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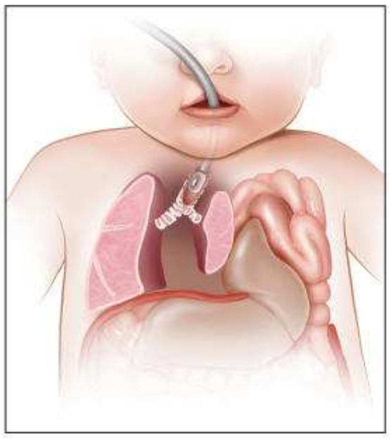

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Diagnostic Utility of Sonography and Correlation Between Sonographic and Clinical Findings in Patients With Carpal Tunnel Syndrome

Tsuyoshi Tajika, MD, Tsutomu Kobayashi, MD, PhD, Atsushi Yamamoto, MD, PhD, Tetsuya Kaneko, MD, PhD, Kenji Takagishi, MD, PhD

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Objectives—First, we investigated the accuracy of carpal tunnel syndrome diagnosis by comparing the cross-sectional area of the median nerve measured at the level of proximal inlet of the carpal tunnel with that measured at the level of the distal radioulnar joint on sonography. Second, we evaluated the correlation between sonographic and neurophysiologic findings and clinical findings assessed by the Carpal Tunnel Syndrome Instrument of the Japanese Society for Surgery of the Hand (JSSH).

Methods—Fifty wrists in 34 patients and 81 wrists in 45 healthy volunteers were examined. The proximal cross-sectional area and the difference (Δ) between the proximal and distal cross-sectional areas were calculated for each wrist. Nerve conduction velocity tests were performed for all patients with carpal tunnel syndrome. The proximal, distal, and Δ cross-sectional areas were compared for the two groups. We examined the correlation between the proximal, distal, and Δ areas, nerve conduction velocity findings, and JSSH scores in the patients.

Results—The diagnosis of carpal tunnel syndrome determined by the Δ cross-sectional area was more accurate than the diagnosis determined by the proximal area on receiver operating characteristic curve analysis ($P = .006$). Statistically significant correlations were found between proximal area, Δ area, and nerve conduction velocity findings (proximal, $r = 0.45$; $P = .0013$; Δ, $r = 0.44$; $P = .001$). The proximal and distal areas were positively correlated with the JSSH symptom severity score (proximal, $r = 0.39$; $P = .005$; distal, $r = 0.35$; $P = .014$).

Conclusions—The cross-sectional area method using sonography has excellent performance for diagnosing carpal tunnel syndrome. It was useful for measuring the proximal and distal cross-sectional areas to evaluated the symptom severity and for calculating the Δ cross-sectional area to assess motor nerve damage in patients with carpal tunnel syndrome.

Key Words—carpal tunnel syndrome; cross-sectional area; sonography

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Address correspondence to Tsuyoshi Tajika MD, Department of Orthopedic Surgery, Gunma University Graduate School of Medicine, 3-39-22 Showa-machi, Maebashi, Gunma 371-8511, Japan.

E-mail: t.tajika@gunma-u.ac.jp

Abbreviations

BMI, body mass index; JSSH, Japanese Society for Surgery of the Hand; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic

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Carpal tunnel syndrome, entrapment neuropathy of the median nerve at the wrist, is an extremely common disease. It is estimated that the annual incidence is 0.1% among adults. The prevalence is 2.1% among men, 3.0% among women, and 2.7% among the general population.[1,2] The diagnosis of carpal tunnel syndrome is based mainly on a typical history, clinical examination, provocative test, and nerve conduction velocity test. However, 10% to 25% of electrophysiologic examination results are falsely negative. Moreover, nerve conduction velocity remains an expensive, time-consuming, and invasive procedure for patients.[3,4]

Several recent reports have described sonography as useful for diagnosis of carpal tunnel syndrome to detect enlargement of the median nerve cross-sectional area in patients with this condition.[5–14] It excludes anatomic variants such as bifid median nerves and space-occupying lesions such as ganglia, neural tumors, and tenosynovitis.[5] Prior studies have been conducted to determine cutoff values for the median nerve cross-sectional area. Nevertheless, a wide range of diagnostic accuracy rates for carpal tunnel syndrome prevails in evaluations of the cross-sectional area at the level of the proximal inlet of the carpal tunnel.[5–14] Several studies have been undertaken to improve diagnostic accuracy for carpal tunnel syndrome by investigating the cross-sectional area more proximally and more distally.[15] Other studies have demonstrated correlations between sonography of the median nerve and nerve conduction velocity findings and clinical symptom assessment using the Boston Carpal Tunnel Questionnaire.[16–19]

