

The usefulness of ultrasonography to diagnose the early stage of carpal tunnel syndrome in proximal to the carpal tunnel inlet

A prospective study

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Abstract

This study aimed to investigate the relationship between the change of median nerve cross-sectional area (CSA) and the severity of carpal tunnel syndrome (CTS) determined by electrodiagnostic study based on the area immediately proximal to the carpal tunnel inlet (IPCTI).

From December 2016 to August 2017, 34 patients (8 men and 26 women; mean age, 61.68 years \pm 11.83; range, 28–80 years) with CTS symptoms were recruited. Electrodiagnostic study was performed in all patients to categorize the severity of CTS according to Bland classification. The CSA of median nerve and carpal tunnel at IPCTI, and carpal tunnel inlet/outlet level was measured by one physician. The Kruskal-Wallis test was used for comparing the CSA of the median nerve and carpal tunnel among CTS severity groups divided by electrodiagnostic study. The Dunn procedure was used for post-hoc comparison.

At IPCTI and the carpal tunnel inlet level, the CSA of the median nerve was statistically larger depending on the severity of CTS ($P < .01$, $P < .01$). In the post-hoc comparison, only the CSA measured at the IPCTI level could differentiate normal reference values from mild CTS indicating the early stage ($P < .05$).

Measuring the CSA of median nerve in IPCTI level is the most sensitive method to diagnose the early stage CTS.

Abbreviations: CMAP = compound motor action potential, CSA = cross-sectional area, CTS = carpal tunnel syndrome, DML = distal motor latency, IPCTI = immediately proximal to the carpal tunnel inlet, NCV = nerve conduction velocity, PWDSLD = palm wrist distal sensory latency difference, SNAP = sensory nerve action potential.

Keywords: anatomy, carpal tunnel syndrome, cross-sectional, electrodiagnosis, median nerve, ultrasonography

1. Introduction

Carpal tunnel syndrome (CTS) affects 1 in every 10 persons and accounts for about 90% of all compressive neuropathies.^[1] The symptoms of CTS include numbness, tingling, or a burning sensation in the thumb and fingers. Weakness and atrophy of the thumb muscles could occur without proper treatment.^[2–4] The CTS is caused by the compression of the median nerve in the carpal tunnel, an anatomical compartment located at the base of the palm. As the disease progresses, the median nerve becomes

increasingly swollen, causing more compression and worsening of symptoms.^[5–7]

The diagnosis of CTS is based on electrodiagnostic study to confirm neuropathy and radiologic examination to confirm the compression of the median nerve.^[8–10] Clinical diagnosis of CTS can also be made with a greater than 80% sensitivity and specificity of 95% or more.^[10,11] Median motor and sensory nerve conduction studies are valid and reproducible in a clinical laboratory setting. However, they are the pain-causing procedure and cannot identify the anatomy around the nerve.

With improvements in the resolution of ultrasonography imaging, CTS is now diagnosed using high-resolution ultrasonography, which is non-invasive, does not cause pain, and takes a short time to complete. Many studies have suggested diagnosing CTS when the cross-sectional area (CSA) of the median nerve in the carpal tunnel is above a certain cut-off value.^[12–16] Ultrasonography offers high diagnostic accuracy and has a high correlation with electrodiagnostic findings and severities.^[7,16–18] However, since the carpal tunnel is limited space, it is difficult to diagnose by ultrasonography until the nerve is swollen enough to exceed the pressure in the carpal tunnel.

In this study, we investigated the changes in the CSA of the median nerve in non-limited spaces, such as immediately proximal to the carpal tunnel inlet (IPCTI), and confirmed the relationship between the CSA of the median nerve and the severity of CTS assessed using electrodiagnostic study.

