Median nerve cross sectional area at the distal wrist and nerve conduction findings in patients with carpal tunnel syndrome: A comparative study

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Abstract. Carpal tunnel syndrome (CTS) is the most common form of peripheral entrapment neuropathy. Ultrasound (US) has emerged as a valuable diagnostic tool for musculoskeletal conditions, including CTS. The aim of the present study was to evaluate the correlation between the cross-sectional area of the median nerve (MN) at the distal wrist (CSA-D) with the severity of CTS, as determined by nerve conduction studies (NCS). For this purpose, a total of 60 female patients with clinical CTS symptoms underwent ultrasound CSA-D measurements at the carpal tunnel inlet, followed by NCS by a blinded electrophysiologist to the US findings. The results revealed that CSA-D exhibited a significant positive correlation with MN distal motor latency (R=0.588, P<0.001) and sensory latency (R=0.541, P<0.001). Conversely, a significant negative correlation was observed with motor conduction velocity (R=-0.373, P=0.003), sensory action potential amplitude (R=-0.592, P<0.001) and sensory conduction velocity (R=-0.562, P<0.001). In discriminating mild vs. severe CTS, US had an area under the receiver operating characteristic (ROC) curve (AUC) value of 0.910 (95% CI, 0.826-0.994, P<0.001), with 95% sensitivity and 86% specificity at CSA-D=17.5 mm^2. On the whole, CSA-D correlates significantly with NCS parameters in CTS. US is more effective in differentiating mild from severe CTS, than mild from moderate CTS. US is a highly effective modality for distinguishing between mild and severe CTS, demonstrating superior diagnostic performance for this specific differentiation compared to distinguishing mild from moderate disease.

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Introduction

Carpal tunnel syndrome (CTS), caused by median nerve (MN) compression at the wrist, is the most prevalent type of entrapment neuropathy of the wrist (1). The median nerve distribution is affected by symptoms, such as pain, tingling and numbness, and the global incidence of this condition has been reported to range from 0.24 to 0.4% (1,2).

A clinical evaluation and nerve conduction studies (NCS) are the two requirements for reaching a diagnosis; nevertheless, NCS tests are not only uncomfortable, but are also time-consuming and prone to producing misleading results (3,4). The measurement of the MN cross-sectional area (CSA) at the flexor retinaculum using ultrasound (US) is a promising alternative that does not involve any invasive procedures. This method enables the direct measurement of the MN CSA (5). In comparison to electrodiagnostic examinations, it is more convenient, less costly and provides morphological data (6). However, the connection between CSA-D and NCS latencies is not yet fully understood, despite the fact that it has the potential to be significant.

The present study thus aimed to determine the correlation between the MN CSA at the distal wrist (CSA-D) with the severity of CTS, as graded by NCS.

Patients and methods

Study design and setting. The present prospective, cross-sectional study was carried out at the Al-Imamen Al-Kadhmin Medical Teaching Hospital (a primary teaching hospital affiliated with the College of Medicine, Al-Nahrain University) in Baghdad, Iraq during the months of September, 2023 and July, 2024. The study cohort comprised 60 female patients. The sample comprised only females as the prevalence of CTS is markedly higher in females than males. There were no male patients during patient recruitment period. Patients were presenting with clinical signs and symptoms suggestive of CTS, as assessed by an orthopedic surgeon. Clinical indicators of CTS included tingling and/or numbness, nocturnal symptoms mostly in MN distribution and positive results on a clinical examination (Phalen test or compression test).

Ethical considerations. Research approval was obtained from the institutional Review Board of Al-Khadimain Teaching Hospital (Reference no. 5563 on April 24, 2023). Following the explanation of the objectives of the study, each participant completed a consent form before the commencement of data collection. Participants were informed of their unconditional right to withdraw at any time, and the confidentiality of all collected data was strictly maintained.

Patient population and data collection. Direct interviews were used to obtain patient demographics [age and body mass index (BMI)]. The inclusion criteria were the following: The presence of typical CTS symptoms, such as numbness, tingling, burning, or pain in the median nerve distribution (thumb, index, middle fingers); a duration of symptoms persisting for a minimum period (e.g., ≥3 months); and clinical signs, i.e., positive provocative tests, such as Phalen's test or Tinel's sign, as assessed by an orthopedic surgeon.

The exclusion criteria were the following: Patients were excluded if they had a history of concomitant illnesses, such as cervical radiculopathy, prior ipsilateral CTS surgery, rheumatoid arthritis, thyroid disease, pregnancy, brachial plexopathy, wrist fractures and polyneuropathy.

NCS and severity grading. An electrophysiologist blinded to the findings of the clinical and US investigations conducted NCS, which consisted of five different motor and sensory nerve measurements. Compound muscle action potentials (CMAPs) and distal motor latencies (DMLs) were recorded for this investigation, and motor latencies were measured over 5-6 cm segments over the MN.

