Correlations of Median Nerve Area, Strain, and Nerve Conduction in Carpal Tunnel Syndrome Patients

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Abstract

Background: The objective of this study was to see if ultrasound-interpreted median nerve strain and cross-sectional area correlate with abnormal nerve conduction studies and thumb opposition strength in patients with carpal tunnel syndrome (CTS). **Methods:** Sixty wrists of 30 idiopathic CTS patients were assessed by ultrasound and nerve conduction study. Distal motor latency, cross-sectional area, and strain ratio of the median nerve were measured. In addition, thumb opposition strength was classified using the manual muscle testing grade from 0 to 5, clinically. The strain ratio was defined as the strain of the reference coupler divided by the strain of the median nerve. The correlations between clinical examinations of distal motor latency, cross-sectional area, strain ratio, and thumb opposition strength were estimated with the Spearman rank correlation coefficients. **Results:** The correlation coefficients between distal motor latency and strain ratio, distal motor latency and cross-sectional area, and strain ratio and cross-sectional area were .597, .352, and .324, respectively. The correlation coefficients between thumb opposition strength and distal motor latency, thumb opposition and cross-sectional area, and thumb opposition and strain ratio were $-.523$, $-.307$, and $-.358$, respectively. All of the correlations showed statistical significance. The correlation coefficients between distal motor latency and strain ratio, and thumb opposition and distal motor latency, were relatively high. **Conclusions:** The results of this study suggest that the nerve conduction delay is related to changes in the material properties of the median nerve. In addition, nerve conduction study was the principal indicator of the thumb opposition strength.

Keywords: median nerve, strain, carpal tunnel syndrome, nerve conduction study, ultrasound

Introduction

Carpal tunnel syndrome (CTS) is a compression neuropathy of the median nerve at the wrist. The diagnosis of CTS is usually based on a typical history, clinical examination, provocative test, and nerve conduction study. The most common symptom in idiopathic CTS is a tingling sensation along the median nerve distribution in the hands. The value of provocative physical tests, such as Tinel's sign or Phalen's test, is controversial, and results are often of doubtful clinical significance.⁴ As there is no clear definition of the severity of numbness, its clinical severity has sometimes been defined by the thumb opposition strength.¹¹

Nerve conduction studies have been reported to be highly specific in some studies.^{1,19} The median nerve shows a delay in the sensory and motor conduction velocities. Nerve conduction studies focus on defining whether there has been damage to the median nerve inside the carpal tunnel to quantify the severity of the nerve damage and to define the physiology of the disease as a conduction block, demyelination, or axonal degeneration. Because of the high

specificity and sensitivity, nerve conduction studies are considered to be the gold standard for CTS diagnosis.

In recent years, imaging techniques such as ultrasonography have been shown to be of value in the diagnosis of CTS. They have the potential advantages of lower cost, shorter examination time, and noninvasiveness. It is well established in the literature that ultrasound imaging can detect pathologies such as thickening and echogenicity alteration of the flexor tendons¹⁷ and flexor retinaculum,⁸ synovial proliferation, swelling of the median nerve in the proximal part of the carpal tunnel, and flattening of the median nerve in the carpal tunnel.^{2,7,14} In addition to the morphological changes, an imaging method for measuring tissue strain

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using a conventional ultrasound machine, so-called ultrasound elastography, has been introduced.^{3,21} Ultrasound elastography can estimate tissue stiffness either by strain analysis of tissue under compression (quasistatic methods) or by the imaging of shear waves.¹⁰ Recently, the application of ultrasound elastography for clinical diagnosis has been expanded.^{5,6,20,24,25} In previous studies, median nerve strain was measured and compared between CTS patients and healthy controls using ultrasound elastography.^{13,22} These studies suggested that the median nerves of CTS patients are harder (lower strain) than those of controls. In addition, it was suggested that the strain ratio (strain of the reference coupler / strain of the median nerve) was useful to standardize the results for the stiffness evaluation.²⁷

With compression of a normal nerve trunk, the structure is deformed when compression tissue is redistributed into noncompressed areas. It has been suggested that large fascicles in a small amount of epineurium are more vulnerable to compression than several small fascicles embedded in a large amount of epineurium.¹⁵ This is because the latter can transform larger than the former. This may be different in the pathological condition. However, the relations among the morphology, material property, and physiological function of the peripheral nerve are still unclear. To understand the pathological basis of nerve compression lesions, it is necessary to understand the effects of all individual characteristics of the nerve components. In this study, we wished to submit a new type of discussion for the progress of entrapment neuropathy by evaluating the relations of morphological, mechanical, and functional diagnostic tests. The objective of this study was to see if ultrasound-interpreted median nerve strain and cross-sectional area correlate with abnormal nerve conduction studies and thumb opposition strength in patients with CTS. We hypothesized that there are correlations between each evaluation; in addition, clinical staging of the disease can be expected with diagnostic tests.

