

Sonographic assessment of carpal tunnel syndrome in diabetic patients with and without polyneuropathy

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Abstract

The objective of this study is to determine whether the cross sectional area (CSA) measurement of the median nerve at the wrist differ between carpal tunnel syndrome (CTS) in diabetic patients with and without diabetic polyneuropathy (DPN).

This study included 44 patients with type II diabetes mellitus (DM) with CTS, 32 patients with CTS and DPN, 46 patients with idiopathic CTS, and 42 healthy subjects. Ultrasonographic measurement of the CSA of the median nerve was made at the level of the wrist, together with nerve conduction studies.

The median CSA at the wrist was significantly larger in all patient groups compared with healthy subjects. The median nerve CSA was significantly larger in diabetic patients with CTS than patients with idiopathic CTS. The median nerve CSA at wrist was significantly smaller in patients with CTS and DPN compared with diabetic patients with CTS only.

The median nerve CSA at the wrist was larger in diabetic patients with CTS than patients with idiopathic CTS and CTS with DPN. Median nerve CSA can help to differentiate between diabetic patients with CTS with and without DPN.

Abbreviations: CSA = cross-sectional area, CTS = carpal tunnel syndrome, DM = diabetes mellitus, DPN = diabetic polyneuropathy.

Keywords: carpal tunnel, diabetes, median nerve, polyneuropathy, ultrasound

1. Introduction

In the past few years the middle East population is experiencing a sharp increase in the incidence of diabetes mellitus (DM), approaching, and in some regions exceeding the levels found in developed countries.^[1] The incidence of diabetes mellitus in the Saudi population reaches up to 11.9%.^[2]

Clinical diagnosis of carpal tunnel syndrome (CTS) is difficult in patients with diabetic polyneuropathy as polyneuropathy symptoms may mimic those of CTS in clinical practice. Since CTS and diabetic polyneuropathy may produce similar changes in median nerve conduction study, the use of standard electrophysiological diagnostic criteria in these patients may result in a high rate of false positive or false negative diagnosis.^[3–6] Previous studies focused on the sonographic measurement of the median nerve at the carpal tunnel in patients with idiopathic CTS, CTS with DM with or without diabetic polyneuropathy (DPN).^[7,8]

Chen et al^[7] reported about larger cross-sectional area (CSA) of the median nerve at the carpal tunnel in diabetic patients with CTS compare with patients with idiopathic CTS and diabetic patients with CTS and DPN. On the other hand, Kim et al,^[8] reported that, the CSA of the median nerve at carpal tunnel did not show the difference between the patients with CTS alone, the diabetic patients with CTS without DPN, and the patients with CTS and DPN. This study concluded that the patients with CTS had larger median nerve CSA at the carpal tunnel, independent of the presence of coexisting DPN.

The aim of this study is to determine whether the CSA of the median nerve at the carpal tunnel differ between CTS in diabetic patients with and without DPN.

2. Subjects and methods

This research was a prospective cross-sectional case control study conducted at a university hospital, from January 2016 to Jun 2017. The study included 42 healthy subjects, 46 patients with idiopathic CTS, and 76 patients with type II DM complaining of tingling and numbness sensation of hands and/or feet. The diagnosis of CTS only, or CTS with DPN in diabetic patients was based on the clinical examination and the results of the nerve conduction study described elsewhere.^[9–12] In order to rule out other possible causes, the patients with long-term alcohol intake, thyroid dysfunction, acromegaly, chronic kidney diseases, connective tissue disorders, malignant disease, distal radius fracture, and pregnancy in etiology, were excluded from the study.

2.1. Procedures

The university research board approval was obtained for this study, and informed consent was provided by all participants. Our patients were recruited from endocrinology, rheumatology, and neurology

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The authors have no conflicts of interest to disclose.

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outpatient clinics of the university hospital. All patients with symptoms suggestive of CTS were evaluated clinically and electrophysiologically to confirm the diagnosis. The diagnosis of DM was established by fasting and 2 hours postprandial serum blood sugar as a short-term glucose measurement, and hemoglobin A1C as a long-term measurement. Patients without diabetes were included in the idiopathic CTS group. The healthy subjects enrolled in this study were free from any diseases related to neuromuscular system, as indicated by history taking and clinical examination.

