

The Diagnostic Value of Ultrasonography in Korean Carpal Tunnel Syndrome Patients

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Objective: The purpose of this study was to assess the diagnostic utility of the wrist ultrasonography (USG) in patients with and without carpal tunnel syndrome (CTS).

Methods: Individuals with electrodiagnostically proven CTS patients and healthy control subjects were enrolled prospectively. USG was done 60 wrists of 48 patients with CTS and 36 wrists of 18 controls. The USG analysis included median nerve cross sectional area (CSA) at the level of carpal tunnel inlet. We also evaluated the relationship between median nerve CSA at the level of carpal tunnel inlet and severity grade of nerve conduction test in CTS patients.

Results: The median nerve CSA at the level of carpal tunnel inlet was significantly larger in CTS patients (13.6 mm² versus 7.7 mm², $p < 0.0001$). And there was an association between median nerve CSA and severity grade of nerve conduction studies ($p = 0.036$). Receiver operating characteristics (ROC) analysis yielded sensitivity of 86.7% and specificity of 88.9% using a cut-off value of 9 mm². But the specificity was increased to 97.2%, although sensitivity was decreased to 78.3%, when using cut-off value at 10.1 mm².

Conclusion: Ultrasonographic measurement of the median nerve CSA at carpal tunnel inlet was useful in diagnosis of CTS. According to ROC analysis, USG is used as a complementary test for electrodiagnostic test.

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KEY WORDS: Carpal tunnel syndrome · Ultrasonography · Electrodiagnosis.

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy. In most cases of CTS, characteristic clinical findings alone may be sufficient for diagnosis.^{17,22)} Although the electrodiagnostic tests (EDT) have been reported to be high sensitivity and specificity, other studies noted a substantial false-positive and false-negative rate of 10–20%.^{6,7,19)}

Since 1992, Buchberger et al.²⁾ has been the first to quantify changes in CTS using ultrasonography (USG), many studies demonstrated a consistent and significantly increased median nerve cross-sectional area (CSA) in patients with

CTS. The most frequently used criterion for USG study is at the level of carpal tunnel inlet, where the median nerve is identified most easily.^{14,22)} However, the normal range and pathologic threshold of median nerve CSA vary widely between laboratories. The pathologic thresholds are ranging from 9 to 14 mm².^{9,22)}

The object of our study is to establish the clinical efficacy of USG in patients with CTS through reestablish the normal range and pathologic threshold of median nerve CSA at the level of carpal tunnel inlet in prospectively recruited patients with and without CTS; and also to correlate ultrasonographic measurements with electrophysiological measurements of CTS severity.

Materials and Methods

Study population

Patients were enrolled prospectively at our institute from September 2008 to April 2012. The USG was carried out on 60 wrists of 48 CTS patients who confirmed by EDT ac-

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cording to the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) criteria. As control group, we performed USG on 36 wrists of 18 healthy adults who did not have signs and symptoms of CTS.

Clinically severe CTS was defined to be present in patients who had two or more of the following criteria: 1) nocturnal paresthesias and pain in the median nerve distribution in the hand, which cause awakes; 2) reproduction or aggravation of paresthesias or pain by Tinel or Phalen signs; 3) aggravation of paresthesias by activities such as driving a car, riding a bike, holding a book, or holding a telephone; and 4) relief of symptoms by shaking the hand. These clinical criteria have been used previously in other studies.^{11,27)} Atrophy of abductor pollicis brevis muscle (APBM) was confirmed by visual inspection and palpation of the muscle. Patients with a history of peripheral neuropathy, diabetes and who underwent previous CTS surgery were excluded in this study.

This study was approved by the institutional review board of our Hospital. All participants provided signed informed consent (SCH-2012-069). No compensation was provided.

Electrodiagnostic test

Nerve conduction studies (NCS) across the affected wrists were performed on all patients. The studies were performed according to the protocol of AANEM,²³⁾ while maintaining the skin temperature at 32°C. The median motor nerve conduction study was performed by supramaximal electrical stimulation of the median nerve at the wrist and recording from an active electrode placed over the motor point of the APBM 8 cm from the stimulation point with the reference electrode over the metacarpophalangeal joint of the thumb. Distal motor latency and baseline-negative peak amplitude of compound muscle action potentials (CMAP) of median nerve were measured. Sensory nerve conduction study was performed by positioning the recording electrode on the index finger and stimulating the proximal median nerve at points 7 cm and 14 cm from the recording electrode. Through these tests, distal sensory latency, baseline-negative peak amplitude of sensory nerve action potentials (SNAPs), and conduction velocity at the wrist segment were measured.