Measurements of sensory nerve action potentials (SNAPs) and distal sensory latencies were made in addition to sensory latencies recorded over 12-13 cm segments of the MN. NCS results were deemed normal when the following criteria were met: MN motor latency <4.0 msec, CMAP amplitude >10 mV, MN sensory latency <3.5 msec, and SNAP amplitude >6 μV. The thresholds were obtained from previous studies on CTS, as well as guidelines from clinical neurology (7-11). The inability to satisfy any of these requirements was the defining characteristic of a positive electrodiagnostic test result for CTS.

Electrophysiological severity grading. The severity of CTS was classified as mild, moderate or severe based on the findings of NCS, in accordance with the electrodiagnostic guidelines that have been developed (12): i) Mild CTS: Prolonged median sensory latency (>3.5 msec) with normal median motor distal latency (≤4.0 msec); ii) moderate CTS: Prolonged median sensory latency and prolonged median motor distal latency (>4.0 msec) with a preserved CMAP amplitude; iii) severe CTS: Prolonged median motor and sensory latencies with either a low CMAP amplitude (<4.5 mV) and/or electrophysiological evidence of axonal loss. In the present study, it was confirmed that all 65 wrists (as in 5 patients, both wrists were affected) were classified using these specific, quantitative metrics.

Ultrasonographic examination. A radiologist, blinded to the results of the electrodiagnostic testing, conducted the ultrasonography of the median nerve. The carpal tunnel entrance at the pisiform bone was utilized to measure the CSA of the MN. A 4-12 MHz linear array transducer (US machine: Affiniti 30 Ultrasound system; Philips Medical System) was employed for the ultrasonography, positioned vertical to the forearm.

On the examination table, the patients lay on their backs, elbows bent at 90˚, and forearms widely splayed. An ellipse function was employed by the US machine to determine the CSA. The hyperechoic epineurium interior area can be determined using this function, which forms an ellipse around the target region (13).

Assessment of measurement reliability. An intra-observer variability assessment was carried out to guarantee the accuracy and reproducibility of the ultrasonographic measurements. Following 1 week, 15 patients (representing 25% of the total sample) were re-measured for CSA-D by the same radiologist who had been blinded to the electrodiagnostic results.

Reproducibility was high, with an intra-class correlation coefficient (ICC) of 0.94 (95% CI, 0.87-0.98) for intra-observer reliability. To reduce the possibility of operator error, the NCS relied on a single, highly trained electrophysiologist to conduct each test according to a predetermined procedure. In conformity with the standards set forth by the American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM), all subjects had identical equipment settings and electrode placements (12).

Statistical analysis. Statistical analyses were executed using SPSS software (version 25.0). Continuous data that were not normally distributed data were analyzed using the Kruskal Wallis test followed by Dunn's multiple comparisons test. The discriminative ability of the MN CSA in distinguishing between mild, moderate and CTS was assessed using receiver operating characteristic (ROC) curve analysis. Pearson's correlation analysis was used to examine potential correlations between MN CSA and other variables. A P-value <0.05 was considered to indicate a statistically significant difference.

Results

Demographic and clinical characteristics of the patients. The study population had a mean age of 49.7±11.34 years. The cohort, comprising exclusively female participants, had a mean BMI of 28.58±3.1 kg/m^2, categorizing the majority of the patients as overweight or obese. In total, 58.46% of the patients had an involvement of the right wrist (Table I).

Electrophysiological parameters and ultrasonography. The mean DML and CMAP of the affected MN were 5.43±2.08 msec and 5.81±1.89 msec, respectively. Abnormalities in conduction velocities and sensory latencies were prevalent, with a mean motor conduction velocity of 53.0±6.42 m/sec, mean sensory latency of 4.56±2.57 msec, and mean sensory conduction velocity of 30.98±23.91 m/sec. The ultrasonography findings revealed that the mean CSA of the affected MN at its distal segment was 17.9±4.1 mm^2 (Table II).

Distribution of disease severity. Based on the American criteria for CTS classification (14), of the 65 affected wrists, 31 (47.69%) were categorized as having mild disease, 13 (20%) as moderate disease, and 21 (32.3%) as severe disease (Fig. 1).

Table I. Demographic characteristics of the patients with carpal tunnel syndrome in the present study (n=60).

Variables	Value
Age, years	
Mean ± SD	49.7±11.34
Range	25-68
Height, cm	
Mean ± SD	165.5±9.4
Range	150-179
Weight, kg	
Mean ± SD	75.18±9.0
Range	67-102
Body mass index, kg/m^2	
Mean ± SD	28.58±3.1
Range	23.2-35.0
Patients (n=60)	Unilateral CTS: 55 Bilateral CTS: 5
Wrists (n=65)	Right: 38 (58.46%) Left: 27 (41.54%)

It should be noted that the total number of wrists affected with CTS was 65 (as in 5 patients. both wrists were affected).