Methods

The protocol for this study was reviewed and approved by our institutional review board. The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Sixty wrists of 30 idiopathic CTS patients (17 females and 13 males; age range, 33-85 years, with a mean age of 62.9 years; 43 affected wrists and 17 unaffected wrists) were evaluated. CTS patients with a history of systemic disease associated with a higher incidence of CTS, such as chronic renal failure, thyroid disease, diabetes, obesity (body mass index greater than or equal to 30), or rheumatoid arthritis, were excluded. In addition, patients who had a history of any upper extremity surgery were excluded. Participants were given a brief description of the

purpose of the research and the testing procedures during the initial contact. Informed consent was obtained from all patients for being included in the study. The CTS diagnosis was confirmed that the patients had clinical symptoms of pain, numbness, tingling in the median nerve distribution of the hand, and at least 1 positive provocative test result (Tinel's sign at the wrist and Phalen's maneuver), in addition to meeting criteria of nerve conduction velocity findings with the American Association of Electrodiagnostic Medicine (AAEM) guidelines.¹² All patients underwent nerve conduction study and ultrasound imaging.

Nerve Conduction Study

The nerve conduction study was performed for all participants according to the recommended protocol of AAEM using a standard electromyography system (Neuropack MEB-2208; Nihon Kohden Co., Tokyo, Japan). All studies were performed by a clinical technician who was blinded to the clinical symptoms. For the motor conduction study, a recording electrode was placed at the middle portion of the abductor pollicis brevis (APB) muscle. The stimulation was applied at the wrist, 7 cm proximal to the recording electrode. The onset of latency, amplitude, distance, and velocity of motor action potentials were measured. The distal latency of the motor action potential of the APB muscle was used for further analysis. Results were excluded from the analysis if there was no motor action potential in severe cases.

Strain Ratio Measurement of Median Nerve

The strain ratio was measured for the evaluation of the median nerve stiffness. As the results of strain measurement for the deep tissues are affected by the stiffness of the surrounding structures or the pressure applied to the structure, it is necessary to standardize the results. The strain ratio enables us to judge the *in vivo* stiffness objectively by comparing the strain of the median nerve to the strain of the reference coupler, which has a fixed value of elasticity.⁹

Each participant was asked to sit and place one's forearm on the table with the palmar side up. An ultrasound scanner (Hi Vision Avius; Hitachi Aloka Medical, Ltd., Tokyo, Japan) equipped with a linear array transducer was set to a depth of 20 mm. The median nerve strain was measured with "Real-time Tissue Elastography" mode in the ultrasound system. For the strain measurement, we used a cyclic compression apparatus. The method to measure the median nerve strain using the apparatus was described in a previous study.²⁷ The apparatus consisted of a forearm table with transducer holder and a programmed controller for the compression-release cycle. The transducer holder can adjust the height of the transducer. The displacement and cycles for the compression-release can adjust with the programmed controller. The transducer was attached to the transducer

Figure 1. An example image of ultrasonic strain measurement.

Note. Regions of interest were set at the imaged median nerve and the part of the reference coupler just above the median nerve. The median nerve strain and the strain ratio (strain of the reference coupler / strain of the median nerve) were each measured 5 times.

holder at the apparatus, and was placed parallel to the wrist crease (proximal carpal tunnel), with the wrist in a neutral position. The transducer was maintained perpendicular to the skin surface of the wrist crease. The median nerve was identified by cross-sectional ultrasonographic imaging. The forearm of the examinee was secured to the table. The reference coupler, which has a fixed value of elasticity, was attached to the transducer.⁹ The reference coupler is made of elastic resin. Its acoustic characteristics are adjusted to minimize image deterioration. Young's modulus of the reference coupler was 22.6 kPa. When the whole surface of the transducer was attached to the skin, the transducer was pressed down to a depth of 4 mm according to the scale that was displayed on the transducer holder. In a preliminary study, it was confirmed that this initial placement was needed to ensure that the compression force reached the median nerve.²⁷ The compression-release cycle was set to 1.5 Hz and was observed with a numeric scale indicator on the monitor. The displacement for the tissue compression was adjusted in the range of -0.7% to 0.7% on the indicator. The outline of the imaged median nerve was traced, and its strain was measured (Figure 1). In addition, the strain of the reference coupler was also measured just above the median nerve. The median nerve strain ratio (strain of the reference coupler / strain of the median nerve) was measured 5 times. The averages of these 5 measurements of strain ratios were used for analysis.