The severity of electrophysiological CTS impairment was

assessed according to the classification reported by Stevens²³⁾ and divided into 3 groups as Table 1.

Ultrasonography

The affected wrist was assessed with USG in patients group immediately after the EDT. In control subjects, both wrists were assessed with USG. USG was performed using a 7–12 MHz linear-array transducer. A radiologist conducted the measurement without any information of the EDT results. Subjects were examined lay down on a hard, flat surface with the arm supinated, the wrist in neutral position, and fingers semi-extended. Median nerve measurements were performed at carpal tunnel inlet, which defined as the proximal margin of the flexor retinaculum between the scaphoid tubercle and the pisiform bone. The distal wrist crease served as an external landmark for initiation of scanning. The CSA measurements were performed by tracing the margin of the inner border of the perineural hyperechoic rim surrounding the hypoechogenic median nerve with electronic calipers.

Statistical analysis

Statistical analyses were performed using the SPSS 17.0 software package (SPSS Inc., Chicago, IL, USA), and statistical significance was set at $p < 0.05$. Student's *t*-test was used to test for differences in the patients and healthy controls. For statistical significance between 3 grade groups of NCS, one-way analysis of variance test was employed.

Receiver operating characteristics (ROC) curves were configured to establish the cut-off points of median nerve CSA with optimal sensitivity and specificity for establishing a diagnosis of CTS.

Results

Study population

Forty-eight (60 wrists) patients and 18 (36 wrists) healthy controls were included in the study. The age and sex distribution of patient and control group are shown in Table 2. The median symptom duration of CTS patients was 12.1 months. Of the 60 wrists, 18 cases were clinically severe CTS and

TABLE 1. Electrophysiological carpal tunnel syndrome grading scheme according to the classification reported by Stevens²³⁾

	DSL (ms)	Samp (μV)	DML (ms)	Mamp (mV)
Mild	>3.5	<20	–	–
Moderate	Abnormal median sensory latencies as above		>4.2	<5
Severe	Abnormal median motor/sensory latencies as above, with absent SNAP or thenar CMAP abnormal spontaneous activity on needle examination			

DSL: distal sensory latency, Samp: sensory amplitude, DML: distal motor latency, Mamp: motor amplitude, SNAP: sensory nerve action potential, CMAP: compound motor action potential

TABLE 2. Summary of carpal tunnel syndrome patients and healthy control subjects

	Patients (n=48)	Controls (n=18)	p
Mean age \pm SD (years)	58.5 \pm 12.1	54.3 \pm 12.9	0.114
Female gender	43 (89.5%)	10 (55.6%)	0.357
Number of wrists (right/left)	60 (29/31)*	36 (18/18)*	
Median duration of symptoms (months)	12.1	N/A	
Clinically severe grade (wrists)	18 (30.0%)	N/A	
Atrophy of APBM	31 (51.7%)	N/A	
Electrodiagnostic grade		N/A	
Mild	6 (10.0%)		
Moderate	28 (46.7%)		
Severe	26 (43.3%)		

*the numbers in parenthesis denote the counts of right/left wrists. APBM: abductor pollicis brevis muscle

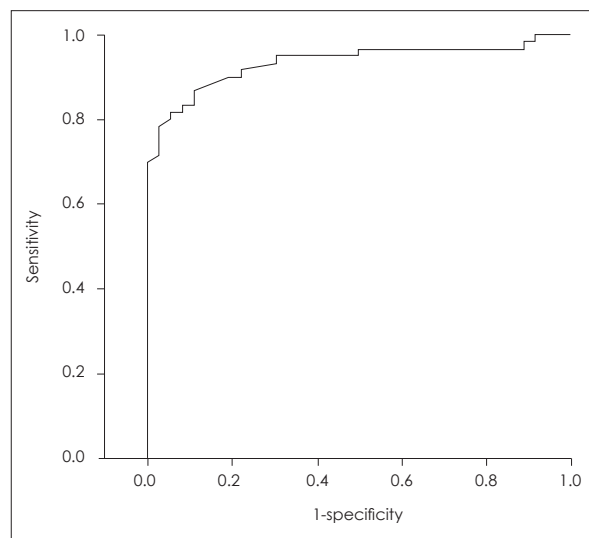


FIGURE 1. Receiver operating characteristics curve for ultrasonographic assessments of median nerve cross-sectional area at carpal tunnel inlet. The area under the curve is 0.935 (95% confidence interval, 0.86–0.98; $p < 0.0001$).