This study was designed to investigate the accuracy of carpal tunnel syndrome diagnosis by comparing the cross-sectional area of the median nerve measured at the level of the proximal inlet of the carpal tunnel with that measured at the level of the distal radioulnar joint and to evaluate the correlation between sonographic imaging and clinical findings assessed by the Carpal Tunnel Syndrome Instrument of the Japanese Society for Surgery of the Hand (JSSH).

Materials and Methods

This study examined 50 wrists of 34 patients, including 25 women and 9 men with a mean age of 59.5 years (range, 30–85 years). The control group comprised 81 wrists of healthy volunteers, including 32 women and 13 men with a mean age of 57.6 years (range, 30–86 years). Patients evaluated consecutively between January 2009 and May 2012 were recruited for this study, and healthy volunteers evaluated between June 2012 and August 2012 were recruited. The carpal tunnel syndrome diagnosis was made according to clinical symptoms (pain, numbness, tingling in the median nerve distribution of the hand, and weakness of pinching strength) and having at least 1 positive provocative test result (Tinel sign at the wrist, Phalen maneuver, and reverse Phalen maneuver), in addition to meeting criteria of nerve conduction velocity findings by the American Association of Electrodiagnostic Medicine (distal terminal latency of the sensory nerve action potential amplitude >3.4 milliseconds or distal terminal latency of the compound muscle action potential amplitude >4.5 milliseconds). All patients with carpal tunnel syndrome underwent sonography and nerve conduction velocity studies. The revised JSSH Carpal Tunnel Syndrome Instrument, which was a version of the Boston Carpal Tunnel Questionnaire proposed by Levine et al[16] and translated into Japanese, was used in our study. The JSSH instrument was validated by Imaeda et al[20] as having evaluation capacities equivalent to the original version. Patients who had bilateral symptoms were asked to answer on each side.

The control group included hospital staff members and their relatives with no clinical symptoms in terms of carpal tunnel syndrome. The control group underwent sonography only. Participants were excluded from this study if they had bifid median nerves or any systemic disorder such as rheumatoid arthritis, diabetes mellitus, connective tissue disorders, chronic renal failure, polyneuropathy, thoracic outlet syndrome, cervical radiculopathy, cervical myelopathy, wrist fracture, and anamnesis of operation at the wrist. Body mass indices (BMIs) of all participants in this study were assessed. The duration of morbidity was recorded for the patients with carpal tunnel syndrome. This study was approved by the Regional Ethics Board, and informed consent was obtained from all patients and volunteers

Sonographic Technique

With a 6–14-MHz linear array transducer and a B-mode portable real-time apparatus (EUB-7500; Hitachi Medical Corp, Tokyo, Japan), sonographic examinations were performed by a hand surgeon (T.T.) with more than 12 years of experience in performing sonography and surgery. Participants were seated facing the examiner to maintain a position of elbows in slight flexion, wrists in slight extension, forearms in supination, and fingers semiextended. The median nerve from the distal forearm to the carpal tunnel outlet was assessed in longitudinal and transverse planes. The angle of the linear array probe was kept perpendicular to the surface of the median nerve. In accordance with a report by Klauser et al,[15] we obtained the cross-sectional area at 2 points: the area was measured at the proximal inlet of the carpal tunnel (Figure 1A) using the pisiform bone as a reference and at the distal radioulnar joint (Figure 1B) using that joint as a reference. The difference (Δ) between the proximal and distal cross-sectional areas was calculated for each wrist. The cross-sectional area was calculated using the direct method with tracing of a continuous line around the inner hyperechoic rim of the median nerve using electronic calipers. Results of sonographic measurements were evaluated by another author (K.T.) without prior information on clinical and electrophysiologic results.