2.2. Electrophysiologic methods

Nerve conduction studies were performed with Nihon-Cohden Neuropack (Tokyo, Japan) device. All studies were performed under standard room temperature of 25°C. Hand temperature was maintained at $\geq 32^\circ\text{C}$. Electrodiagnostic studies were performed on both hands and in one of the lower limbs in all patients by an investigator blinded to the results of the clinical evaluation. Patients whose hands shown normal median nerve conduction study were excluded. Needle electromyography was carried out in biceps brachii, pronator teres, and first dorsal interossei.

For the diagnosis of median nerve entrapment at wrist (CTS) the median nerve compound muscle action potential (cMAP) was recorded from the abductor pollicis brevis with stimulation 8 cm proximal to the recording electrode. The distal latency and cMAP amplitude were measured. Sensory nerve action potential (SNAP) was recorded from the middle finger with ring electrodes. The palmar stimulation was 7 cm proximal to the recording electrode while the wrist stimulation was 14 cm from it.

2.3. Diagnosis of idiopathic CTS

Idiopathic CTS was diagnosed if 3 of the following criteria were fulfilled: median SNAP peak latency was >3.7 ms; SNAP peak latency of the proximal 7-cm segment was more than the peak latency of the distal 7-cm segment; SNAP amplitude was $<20 \mu\text{V}$, including a conduction block (an SNAP amplitude drop of $>50\%$ with respect to the proximal stimulation, as compared with that of the distal stimulation); median CMAP distal latency was >4.2 ms; and CMAP amplitude was <4.5 mV.^[8–13]

2.4. Diagnosis of CTS in diabetic patients

CTS was diagnosed in patients with diabetic neuropathy if they met the following criteria: the ratio of the distal motor latency of

the median to the ulnar nerve was >1.5 ; the ratio of the distalsensory latency of the median to the ulnar nerve was >1.2 ; the amplitude ratio of the median SNAP to the ulnar SNAP was <0.6 .^[8–14]

2.5. Diagnosis of diabetic polyneuropathy

Diabetic polyneuropathy was diagnosed according to the American Academy of Electrodiagnostic Medicine (AAEM) criteria (2005).^[11]

2.6. Ultrasound assessment technique

All patients underwent a sonographic (US) evaluation within 24 hours from the electrophysiologic evaluation. The ultrasound scanning of the median nerve was performed at the entrance of carpal tunnel with ultrasound diagnostic scanner (Epic 7 version 1.5, Ultrasound system: Philips, Bothell, WA) using a L18–5 MHz linear transducer. An experienced radiologist (MB), with 11 years experience in neuromuscular ultrasound performed all ultrasound scans. Each exam was performed bilaterally and for 3 times to assess for intrarater reliability. To minimize anisotropy, the probe was positioned in a perpendicular position to the nerve. Minimal pressure was exerted on the probe to optimize image quality. The median nerve was scanned bilaterally.

Based on anatomic landmarks, the CSA was measured at the entrance of the carpal tunnel, identified by its fascicular pattern. The power and color Doppler modes were used to properly identify nerves at their anatomic sites. The cross-sectional area of the median nerve was measured by circumferential tracing inside the hyperechoic rim of each nerve (Fig. 1 median nerve with normal CSA, Fig. 2 enlarged median nerve with increased CSA). Images and results were saved electronically and analyzed.

2.7. Statistical analysis

Statistical analysis was performed using SPSS for Windows (Version 15, Chicago, IL). Descriptive statistics (mean, maximum, minimum, and standard deviation) were determined for each nerve conduction parameter, as well as for the median nerve CSA for all groups. Analysis of variance (ANOVA) was used to test the differences in nerve conduction parameters, and median nerve CSA among groups. The *t* test was performed for statistical evaluation of demographic features, duration of diabetes mellitus, and the HbA1C levels between groups. The analyses