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2. Methods

2.1. Participants

This study was approved by the Ethics Committee, and all patients provided written informed consent. A total 68 hands of 34 patients over the age of 20 years who visited the clinic on account of symptoms such as a tingling sense, numbness, and pain in the hand were enrolled in this prospective study, which was conducted from December 2016 to August 2017. Patients who had previously undergone surgery on the wrist (including for CTS), those who received steroid injection for CTS within the last 3 months, those with peripheral neuropathy, and those with Martin-Gruber anastomosis were excluded (Fig. 1).

2.2. Electrodiagnostic study

All patients underwent a nerve conduction study (Cadwell Sierra Wave; Cadwell Laboratories, Kennewick, WA) based on the American Academy of Neurology statement about the protocol for patients suspected to have CTS. Electrodiagnostic study was performed on both hands in all patients regardless of the symptom. Electrodiagnostic indices included 8-cm transcarpal orthodromic median and ulnar sensory peak latencies, 8-cm median motor

compound muscle action potentials, distal motor latencies, and median conduction velocities.^[10,11] These parameters were measured using the standard techniques of supramaximal stimulation and surface electrodes with adjustment for skin temperature.

The severity of CTS was categorized using the Bland classification according to the electrodiagnostic results. The severity based on the Bland classification were as follows: normal (grade 0); very mild (grade 1), CTS demonstrable only with the most sensitive tests; mild (grade 2), sensory nerve conduction velocity slow on finger/wrist measurement, normal terminal motor latency; moderate (grade 3), sensory potential preserved with motor slowing, distal motor latency to the abductor pollicis brevis < 6.5ms; severe (grade 4), sensory potentials absent but motor response preserved, distal motor latency to the abductor pollicis brevis < 6.5 ms; very severe (grade 5), terminal latency to the abductor pollicis brevis > 6.5 ms; extremely severe (grade 6), sensory and motor potentials effectively unrecordable (surface motor potential from the abductor pollicis brevis < 0.2 mV amplitude).^[19] In this study, patients with a normal finding were defined as group 1, those with neurapraxia (grades 1 and 2) as group 2, those with mixed neurapraxia and axonotmesis (grades 3 and 4) as group 3, and those with axonotmesis (grades 5 and 6) as group 4 (Table 1).