The intratester reliability of the cross-sectional area measurements was evaluated by the primary investigator. Twenty healthy wrists were measured 3 separate times during the same testing session. The intraclass correlation coefficient was 0.88. The prior test-retest reliability of the cross-sectional area was assessed by the primary investigator. Twenty healthy wrists were measured and then remeasured 5 days later. The intraclass correlation coefficient was 0.96. The intertester reliability for sonography was evaluated in 10 healthy wrists by the primary investigator and another investigator. The intertester correlation coefficients were 0.94 and 0.89 for measurements at the proximal inlet of the carpal tunnel and the distal radioulnar joint, respectively.

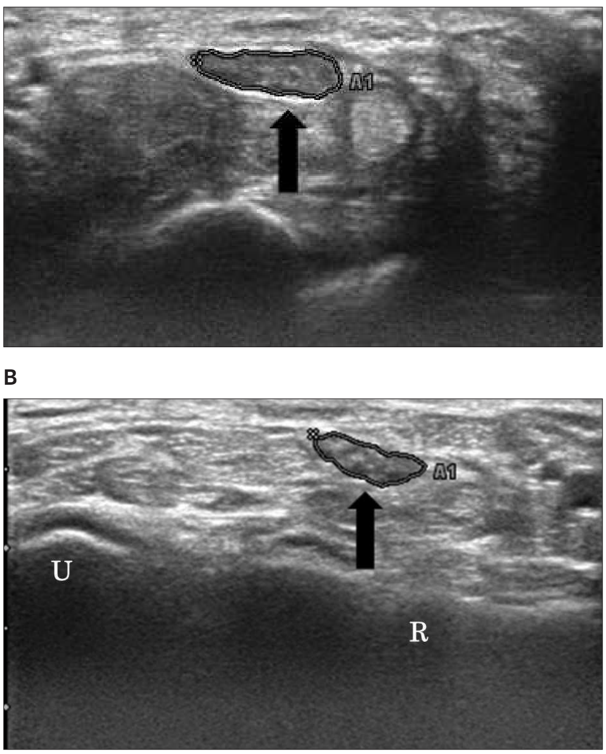
Electrophysiologic Studies

Nerve conduction velocity tests were conducted for the patients referred for carpal tunnel syndrome in this study according to the protocol proposed by the American Association of Electrodiagnostic Medicine. All nerve conduction velocity tests were performed with a standard electromyographic system (Neuropack MEB-2200; Nihon Kohden Corp, Tokyo, Japan) in the same room with the same temperature and for both hands. The patients suspected of having carpal tunnel syndrome also underwent median and ulnar nerve conduction velocity tests. Standard techniques of supramaximal percutaneous stimulation with a constant-current stimulator and standard surface ring electrodes were used for the nerve conduction velocity tests. The tests included measurements of the distal motor latency of the median nerve from the wrist joint to the thenar muscle, the distal sensory latency of the median nerve from the wrist joint to the second finger segment, as assessed by the compound muscle, and sensory nerve action potential amplitudes of the median nerve.

Figure 1. Carpal tunnel syndrome of the left wrist in a 38-year-old woman. **A**, Transverse sonogram of the median nerve (arrow) at the proximal inlet of the carpal tunnel. The proximal cross-sectional area is 13 mm^2. **B**, Transverse sonogram of the median nerve (arrow) at the radioulnar joint. The distal cross-sectional area is 9 mm^2, and the Δ area is 3 mm^2. R indicates radius; and U, ulna.

A

B



Statistical Analysis

The sexes, ages, and BMIs of the two groups were compared by the Fisher exact test or Mann-Whitney *U* test. The proximal, distal, and Δ cross-sectional areas of the carpal tunnel syndrome and control groups were compared by Mann-Whitney *U* tests. The Spearman correlation coefficient by rank test was used to correlate the Δ area with nerve conduction velocity findings (distal motor latency of the compound muscle action potential and distal sensory latency of the sensory nerve action potential), the Carpal Tunnel Syndrome Instrument scores (functional and symptom scores), the BMI of the carpal tunnel syndrome group, and the mean duration of carpal tunnel syndrome symptoms. Receiver operating characteristic (ROC) curve analysis was performed to evaluate whether the Δ or proximal cross-sectional area was more accurate for the diagnosis of carpal tunnel syndrome. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated to assess the accuracy of sonography for diagnosis of carpal tunnel syndrome using proximal area measurements only with threshold values of 10, 11, and 12 mm^2 and Δ area calculations with threshold values of 1, 2, and 3 mm^2. The results reported herein are given as mean (SD); $P < .05$ was considered statistically significant.