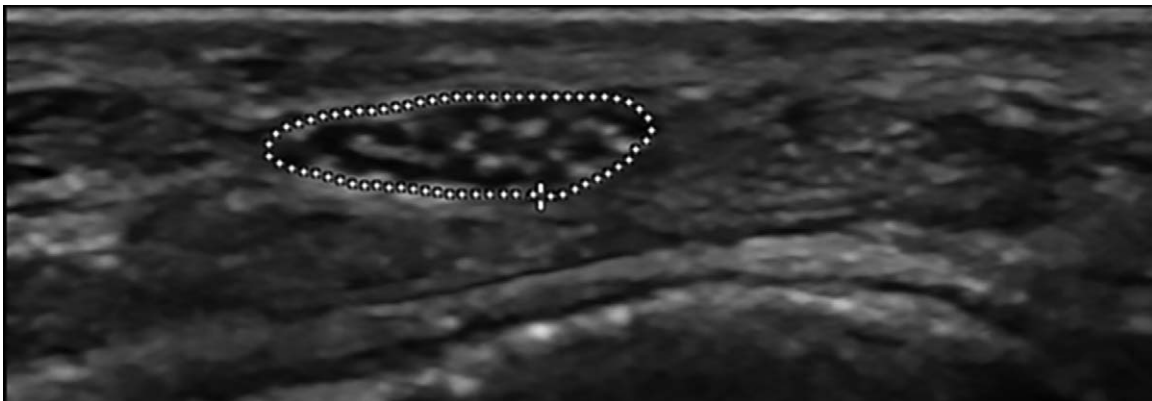


Figure 1. Short axis scan of a normal median nerve at the wrist, CSA = 7.7 mm². CSA = cross-sectional area.

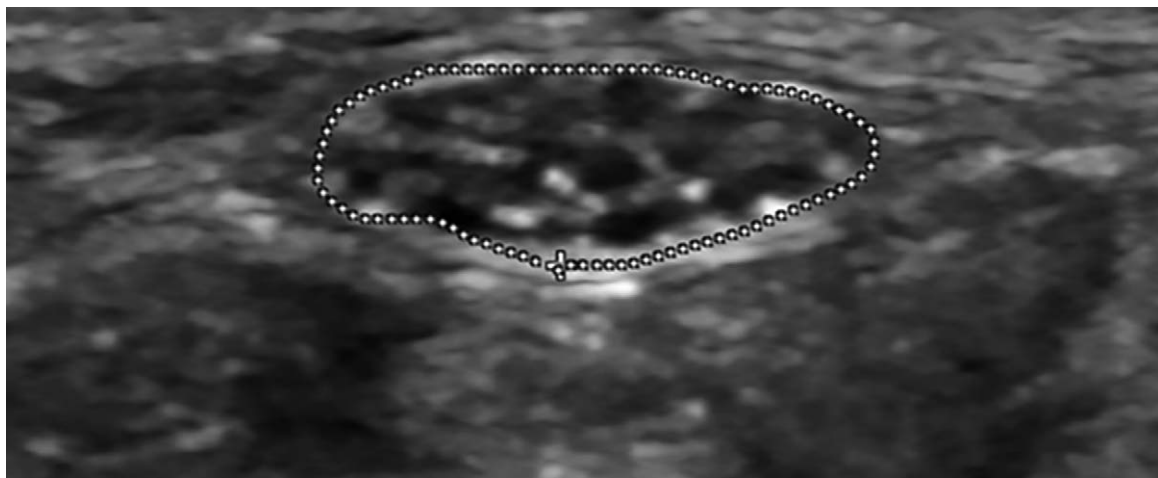


Figure 2. Short axis scan of an enlarged median nerve at the wrist, CSA=15.2mm². CSA=cross-sectional area.

also evaluated the correlations between CSA of the median nerve and the electrophysiologic parameters in CTS groups, using Pearson correlation coefficient. Statistical significance was set at a P value of ≤0.05.

3. Results

The present study included 42 healthy subjects (84 hands), 46 patients with idiopathic CTS (78 hands), 44 diabetic patients with CTS (74 hands), and 32 patients with CTS and DPN (56 hands). Most of our subjects were women. They represent (66.7%, 82.6%, 86.4%, and 56.2%), respectively. Group of patients with CTS and DPN has the highest mean (±SD) of age, duration of DM, and HbA1C. The body mass index was not significantly different between the 3 groups of CTS (Table 1). The median nerve CSAs measured at the wrist are listed in (Table 2). The CSA at the wrist was significantly larger in all patient groups compare with the healthy subjects. Regarding the patient subgroups, it was significantly larger in diabetic patients with CTS than patients with idiopathic CTS. On the other hand, median nerve CSA at

wrist was significantly smaller in patients with CTS and DPN compared with diabetic patients with CTS. The results of nerve conduction studies for median and ulnar nerves are shown in (Table 3). The median nerve CSA was well correlated positively with SNAP distal sensory latency (peak) in patients with idiopathic CTS (P=.04), diabetic patients with CTS (P=.019), and diabetic patients with CTS and DPN (P=.001).