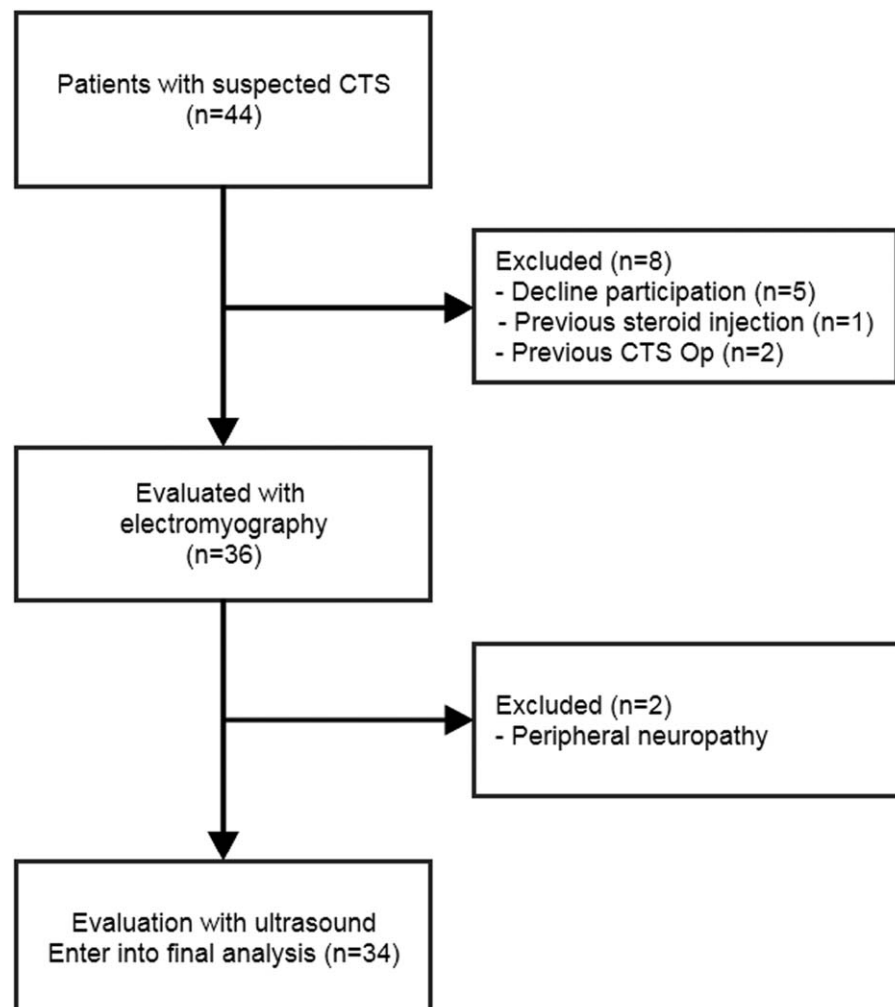


Figure 1. Flowchart of study population. CTS = carpal tunnel syndrome.

Table 1
Group Categorization according to Grade of Bland Classification.

Grade	Electrodiagnostic abnormality	Categorize
0 – normal	No abnormality	Group 1
1 – very mild	CTS detected by only PWDSLD*	Group 2
2 – mild	Median DML < 4.5 ms and sensory NCV < 40 m/s	Group 3
3 – moderately severe	Median DML > 4.5 ms and < 6.5 ms with preserved SNAP	
4 – severe	Median DML > 4.5 ms and < 6.5 ms with absent SNAP	
5 – very severe	Median DML > 6.5 ms with CMAP > 0.2 mv	Group 4
6 – extremely severe	Median CMAP < 0.2 mv	

CMAP = compound motor action potential, CTS = carpal tunnel syndrome, DML = distal motor latency, NCV = nerve conduction velocity, PWDSLD = palm wrist distal sensory latency difference, SNAP = sensory nerve action potential.

2.3. Ultrasonography study

Ultrasonography examinations were performed within 1 week after electrodiagnostic study, by a rehabilitation specialist with 5 years’ experience in musculoskeletal ultrasonography. Ultrasonography was performed using a 12–4 MHz linear-array transducer (EPIQ 5; Philips Diagnostic Ultrasound System and Transducers, Bothell, WA) in a quiet environment with an ambient temperature of 20°C. The patients were seated facing the examiner. The arms were extended; the wrists were rested on a hard flat surface; the forearms were supinated; and the fingers were semi-extended. Transverse images were obtained at 3 levels: at IPCTI, at the carpal tunnel inlet, and at the carpal tunnel outlet. The flexor retinaculum was used as a landmark, in preference to the bone landmarks, to the margins of the carpal tunnel. On high-resolution ultrasonography, the flexor retinaculum was seen as a variably bowed echogenic band that spans the carpus. The examiner measured the CSA of the median nerve and that of the

carpal tunnel at each level and measured the depth from the skin to the top of the median nerve (at the IPCTI level, as there is no carpal tunnel, the CSA was not measured) (Fig. 2).

2.4. Statistical analyses

Following previous studies, the sample size was calculated a priori, taking into account the values of the CSA of the median nerve in the affected and unaffected sides.^[20] The sample size was calculated using G*Power software (version 3.0; Franz Faul, Universitat Kiel, Kiel, Germany). All statistical analyses were performed using software (SPSS version 22; SPSS Inc., Chicago, IL). The Kruskal-Wallis test was used to compare the groups divided by the severity of electrodiagnostic study, in terms of age, symptom duration, and the CSAs of the median nerve and carpal tunnel. The Dunn procedure was used for the post-hoc test. One-way analysis of variance was used to determine the depth difference according to the measurement location.