Results

The demographic data of the carpal tunnel syndrome and control groups were comparable. The carpal tunnel syndrome was bilateral in 16 cases (47.1%) and unilateral in 18 (52.9%). The mean carpal tunnel syndrome symptom duration was 11.2 (14) months (range, 0.75–48 months).

The mean distal cross-sectional areas were 7.7 (1.8) mm^2 in the carpal tunnel syndrome group and 7.8 (1.9) mm^2 in the control group ($P < .05$). The mean proximal areas were 13.9 (3.2) mm^2 in the carpal tunnel syndrome group and 8.0 (2.0) mm^2 in the control group ($P < .0001$). The mean Δ areas were 6.2 (2.8) mm^2 in the carpal tunnel syndrome group and 0.2 (0.8) mm^2 in the control group ($P < .0001$). The mean JSSH functional status and symptom severity scores were 2.78 (1.01) and 2.82 (0.88) in the carpal tunnel syndrome group.

Table 1 shows the correlation between the sonographic and electrophysiologic findings and the symptom severity and functional status scores in the patients with carpal tunnel syndrome. A statistically significant correlation was found between the proximal cross-sectional area and the distal motor latency ($r = 0.45$; $P = .0013$), the symptom severity score ($r = 0.39$; $P = .005$), and the duration of morbidity in the patients with carpal tunnel syndrome ($r = 0.34$; $P = .017$). The distal area was positively correlated with the JSSH symptom severity score ($r = 0.35$; $P = .014$). A significant correlation was found between enlargement of the Δ area and distal motor latency ($r = 0.44$; $P = .001$), but no relationship was found between enlargement of the Δ area and the JSSH functional status and symptom severity scores. Table 2 shows the accuracy of sonography for diagnosis carpal tunnel syndrome for each cutoff value.

Receiver operating characteristic curve analysis revealed excellent diagnostic ability with the use of both the proximal cross-sectional area (area under the ROC curve = 0.950) and the Δ area (area under the ROC curve = 0.996). However, the diagnostic performance of the Δ area was significantly superior to that of the proximal area ($P = .006$).

Discussion

Standard diagnosis of carpal tunnel syndrome is usually based on clinical signs and symptoms and positive provocation test and electrodiagnostic examination results. However, the most recent developments of sonographic technology can visualize peripheral nerves more clearly. Numerous studies have examined the utility of sonography for evaluating carpal tunnel syndrome.[5–14] Experimental animal models demonstrated that mechanical compression and local ischemia of the peripheral nerve induced morphologic changes because of intraneural edema.[21,22] For diagnosis of carpal tunnel syndrome using sonographic findings, it has been established well in the literature that swelling of the median nerve, indicated by the cross-sectional area of the nerve, should be detected.[5–14] Previous reports have proposed a range of median nerve proximal cross-sectional area cutoff values. The thresholds reported for the median nerve proximal area cutoff for diagnosis of carpal tunnel syndrome vary from 6.5 to 15 mm^2, and the sensitivity reported in these studies ranged from 57% to 98%, with specificity ranging from 63% to 100%.[5–14] A wide range of diagnostic accuracy rates for carpal tunnel syndrome has been shown in evaluations of the proximal cross-sectional area on sonography.

To enhance the diagnostic accuracy for carpal tunnel syndrome, different sonographic measurement techniques have been reported. Klauser et al[15] calculated the difference between the proximal cross-sectional area and the area at the level of the pronator quadratus muscle to compensate for the interindividual variation in the cross-sectional area of the median nerve. Their study revealed that the use of the Δ area with a 2-mm^2 threshold yielded the greatest sensitivity (99%) and specificity (100%) for the diagnosis of carpal tunnel syndrome, and the Δ parameter

Table 1. Correlations Between Sonographic and Clinical Findings in the Patients With Carpal Tunnel Syndrome

Parameter	Distal Sensory Latency	Distal Motor Latency	Symptom Severity Scale	Functional Status Scale	BMI	Symptom Duration
CSAc	0.23	0.45[a]	0.39[a]	0.13	0.18	0.34[a]
CSAd	−0.04	0.02	0.35[a]	0.23	−0.02	0.07
ΔCSA	0.29	0.44[a]	0.13	−0.03	0.1	0.27