4. Discussion

Carpal tunnel syndrome and DPN commonly occur in patients with DM and can occur separately or more frequently concomitantly.^[15,16]

The present study found a larger median nerve cross-sectional area at the wrist in patients with idiopathic CTS, and CTS in diabetic patients with and without DPN compared with healthy subjects. A large median nerve cross-sectional area at the wrist, in patients with idiopathic CTS, is a well-established U/S finding.^[7,17-19] Although our patients have a higher mean of body mass index (BMI) compare with healthy subjects, this finding do not explain the difference between healthy subjects and patient’s subgroups, regarding median nerve CSA, in agreement with

Table 1
Patients characteristics.

| Variables | Healthy subjects | Idiopathic CTS | CTS with DM | CTS with DPN |
|--------------------|------------------|----------------|-------------|--------------|
| Gender: | | | | |
| Male: N% | 14 33.3% | 8 17.4% | 6 13.6% | 14 43.8% |
| Female: N% | 28 66.7% | 38 82.6% | 38 86.4% | 18 56.2% |
| Age: mean±SD | 46.5±12.2 | 46.2±11.9 | 50.9±8.7 | 57.1±7.6* |
| Min Max | 29 70 | 28 68 | 37 67 | 43 69 |
| BMI: mean±SD | 27.3±3.4 | 28.2±4.2 | 29.2±4.5** | 28.5±5.1 |
| Min Max | 20 34 | 20 36 | 22 38 | 22 37 |
| DDM, y: mean±SD | | | 12.8±9.1 | 17.6±10.8*** |
| Min Max | | | 2 29 | 4 30 |
| HbA1c (%): mean±SD | | | 8.6±2.3 | 9.1±1.3# |
| Min Max | | | 6.6 12.1 | 7.6 12.7 |

BMI=body mass index, CTS=carpal tunnel syndrome, DDM=duration of diabetes mellitus, DM=diabetes mellitus, DPN=diabetic polyneuropathy.

* P<.05 diabetic patients with CTS and CTS compared with healthy subjects, idiopathic CTS, and diabetic patients with CTS only.

** P=.49 diabetic patients with CTS only compared with healthy subjects.

*** P=.014 diabetic patients with CTS and DPN compared with diabetic patients with CTS only.

P=.045 diabetic patients with CTS and DPN compared with diabetic patients with CTS only.

Table 2
CTS diagnosis and median nerve CSA at the wrist.

| Variables | Healthy subjects N=84 | Idiopathic CTS N=78 | CTS with DM N=74 | CTS with DPN N=56 |
|---|--------------------------|------------------------|---------------------|----------------------|
| Right CTS N% | 0 0% | 10 12.8% | 8 10.8% | 47.1% |
| Left CTS N% | 0 0% | 4 5.1% | 6 8.1% | 4 7.1% |
| Bilateral CTS N% | 0 0% | 32 41% | 30 40.5% | 24 42.9% |
| Median nerve CSA at wrist, mm ² : mean±SD | 10.6±2 | 13.7±1.6 | 17±3.4 | 13.4±1.1 |
| Min Max | | P=.000* | P=.000* | P=.000* |
| | | | P=.000** | P=.000*** |
| | 7.1 14.4 | 12.5 18.2 | 13 26 | 12 16.7 |

CTS=carpal tunnel syndrome, CSA=cross-sectional area, DM=diabetes mellitus, DPN=diabetic polyneuropathy.

* Compared to healthy volunteer.