31 cases showing atrophy of APBM.

Electrodiagnostic test

The severity of CTS according to classification reported by Stevens was mild in 6 wrists, moderate in 28 wrists and severe in 26 wrists. The mean values of NCS were followings: sensory latency, 3.05 ms; sensory amplitude, 11.76 μ V; sensory velocity, 29.78 m/s; motor latency, 5.45 ms; and motor amplitude, 9.18 mV. CMAPs were absent in 2 cases and median SNAPs were completely absent in 13 cases.

Ultrasonography and statistical analysis

The mean value of CSA was 13.6 ± 4.8 mm² (range 6.2–31.2 mm²) in patient group, and 7.7 ± 1.2 mm² (range 5.4–10.5 mm²) in control group. The mean CSA at carpal tunnel inlet was significantly larger in patients than in controls ($p < 0.0001$). The ROC analysis demonstrated the area under

TABLE 3. Median nerve CSA according to NCS grade

NCS grade	Median nerve CSA (mm ²)	p
Mild	9.4 \pm 2.4	0.036*
Moderate	13.3 \pm 4.2	
Severe	14.9 \pm 5.4	

*statistically significant was obtained through one-way analysis of variance test ($p < 0.05$). NCS: nerve conduction test, CSA: cross sectional area

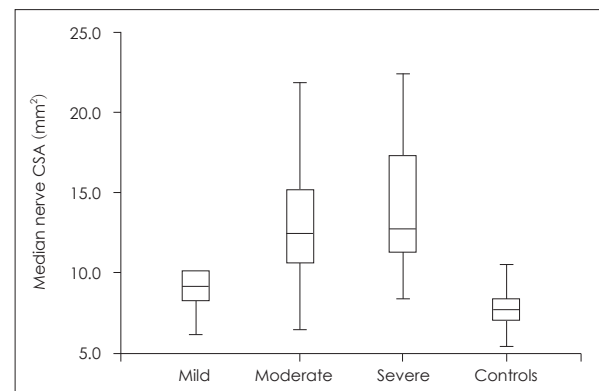


FIGURE 2. Box plot showing median nerve cross-sectional area (CSA) according to severity of nerve conduction study, and control subjects.

the curve at 0.935 for median nerve CSA (95% confidence interval, 0.86–0.98; $p < 0.0001$) (Figure 1). The cut-off value which defined to the best sensitivity over specificity ratio was at 9 mm² (sensitivity of 86.7% and specificity of 88.9%). The 2 standard deviation (SD) above the mean control value was 10.1 mm². With the cut-off value of 10.1 mm² the specificity was increased to 97.2%, whereas the sensitivity was slightly decreased to 78.3%.

Mean median nerve CSA of the patient group who classified with mild, moderate and severe NCS grade was 9.4 mm², 13.3 mm², and 14.9 mm², respectively (Table 3). There was an association between median nerve CSA and severity grade of NCS ($p = 0.036$) (Figure 2). The severe grade of NCS showed significantly larger median nerve CSA.

Discussion

This study has demonstrated that median nerve CSA at the carpal tunnel inlet is significantly increased in electrodiagnostically proven CTS patients compared with healthy controls.

The advantage of USG is less invasive than EDT, which can make one discomfort from the electrical stimulations. And, USG may also be advantage in advanced CTS patients with severe APBM atrophy where NCS shows no more response.¹⁴⁾ Anatomical variations of median nerve and other morphological changes, such as cysts, neuromas, and aberrations of muscles and nerves, at the wrist are relatively common.^{1,4,8,13,16)} Therefore USG can provide an anatomical profile which is important when minimal invasive surgery, such as endoscopic median nerve release, is performed.