Measurement of Median Nerve Morphology

The median nerve cross-sectional area was measured as a morphological index. The median nerve was imaged at the same level as the strain measurement without pressure. The cross-sectional ultrasonographic images of the carpal tunnel

were reviewed using Analyze 10.0 Software (Biomedical Imaging Resource, Mayo Clinic, Rochester, Minnesota).²⁸ The median nerve was outlined, and its area was calculated. All ultrasound studies were performed by a hand surgeon who was blinded to the nerve conduction studies.

Evaluations of Thumb Opposition

For the assessment of thumb opposition, the patient sat with the forearm in supination and the wrist in a neutral position. The examiner stabilized the hand by placing the dorsal aspect of his fingers on the palmar aspect of the patient's fingers, and the same with the thumb. Resistance was applied on the palmar side of the thumb in the direction of extension. The patient actively flexes the thumb toward the little finger. The strength was classified using the manual muscle testing (MMT) grade from 0 to 5. Each grade was defined as follows: 5, holding the test position against maximal resistance; 4, holding the test position against moderate resistance; 3, holding the test position against gravity; 2, able to move through the full range of motion when the effect of gravity is eliminated; and 0 to 1, no visible movement, palpable, or observable tendon prominence/flicker contraction, or no observable muscle contraction. As it was difficult to distinguish 0 and 1 clinically, we defined them in the same group as grade 1 in this study. This evaluation was performed by a hand surgeon.

Statistical Analysis

The results are expressed as means $\pm$ standard deviations. The correlations between diagnostic tests of distal motor latency, strain ratio, and cross-sectional area were evaluated. In addition, the correlations between diagnostic tests

Figure 2. Results of the correlations among distal motor latency, strain ratio, and cross-sectional area.

Note. (a) The correlation between strain ratio and cross-sectional area. (b) The correlation between distal motor latency and strain ratio. (c) The correlation between distal motor latency and cross-sectional area. The correlation coefficients between distal motor latency and strain ratio, distal motor latency and cross-sectional area, and strain ratio and cross-sectional area were .597, .352, and .324, respectively.

and thumb opposition strength were evaluated. To measure the relationship among different clinical evaluations, Spearman rank correlation coefficients were used. The correlation coefficients were defined as follows: greater than 0 implies positive agreement among ranks, less than 0 implies negative agreement (or agreement in the reverse direction), and 0 implies no agreement. A *P* value of less than .05 was considered to indicate a statistically significant correlation. All analyses were performed using Excel Statistics 2012 software (SSRI Co., Tokyo, Japan).

Results

Figure 2 shows the results of the correlations among distal motor latency, strain ratio, and cross-sectional area. The correlation coefficients between distal motor latency and strain ratio, distal motor latency and cross-sectional area, and strain ratio and cross-sectional area were .597, .352, and .324, respectively. All of these correlations showed statistical significance ($P < .05$). The correlation coefficient between distal motor latency and strain ratio was relatively high ($P < .01$).

The average results of diagnostic tests according to the MMT grades of the thumb opposition strength are shown in Table 1. On the basis of the MMT grading of the thumb

opposition, 24 wrists were in grade 5, 23 wrists in grade 4, 4 wrists in grade 3, 1 wrist in grade 2, and 5 wrists in grade 1. In 4 of the 5 wrists in the grade 1 group, motor action potential of the APB muscle was not observed in the nerve conduction study. Thus, the result of the nerve conduction study in grade 1 was from 1 patient. The correlation coefficients between thumb opposition strength and distal motor latency, thumb opposition and cross-sectional area, and thumb opposition and strain ratio were $-.523$, $-.307$, and $-.358$, respectively. All of these correlations showed statistical significance ($P < .05$). The correlation coefficient between thumb opposition strength and distal motor latency was relatively high ($P < .01$).

Discussion

In this study, we assessed the correlations among diagnostic tests of nerve conduction study, strain ratio, and cross-sectional area in CTS patients. In terms of the results, it was found that there were significant correlations among these diagnostic tests. In particular, there was the highest correlation between the distal motor latency and the strain ratio. In addition, there were significant correlations between the diagnostic tests and the thumb opposition strength.

Table 1. The Results of Clinical Examinations According to the MMT Grades of the Thumb Opposition Strength.

MMT grading	Latency, average, ms	SD	Ratio, average	SD	Area, average, mm ²	SD
5	4.93	0.88	2.85	0.57	12.84	1.87
4	6.33	1.41	3.75	1.24	14.43	3.59
3	8.54	3.12	4.24	1.82	15.11	2.05
2	4.68	—	8.77	—	17.55	—
1	6.90	—	3.79	0.79	17.63	5.92

Note. As there was only 1 result in the grade 2 group and the nerve conduction study in grade 1 group, there was no standard deviation. MMT, manual muscle testing.