** CTS with DM compared with idiopathic CTS.

*** CTS with DPN compared with CTS with DM.

Table 3**Nerve conduction study parameters for the median and ulnar nerves.**

| Variables | Idiopathic CTS Mean ± SD | CTS with DM Mean ± SD | CTS with DPN Mean ± SD |
|---------------------------|-----------------------------|--------------------------|---------------------------|
| Median DSL, ms | 4.1 ± 0.4 | 4.3 ± 0.4 | 4.3 ± 0.4 |
| Min Max | 3.7 5.2 | 3.8 5.9 | 3.9 5.1 |
| Median SCV, m/s | 33.9 ± 6.5 | 27.8 ± 8.8 | 31.3 ± 5.9 |
| Min Max | 20.7 42.4 | 10.9 41.4 | 17.3 39.6 |
| Median SNAP amplitude, μV | 16.7 ± 2.6 | 15.5 ± 2.4 | 14.7 ± 2.8 |
| Min Max | 10.2 19.9 | 10.1 18.9 | 8.9 17.9 |
| Median DML, ms | 5.1 ± 0.8 | 5.5 ± 0.8 | 5.2 ± 0.7 |
| Min Max | 3.9 7.6 | 4.1 6.8 | 4.6 7.3 |
| Median MCV, m/s | 55.6 ± 3.5 | 53.2 ± 2.2 | 45.3 ± 2.5 |
| Min Max | 52.1 66.9 | 50.1 57.3 | 40.2 49.7 |
| Median cMAP amplitude, mV | 6.9 ± 2.9 | 6.6 ± 2.6 | 5.2 ± 1.7 |
| Min Max | 3.1 12.5 | 2.9 11.3 | 3.3 9.5 |
| Ulnar DSL, ms | 1.9 ± 0.1 | 1.9 ± 0.1 | 2.2 ± 0.2 |
| Min Max | 1.5 2.2 | 1.8 2.2 | 1.9 2.8 |
| Ulnar SCV, m/s | 54.2 ± 1.3 | 53.3 ± 1.2 | 52 ± 1.9 |
| Min Max | 52.1 59.4 | 50.1 55.4 | 43.3 53.5 |
| Ulnar SNAP amplitude, μV | 37.5 ± 4 | 35.3 ± 3.1 | 30.3 ± 4.4 |
| Min Max | 29.5 45.5 | 28.9 40.5 | 19.2 35.9 |
| Ulnar DML, ms | 2.7 ± 0.1 | 2.8 ± 0.3 | 3 ± 0.5 |
| Min Max | 2.3 3.1 | 2.3 3.3 | 2.3 4.1 |
| Ulnar MCV, m/s | 55.6 ± 1.5 | 54.8 ± 1.2 | 53.3 ± 1 |
| Min Max | 54 61.1 | 52.8 56.3 | 50.1 53.9 |
| Ulnar cMAP amplitude, mV | 11.5 ± 3.2 | 11.2 ± 2.9 | 9 ± 2.3 |
| Min Max | 5.9 16.9 | 5.8 15.7 | 5.3 13.9 |

cMAP = compound muscle action potential, CTS = carpal tunnel syndrome, DM = diabetes mellitus, DML = distal motor latency, DPN = diabetic polyneuropathy, DSL = distal sensory latency, MCV = motor conduction velocity, SCV = sensory conduction velocity, SNAP = sensory nerve action potential.

Werner et al,^[20] who reported no significant correlation between BMI and median nerve CSA.

We found a smaller CSA of the median nerve at the wrist in patients with idiopathic CTS than CTS in diabetic patients without DPN. These findings were contradictory to the study of Kim et al,^[18] who reported no significant difference between patients with idiopathic CTS and patients with CTS and DM. In accordance with study of Chen et al,^[7] who found a larger median nerve CSA in patients with CTS and DM than patients with idiopathic CTS. The basic mechanism for the increased incidence of CTS in DM is not known, but nerve swelling and edema is observed by US and MRI studies.^[21,22] The nerve fibers and microvascular pathology has been attributed in part to increased vascular permeability and angiogenesis as a result of enhanced expression of vascular endothelial growth factor (VEGF) and its receptors,^[23,24] most probably, in response to hypoxia-inducible factor 1α (HIF-1α).^[25–27] Patients with DM showed endoneurial microcirculatory abnormalities and microangiopathy,^[28] which may lead to upregulation of HIF-1α and VEGF through increasing endoneurial hypoxia,^[29] with subsequent lack of autoregulation of the endoneurial vascular bed, median nerve swelling, and increased median nerve susceptibility to entrapment at carpal tunnel.^[30] The increased median nerve swelling could explain the larger median nerve CSA in diabetic patients with CTS than patients with idiopathic CTS.

In the present study the median nerve cross sectional area at the wrist was smaller in diabetic patients with CTS and DPN than diabetic patients with CTS only. This was in accordance with the study by Chen et al.^[7] The severity of DPN is related to the degree of diabetic microvascular disease, the duration of diabetes as well

as the type of diabetes.^[31] Our patients with DPN and CTS had longer duration of diabetes, than diabetic patients with CTS only. Moreover, diabetic polyneuropathy is associated with axonal and neuronal degeneration along with impaired peripheral nerve regeneration most probably due to microangiopathy and endoneurial hypoxia, excessive oxidative stress, abnormalities of macrophages and defective inflammatory repair, schwannopathy, or deficient neurotrophic support.^[32] The early deficient regeneration will later lead to decreased myelin thickness and axonal diameter, which might explain the reduced CSA of the median nerve in patients with CTS and DPN. In conclusion, the median nerve CSA at the wrist was larger in diabetic patients with CTS than patients with idiopathic CTS and CTS with DPN. Median nerve CSA can help to differentiate between diabetic CTS in patients with and without DPN.

Author contributions

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Writing – review and editing: Mamdouh Ali Kotb, Mohamed Abdelmohsen Bedewi.

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