Mean normal value of median nerve CSA at the carpal tunnel inlet have varied among reports, ranging from 6.1 to 10.4 mm².^{3,21,24,28)} In our healthy control group, mean value of median nerve CSA at the carpal tunnel inlet was 7.7 mm², which fall within the range of previous reports. Some studies considered that differing demographic and biometric features, such as older age, male gender, body mass index, and handedness, may contribute to the range of normal value.^{3,5)} However, the debates are still remains, other studies found no significant association between biometric characteristics of subjects and median nerve CSA at wrist and forearm in their well-matched case control study.^{6,9)} Thus, it can be said that the range of normal values for median nerve CSA in the literatures more likely reflects variations in study design and USG technique.

The patients who proven electrodiagnostically CTS had significantly increased median nerve CSA than control subjects. There is no clear explanation why median nerve is found to be thickened or enlarged on USG in CTS. One possible pathophysiology can be assumed based on the result of experimental study for entrapment neuropathy. The cascade of the biological response to compression in peripheral nerves includes endoneurial edema, demyelination, inflammation, distal axonal degeneration, fibrosis, growth of new axons, remyelination, and thickening of the perineurium and endothelium. The degree of axonal degeneration is associated with the amount of endoneurial edema.^{18,20)} Therefore, a more severe grade of median neuropathy as defined by EDT can produce increased endoneurial edema. And this increased swelling will appear as higher median nerve CSA in USG. This was confirmed by our result of significant correlation between median nerve CSA and the NCS severity scale.

ROC analysis in previous studies yields sensitivities ranging from 62% to 97.9% and specificities ranging from 83% to 100% using a cut-off value which makes best sensitivity over specificity ratio.^{1,9,16,26,28)} Our ROC analysis yielded a cut-off value of 9 mm² with 86.7% sensitivity and 88.9% specificity. Those results are similar to previous reports and comparable with sensitivities and specificities of the EDT results. Therefore, if EDT is not available or not tolerable, ultrasonographic assessment of median nerve CSA can be used as a first-line test for diagnosis of CTS. In this setting, a cut-off value with maximal sensitivity and specificity should be used.

The sensitivity and specificity of EDT for diagnosis of CTS has been estimated to be 80–90% and 82–85%, respectively.^{10,13,15,25)} Eventually, approximately 10 to 15% of subjects are the “milder” cases of CTS, those with clinical symptom of CTS but normal NCS results. Koyuncuoglu et al.¹³⁾ found that such “milder” cases of CTS were significantly higher median nerve CSA than healthy control subjects. And they confirmed the diagnosis of CTS in 30% of subjects using cut-off value of 10.5 mm², which predicted specificity as 94.7%.²⁹⁾ Some authors reported very high specificity for diagnosis of CTS using 2SD above the mean control value of median nerve CSA.^{9,14)} Our ROC analysis also yielded better specificity (97.2%) using cut-off value of 10.1 mm² (but decreased sensitivity to 78.3%). Thus, USG has a better specificity than NCS when using cut-off value of median nerve CSA as 2SD above the mean control value. The USG assessments of median nerve CSA using cut-off value with high specificity can be used as a complementary with EDT. If EDT is not available or not tolerable, USG can be used as a stand-alone test for diagnosis of CTS. In this setting, a cut-off value with maximal sensitivity and specificity based on ROC analysis should be used. If there is high clinical suspicion for CTS, but the EDT results are not sufficient for diagnosis of CTS, the USG could be used to confirm the diagnosis. In this case, a cut-off value of median nerve CSA with high specificity (e.g., 2SD above the mean control value) should be used.

Our study has several limitations. First, we included both wrists from each control subjects. And there were relatively small number of control subjects. Second, we measured median nerve CSA only at the level of carpal tunnel inlet. The value of USG for CTS diagnosis could be more increased by measuring median nerve CSA in multiple location at the wrist^{12,14)} or considering other ultrasonographic features (such as flattening ratio of the median nerve, palmar bowing of the flexor retinaculum) not included in this study.

Conclusion

In this study, we showed that ultrasonographic assessments of the median nerve CSA at carpal tunnel inlet were useful in diagnosis of CTS. And when using a cut-off value of 10.1 mm² may help the diagnosis of CTS in patients with negative EDT results.

■ The authors have no financial conflicts of interest.

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