by the coefficient of 1.608 and multiplying the MMDA value by 6.229 then subtracting 25.439 from the total. According to this, a fall in the MSWSegLev and the MMDA values will cause a fall in MUNE count.

DISCUSSION

Electrophysiological tests are useful in supporting CTS diagnosis, and in determining the level of entrapment and the severity of median nerve pressure. The correlation between electrophysiological findings and clinical characteristics has high sensitivity in correct decision-making in CTS diagnosis and treatment (18,19).

In a study, electrophysiological evaluation was shown to be a sensitive method that reflects the pathology independent of the intensity of clinical features (20). Padua et al. (21) showed a significant correlation between the electrophysiologic staging and the severity of clinical symptoms.

In our study, there was a positive correlation between electrophysiological evaluation and symptom duration, VAS, Boston SSS, FSS, Tinel-Phalen-Compression tests positivity, APB muscle atrophy, median nerve latency, MSDP index and MULat difference values. Additionally, a negative correlation was determined with median nerve amplitude, area and transmission rate, ulnar sensory nerve amplitude, MTLI, muscle strength and MUNE values.

Bayrak et al. (22) reported that the mean MUNE values were 48.89±26.30 in the CTS group and 94.33±48.45 in the control group in their study. A statistically significant negative correlation was determined between electrophysiologic evaluation grading and MUNE with low MUNE values seen in severe CTS patients.

In another study, MUNE values were found to be 115.62 ± 31.39 in a CTS patient group and 150.47±33.6 in the control group (23). A statistically significant difference was found between the CTS patients and the control group in terms of median nerve amplitude, distal latency, transmission rate, F wave and MUNE values.

In another study (24), especially in the early stages of CTS that are seen to be silent or with slow sensory transmission, the MUNE technique was found to be sensitive in the determination of motor nerve involvement in CTS patients with sensory findings, and thus it was emphasised that MUNE evaluation in the determination of motor unit loss in the early stages of CTS could be useful in diagnosis and treatment.

In the current study, the MUNE values were determined as 134.66±41.00 in the control group and 68.72 ± 32.16 in the CTS patients. These values were similar to MUNE values obtained in previous studies. That the MUNE values reported in other studies in literature are in a wide range such as 100-300 can be explained by the variations in patients included in the studies and different techniques used. (Table 3).

In a study of 100 hands by Caetano the CTS patients were separated as mild, moderate and severe, and were compared with 50 control hands in terms of median palmar sensory amplitudes and those with normal median sensory amplitude were evaluated as cases seen to have no axonal degeneration (25). In the mild CTS group and in 40.3% of the moderate CTS group, the sensory nerve action potential (SNAP) amplitude value was normal and no axonal degeneration was seen, whereas in the severe CTS group and in more than half of the moderate cases (59.7%), the SNAP amplitude was low or absent and axonal degeneration was seen. It was reported that as low SNAP amplitude is a marker of axonal degeneration and poor prognosis, the use of SNAP amplitude could be of guidance in CTS monitoring and treatment.

Similarly in the current study, a negative correlation was determined between CMAP amplitude, SNAP amplitude and electrophysiological grading, a positive correlation was determined between MUNE values and amplitude and a negative correlation was determined between electrophysiological grading and MUNE values. As a negative correlation was found between the electrophysiological grading and the MUNE value obtained from the APB muscle, this indicates an increase in the degree of axonal loss that develops secondary to demyelinisation as the severity of CTS increases.

According to the regression analysis of our study, although the MSWSeg Lev and MMDA values were seen to be a factor affecting MUNE, no other study could be found which used MUNE estimation with regression analysis. A positive correlation was determined between MUNE values and median nerve amplitude and nerve transmission rate values. The CMAP amplitude is known to be directly proportional to the number of intact axon fibres and this was confirmed by the positive relationship of CMAP amplitude and axon count determined in this study.

Low sample size which was due to patient compliance partially because of the length of time taken for the application of the MUNE technique, and due to the inclusion of a specific age group (20-62 years) and the exclusion of endocrine disorders, such as diabetes mellitus and thyroid function disorders, which often play a role in CTS etiology is a limitation of the study. Furthermore, as the MUNE method is not frequently applied in the treatment and follow-up of CTS, that there were insufficient studies for comparison was also a factor limiting this examination.

CONCLUSION

In the planning of the treatment and management of CTS patients, the individual must be considered as a whole, with evaluations made together of age, gender, occupation, clinical status, symptom duration and severity, functional status and electrophysiological findings. If possible, the axon count should be determined in CTS patients using the MUNE technique. Surgical treatment should be applied to those of electrophysiological evaluation grade 3 and/or...
MUNE count lower than 2 standard deviations of normal, and for other cases, clinical and electrophysiological follow-up should be added to conservative treatment. As the number of cases in this study was limited, there is a need for further studies with greater participation and longer follow-up.

Competing interests: The authors declare that they have no competing interest.

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Ejder Berk ORCID: 0000-0002-0816-0960
Vedat Nacitarhan ORCID: 0000000317568615

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