CSAc indicates cross-sectional area of the median nerve measured at the level of the proximal inlet of the carpal tunnel; CSAd, cross-sectional area of the median nerve measured at the level of the distal radioulnar joint; and ΔCSA, difference between the proximal and distal cross-sectional areas.
[a]Statistically significant ($P < .05$)

was superior to the proximal area for diagnosing carpal tunnel syndrome by ROC analysis. Previous studies revealed a correlation between the degree of the proximal area and neurophysiologic impairment. Klauser et al[15] also reported that the Δ and proximal areas showed a significant tendency to be as large as the severity of the electrodiagnostic examination findings. However, they did not evaluate the correlation between the Δ and proximal areas and the severity of the subjective symptoms in patients with carpal tunnel syndrome.

We also evaluated the cross-sectional area of the median nerve in the 2 places described by Klauser et al[15] to correct the variation of the proximal cross-sectional area evaluation. We measured the cross-sectional area at the inlet of the carpal tunnel and at the level of the distal radioulnar joint. We selected the inlet of the carpal tunnel, as other studies have adopted, because it was easy to image the proximal area where the median nerve was parallel to the skin surface. However, we measured the cross-sectional area at the distal radioulnar joint, unlike the proximal point Klauser et al[15] imaged. We concluded that this joint was also technically easy to image reproducibly as a bony landmark.

Our study revealed that the mean proximal cross-sectional area in the patients with carpal tunnel syndrome was significantly larger than the mean proximal area in the healthy volunteers ($P < .0001$), but no significant difference was found between the mean distal area in the patients with carpal tunnel syndrome and the volunteers ($P = .83$). Our results show that that the mean Δ cross-sectional area in the patients with carpal tunnel syndrome was significantly greater than the mean Δ area in the volunteers ($P < .0001$). Table 2 shows the sensitivity and specificity of each proximal and Δ cross-sectional area cutoff value for diagnosing carpal tunnel syndrome. The use of a Δ area cutoff value of 2 mm^2 or greater yielded 100% sensitivity and 99% specificity. It had a PPV of 98% and an NPV of 100%. Our study also demonstrated that the Δ area was superior to the proximal area for diagnosing carpal tunnel syndrome by ROC analysis, as Klauser et al[15] reported. Our study also revealed a significant relationship between enlargement of the Δ area and distal motor latency in patients with carpal tunnel syndrome. These findings show that evaluation of the Δ cross-sectional area by sonography is very useful for diagnosing carpal tunnel syndrome.

In a recent report, Karadağ et al[18] revealed that the proximal cross-sectional area was positively correlated with Boston Carpal Tunnel Questionnaire symptom severity scores and not just electrophysiologic severity. They reported that the degree of median nerve swelling reflected the degree of nerve damage and carpal tunnel syndrome symptom severity. Padua et al[14] stated that symptom severity did not worsen with an increase in the proximal cross-sectional area, but the functional status was strongly related to the proximal area. Furthermore, Mondelli et al[19] reported no association between the proximal area and Boston Carpal Tunnel Questionnaire scores, and Kaymak et al[17] found that neither the proximal nor the distal area was associated with the functional status or symptom severity in the Boston Carpal Tunnel Questionnaire. The relationship between the proximal and distal cross-sectional areas and patient-oriented findings is controversial.

We investigated the relationship between the Δ, proximal, and distal cross-sectional areas calculated on sonography and the functional status and symptom severity in the patients with carpal tunnel syndrome. No significant relationship was found between the Δ area and the JSSH

Table 2. Diagnostic Accuracy of Median Nerve Measurements in Patients With Carpal Tunnel Syndrome