It is interesting to note that the correlation coefficient between distal motor latency and strain ratio was the highest. This suggests that the stiffness of the nerve structure is related to nerve conduction. It was reported that failure of the blood-nerve barrier after mechanical compression ischemia induced intraneural edema and affected nerve function.²⁶ Mechanical pressure levels and the duration might influence structural changes in the median nerve. Nerve fiber anatomy facilitates the conduction of electrical impulses to convey information over a distance for normal function. Nerve connective tissues serve a protective function as the limb is subjected to the stresses of myriad limb positions and postures.²³ Because of the higher baseline pressure inside the carpal tunnel, the normal nerve function was disturbed with a change of the mechanical properties of the nerve trunk. This may be a way to show the relationship between the changes of mechanical properties and nerve conduction, clinically. Further research with a large sample size and a wide spectrum of CTS severity may clarify the entire process and pathophysiology of the compression neuropathy.

To some extent, the increase of the cross-sectional area corresponded to the increase of the strain ratio. In addition, there was a negative correlation between cross-sectional area and thumb opposition strength. This suggests that the strain changes that were observed in the CTS patients were the result of measuring the stiffness of the pseudoneuroma. As chronic nerve compression is known to be followed by pathological changes in the nerve trunk, that is, endoneurial edema, fibrosis, and thickening of the epineurium,¹⁶ these histological findings may cause changes in the cross-sectional area and the material properties of the nerve.

Numerous studies have shown the utility of ultrasound imaging for the diagnosis of CTS. It is well established in the literature that swelling of the median nerve can be indicated by the cross-sectional area of the nerve under ultrasound.² More recently, it was found that the structures of the median nerve were harder (lower strain) in CTS patients than in normal subjects.¹⁸ This suggests that chronic focal nerve compression of the median nerve can lead to alteration in its morphology and cause

demyelination by mechanical stress, deforming the myelin lamellae.¹⁶ It was confirmed that the weakness of the thumb opposition strength related to the morphological and mechanical property changes of the nerve. However, the correlations between thumb opposition strength and ultrasound parameters were relatively low. This is because the loss of thumb opposition strength occurs in the latter stages of the disease. This may not be obvious in the early stage of the disease, even when there were swelling and stiffness of the nerve in the ultrasound study.

The higher correlation between thumb opposition and distal motor latency suggests that nerve conduction study reflects the motor function of the nerve more than other imaging studies. Electrodiagnostic parameters are abnormal if there is significant demyelination of axonal loss in the large myelinated fibers. It is reported that, in patients with a clinical diagnosis of CTS, the accuracy of ultrasound imaging is similar to that of nerve conduction study. It may be favored by patients because it is painless and easy to undergo. However, the findings of the present study further support the importance of nerve conduction study in confirming the extent of median nerve disfunction in CTS patients.

There are, however, several limitations to our study. First, we did not evaluate sensory nerve conduction velocity. This was because the skin temperature and humidity easily affect this variable. In addition, it is often impossible to measure sensory nerve conduction in CTS patients. Second, thumb opposition strength may be affected by other factors besides CTS, that is, carpometacarpal arthritis, the effect of adductor pollicis, Martin-Gruber anastomosis, and so forth. Third, the majority of the patients were classified as the grade 4 or 5 in the MMT evaluation. The patients classified as grade 1 to 3 were few. The loss of thumb opposition strength is a late sign. Quantitative assessment of the thumb opposition strength may be required to detect early signs of muscle weakness. Fourth, ultrasound strain measurement is known to be affected by the surrounding structures, so it may be necessary to standardize the method by confirming the measurement with other objective indicators. Fifth, there was no control group in this study. Finally, our measurements were taken only at the proximal carpal tunnel because this is

where pseudoneuroma is observed. In addition, it was easy to identify those with CTS by their median nerve size. The results may differ when measured at several different levels.

In conclusion, we assessed whether there was a correlation between the use of ultrasound-derived cross-sectional area and nerve strain with abnormal nerve conduction studies and thumb weakness. The strength of our study is that we could compare median nerve stiffness with the functional assessment. This can help us to understand how the pathological changes affect nerve function. As a result, it was found that there were significant correlations for these clinical evaluations. In particular, there were higher correlations between distal motor latency and strain ratio, and thumb opposition strength and distal motor latency. This suggests that the nerve conduction delay is related to changes in the material properties of the median nerve. In addition, nerve conduction study remains the principal indicator of the thumb opposition strength.

Ethical Approval

The protocol for this study was reviewed and approved by our institutional review board.

Statement of Human and Animal Rights

The procedures described in this article were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000.

Statement of Informed Consent

Participants were given a brief description of the purpose of the research and the testing procedures during the initial contact. Written informed consent was obtained from all patients for being included in the study.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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