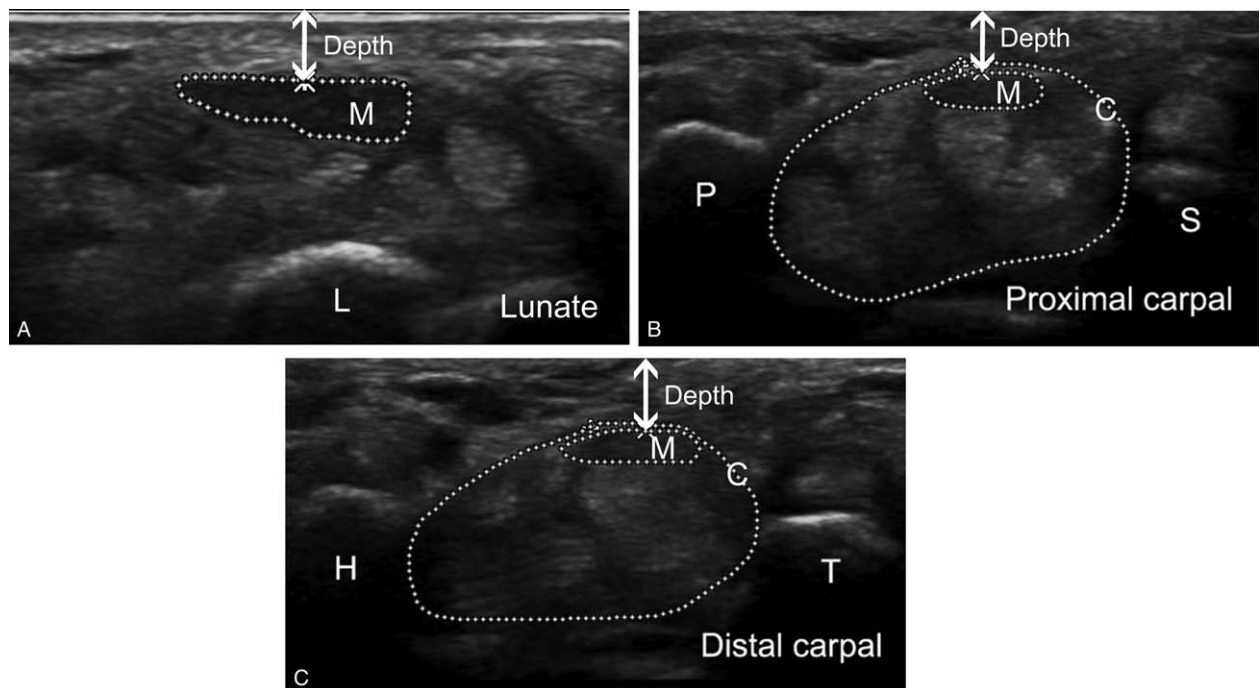


Figure 2. Representative transverse ultrasonography images of the left hand of 55-year-old women. (a) median nerve (outlined) and depth (arrow) at IPCTI level (b) median nerve, carpal tunnel (outlined) and depth (arrow) at carpal tunnel inlet level (c) median nerve, carpal tunnel (outlined) and depth (arrow) at carpal tunnel outlet level. CT = Carpal tunnel, H = Hamate, IPCTI = immediately proximal to the carpal tunnel inlet, L = Lunate, M = Median nerve, P = Pisiform, S = Scaphoid, T = Trapezium.

Table 2
Demographics and clinical characteristics.