Measurement Cutoff	Sensitivity, %	Specificity, %	PPV, %	NPV, %
CSAc with 10-mm^2 threshold	98 (49/50) [89.4–99.9]	83 (67/81) [73.0–90.5]	78 (49/63) [65.7–87.6]	99 (67/68) [92.6–100]
CSAc with 11-mm^2 threshold	86 (43/50) [73.3–94.2]	91 (74/81) [82.4–96.3]	86 (43/50) [73.3–94.2]	91 (74/81) [82.4–96.3]
CSAc with 12-mm^2 threshold	64 (32/50) [49.2–77.1]	96 (77/81) [89.0–99.2]	89 (32/36) [73.6–97.3]	81 (77/95) [71.6–88.3]
ΔCSA with 1-mm^2 threshold	100 (50/50) [94.2–100]	84 (68/81) [74.1–91.3]	79 (50/63) [66.8–88.3]	100 (66/66) [95.6–100]
ΔCSA with 2-mm^2 threshold	100 (50/50) [94.2–100]	99 (80/81) [93.3–100]	98 (50/51) [89.5–99.9]	100 (80/80) [96.3–100]
ΔCSA with 3-mm^2 threshold	92 (46/50) [80.3–98.0]	100 (81/81) [96.4–100]	100 (46/46) [93.7–100]	95 (81/85) [87.8–98.6]

Numbers in parentheses are numbers of wrists used to calculate the percentages; numbers in brackets are 95% confidence intervals. Abbreviations are as in Table 1.

symptom severity score. However, the proximal area was positively related to symptom severity but not the functional status. In addition, the distal area was positively correlated with the JSSH symptom severity score in the patients with carpal tunnel syndrome. No significant difference was found between the distal area in the patients with carpal tunnel syndrome and the control group. The proximal area was positively correlated with the distal area in the patients with carpal tunnel syndrome ($r = 0.48$; $P = .0004$). The Δ area method might be unsuitable for quantifying the subjective symptom severity in patients with carpal tunnel syndrome because the possibility exists that the value of the Δ area is canceled out by the positive correlation between the JSSH severity score and the proximal and distal areas. Yayama et al[22] reported that failure of the blood-nerve barrier after intraneural ischemia might induce intraneural edema and affect nerve function and the severity of symptoms associated with nerve compression in an experimental animal model. In our study, the proximal area was positively correlated with the duration of symptoms in the patients with carpal tunnel syndrome. The mean symptom duration was 11.2 (14) months. Mechanical pressure levels and the duration might influence structural changes in the median nerve. The distal cross-sectional area, which maintains a distance from the entrance of the carpal tunnel, might be larger in patients with carpal tunnel syndrome and a longer disease duration than in the patients with carpal tunnel syndrome investigated in this study. No significant association was found between the Δ, proximal, and distal areas and the JSSH functional status score. However, the Δ and proximal areas were positively related to distal motor latency. These results might have been affected by the sample size and the degree of disease severity among the patients. Further research with a larger sample and a wide spectrum of carpal tunnel syndrome severity is necessary to elucidate the relationship between morphologic changes in the median nerve and the severity of median nerve damage and patient-oriented perceptions of hand function.

Several reports have described a positive correlation between the proximal cross-sectional area and BMI in patients with carpal tunnel syndrome.[23] In addition, one risk factor for carpal tunnel syndrome was reported as a high BMI.[24] In our study, the mean BMI in the patients with carpal tunnel syndrome was significantly higher than that in the healthy volunteers ($P < .05$). However, the cross-sectional areas showed no significant relationship with the BMI. Additional data are necessary to clarify the association between sonographic findings, carpal tunnel syndrome severity, and BMI.

Our research included several limitations. First, our sample size was small. Second, we did not attempt to quantify sensory and motor tests. Additional studies must be conducted to confirm the association between the proximal, distal, and Δ cross-sectional areas and results of quantitative sensory and motor tests. Third, we were unable to investigate patients who had clinical symptoms of carpal tunnel syndrome with negative electrophysiologic findings or without nerve conduction studies because the patient criteria in this study included both clinical symptoms of carpal tunnel syndrome and abnormal electrophysiologic findings. Koyuncuoglu et al[25] reported that electrodiagnostic findings might be normal in patients with clinical carpal tunnel syndrome, as only numbness and paresthesia are evident in early stages. Therefore, nerve conduction tests mainly assessed the function of large myelinated nerve fibers but not small fibers. Additional studies should be undertaken for these patients to ascertain the relationship with the Δ cross-sectional area.

Our results show that the Δ cross-sectional area method using sonography has excellent performance for diagnosing carpal tunnel syndrome. In addition to carpal tunnel syndrome diagnosis, it was useful for measuring the proximal and distal cross-sectional areas to evaluate the symptom severity and helpful for calculating the Δ cross-sectional area to assess median motor nerve damage in patients with carpal tunnel syndrome.

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