Variables	Group 1 [*]	Group 2	Group 3	Group 4	Total
Sex					
Woman	4	28	14	6	52
Men	2	9	1	4	16
Mean age (yr)	58.67 ± 2.50	58.14 ± 11.45	59.33 ± 11.68	67.10 ± 2.53	61.68 ± 11.83
Symptom duration (month) [†]	4.17 ± 3.87	15.68 ± 16.23	14.33 ± 8.85	25.60 ± 6.58	16.72 ± 18.04
Diabetes Mellitus	0	3	2	1	6
Right/Left	1/5	16/21	9/6	8/2	34/34

^{*} Group was categorized according to bland classification based on electromyography finding. Group 1: grade 0 (normal), Group 2: grade 1 and 2, Group 3: grade 3 and 4, Group 4: grade 5 and 6.

[†] Kruskal-Wallis test was used to compare relationship between each group and Dunn procedure was used for post hoc comparison. There was a statistically significant relationship between group 1 and other groups.

Table 3
Outcome measurements of ultrasound of carpal tunnel syndrome.

Outcome Measurement (Cross-sectional area)	Group 1 [*] (mm ²)	Group 2 (mm ²)	Group 3 (mm ²)	Group 4 (mm ²)	P value [†]	P value (Between-Group Comparison)					
						Group 1 and 2	Group 1 and 3	Group 1 and 4	Group 2 and 3	Group 2 and 4	Group 3 and 4
IPCTI level (median nerve)	9.65 (8.83, 11.58)	13.20 (11.20, 16.25)	14.90 (12.00, 22.50)	16.20 (12.63, 19.08)	< .006 [*]	.044 [*]	.012 [*]	.006 [*]	1.000	.869	1.000
Carpal tunnel inlet level (median nerve)	10.15 (9.08, 10.68)	12.10 (11.05, 14.15)	12.20 (10.40, 16.10)	16.05 (14.65, 21.30)	.001 [*]	.127	.086	< .001 [*]	1.000	.019 [*]	.181
Carpal tunnel inlet level (carpal tunnel)	171.00 (163.25, 196.50)	187.00 (170.05, 207.00)	182.00 (174.00, 197.00)	209.00 (174.25, 247.00)	.280						
Carpal tunnel outlet level (median nerve)	10.80 (9.98, 11.13)	13.00 (10.95, 14.10)	12.90 (10.80, 15.90)	14.55 (11.78, 19.43)	.053						
Carpal tunnel outlet level (carpal tunnel)	149.50 (138.50, 164.25)	158.00 (141.00, 172.50)	15.10 (14.60, 19.30)	188.50 (141.75, 225.25)	.216						

IPCTI = immediately proximal to the carpal tunnel inlet.

^{*} Group was categorized according to bland classification based on electromyography finding. Group 1: grade 0 (normal), Group 2: grade 1 and 2, Group 3: grade 3 and 4, Group 4: grade 5 and 6.

[†] Kruskal-Wallis test was used to compare relationship between each group and Dunn procedure was used for post hoc comparison.

3. Results

The demographic data of each group were not statistically significant except for the symptom duration (Table 2). The normal group had shorter symptom duration than the other groups. As the severity of CTS increased, average age and symptom duration tended to increase.

At the IPCTI and carpal tunnel inlet levels, the CSA of the median nerve was statistically larger depending on the severity of CTS ($P < .01$, $P < .01$). The CSA of median nerve and carpal tunnel measured elsewhere did not show significant value according to the severity of CTS. In the post-hoc comparison, at the IPCTI level, the CSA of median nerve was significant in the comparison between group 1 and the other groups. At the carpal tunnel inlet level, statistically significant results were obtained when comparing group 1 with group 4 and group 2 with group 4 (Table 3).

The measured depth at each level was statistically significant, and the measured depth at the IPCTI level showed the smallest value (Table 4).

Table 4
Depth at the measurement level^{*}.

Outcome Measurement	Depth from the skin (mm)
IPCTI level	29.05 ± 5.17
Carpal tunnel inlet level	51.90 ± 10.84
Carpal tunnel outlet level	78.95 ± 11.41

IPCTI = immediately proximal to the carpal tunnel inlet.

^{*} Depth measures from the skin to the top of the median nerve. One-way analysis of variance test was done and the P value was $< .05$.

4. Discussion

CTS means damage to the median nerve in the carpal tunnel, which usually occurs when it is compressed by other structures in the carpal tunnel. Ultrasonography can be applied in most CTS because it can identify morphological changes that occur due to the compression of the median nerve. CTS occurs when the median nerve is compressed in a limited space consisting of flexor retinaculum and hand bones.^[21,22] In peripheral nerves, the internal environment is kept stable by the blood-nerve barrier of the vascular endoneurium and perineurium, which acts as a diffusion barrier.^[23–25] Continuous mechanical compression destroys the blood-nerve barrier and causes endoneurial edema, which is a main contributing factor to the onset of neuropathy.^[5,6,26] However, median nerve in the carpal tunnel area may not swell because of the pressure around the nerve at the early stage. The nerve swelling of the just proximal or distal CT areas are more clearly observed, and the same results have been confirmed in other studies.^[13,27] In this study, the CSA of the median nerve measured at the IPCTI level was the only area that distinguished normal from very mild to severe CTS.

As the diagnosis of CTS with ultrasonography is focused on the change of the CSA of the median nerve in the carpal tunnel, it can be confirmed only after nerve damage is evident. At the IPCTI level, more fluid accumulation may occur and nerve swelling in the early stages of CTS could be easily detected. In previous studies, nerve swelling at the IPCTI level was also observed in the early stage.^[13]

Although the median nerve at the IPCTI level may swell at the early stage, the swelling does not proceed constantly as the stage progresses. The CSA of the median nerve at the IPCTI level was

not significantly different between group 2 and groups 3 or 4 and between group 3 and group 4. This may be due to the accumulation of fluid in the endoneurial space of the median nerve initially in the IPCTI level, but not as much fluid accumulation as the stage progresses. On the other hand, the CSA of the median nerve at the carpal tunnel inlet level was statistically different between groups 1 and 4 and between groups 2 and 4, suggesting that this measurement would be more effective in distinguishing other groups from the very severe group.

The carpal tunnel has proximal and distal sides based on the flexor retinaculum. In the early stages of CTS, nerve swelling can occur on both sides. However, the depth from the skin to the median is closer to the proximal portion than to the distal portion. Considering that the resolution of ultrasonography is inversely proportional to the square of the distance, the detection of CTS at the IPCTI level is much more accurate than at immediately distal to the carpal tunnel outlet.

This study has some limitations. We did not consider the difference in the CSA of the median nerve itself according to individual patients. Moreover, it was difficult to present a diagnostic cut-off value at the IPCTI level owing to insufficient patients. A number of studies with larger numbers of patients would provide cut-off values in the future. In this study, there was no patient with grade 6 CTS based on the Bland classification (i.e., extremely severe). However, patients with grade 5 CTS showed delayed sensory and motor latency on electrodiagnostic study, which could reflect axonotmesis like in grade 6 CTS.

Most studies have been conducted to identify morphological changes, especially swelling, of the median nerve at the carpal tunnel level.^[28,29] These methods are useful for diagnosing CTS, but only after the electrophysiological abnormality of the median nerve is sufficiently advanced. Measuring the CSA of median nerve at the IPCTI level has the advantage of being able to diagnose mild CTS, which is a more early stage.

5. Conclusions

This study is the first to confirm the relationship between the CSA of the median nerve measured at the IPCTI level and the severity of CTS measured using electrodiagnostic study. The CSA of the median nerve measured at the IPCTI level is the most sensitive parameter in diagnosing mild CTS that represents the early stage. Evaluation of nerve entrapment syndrome at other sites and studies with a large number of patients will be needed.

Author contributions

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Hyoung Seop Kim: study design, statistical analysis, and writing.
Jong Moon Kim: literature search, figures, study design, data collection, data interpretation, statistical analysis, data interpretation, and writing.

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Investigation: Myeonghwan Bang.

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