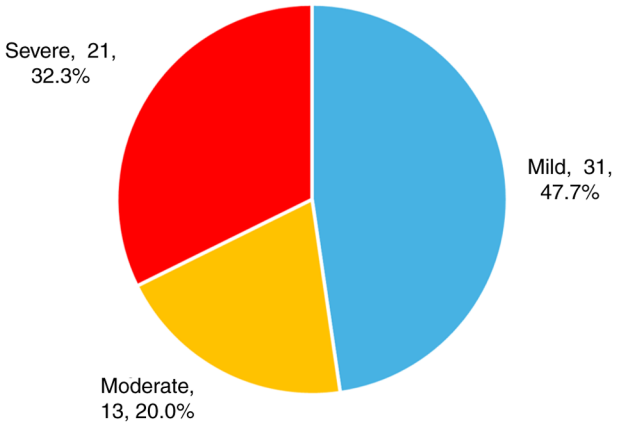

Figure 1. Severity of carpal tunnel syndrome in the patients in the present study.

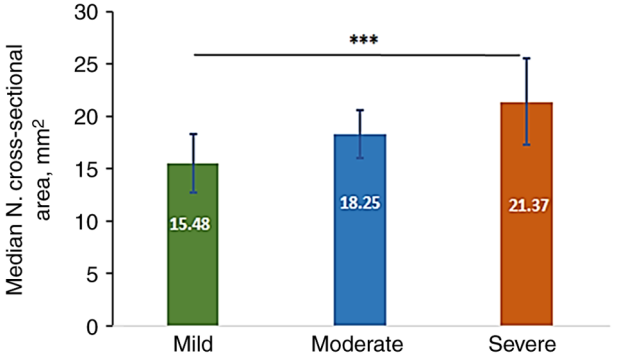

Figure 2. Association of cross-sectional area of the median nerve with disease severity as analyzed using the Kruskal-Wallis test followed by Dunn's post hoc test for multiple comparisons. ***P<0.001, indicates a highly statistically significant difference.

Association between median nerve CSA-D and disease severity. The mean CSA-D in mild, moderate and severe cases was 15.48±2.82, 18.25±2.62 and 21.37±4.14 mm^2, respectively, with highly significant differences observed between mild and severe categories, as analyzed using the Kruskal-Wallis test followed by Dunn's test for multiple comparisons (Fig. 2).

Correlation of CSA-D with electrophysiological parameters. Pearson's correlation analysis was performed to examine the correlation between the CSA-D and other parameters in patients with CTS. The CSA-D exhibited a significant positive correlation with both MN distal motor latency (R=0.588, P<0.001) and MN sensory latency (R=0.541, P<0.001). Conversely, significant negative correlations were observed with MN motor conduction velocity (R=-0.373, P=0.003), sensory action potential amplitude (R=-0.592, P<0.001) and sensory conduction velocity (R=-0.562, P<0.001), as presented in Table III and Figs. 3-7.

Diagnostic performance of ultrasonography. The diagnostic accuracy of MN CSA-D measured by US in detecting and differentiating CTS was assessed using the ROC curve. When comparing mild and moderate CTS, the area under the curve (AUC) was 0.763 (95% CI, 0.618-0.908; P=0.009). As shown in Fig. 8, ultrasonography exhibited a sensitivity of 67% and a specificity of 62% when the cut-off value of CSA-D was 16.5 mm^2.

In distinguishing between mild and severe CTS, the AUC was 0.910 (95% CI, 0.826-0.994; P<0.001). At a cut-off value of CSA-D of 17.5 mm^2, ultrasonography exhibited a sensitivity of 95% and a specificity of 86% (Fig. 9).

For distinguishing between moderate and severe CTS, the AUC was 0.774 (95% CI, 0.607-0.942, P=0.011). At a cut-off value of CSA-D of 20.5 mm^2, ultrasonography demonstrated a sensitivity of 63% and a specificity of 83% (Fig. 10).

Discussion

A positive electrodiagnostic test is primarily used to corroborate the diagnosis of CTS, which is often based on characteristic clinical signs and symptoms (15). According to recent research, MN sonography can detect CTS with sensitivity that is comparable to that of the gold-standard electrophysiological testing (16,17).

The present study identified a positive correlation between the CSA-D of MN and both MN distal motor latency and sensory latency. Conversely, the CSA-D demonstrated a significant negative correlation with MN motor conduction velocity, sensory action potential amplitude, and sensory conduction velocity. These results validate the utility of US in diagnosing CTS and align with findings from other studies (18-21).

Reported cut-off values for the CSA of the MN at the pisiform bone using US vary widely, ranging from 9 to 14 mm^2 (16,22,23) which affect the sensitivity and specificity of this parameter for diagnosing CTS. In the present study, the

Table II. Electrophysiological parameters and sonography (60 wrists).

Variables	Mean ± SD	Range
MN distal motor latency, msec	5.43±2.08	2.8-11.2
MN compound muscle action potential (msec)	5.81±1.89	1.9-9.7
MN motor conduction velocity, msec	53.0±6.42	35.5-68.8
MN sensory latency msec	4.56±2.57	2.5-11
MN sensory action potentials amplitude, μv	30.98±23.91	3.5-98.4
MN sensory conduction velocity, msec	31.66±10.77	10.8-48.0
MN cross sectional area, mm^2	17.9±4.1	10.0-31.0

MN, median nerve.

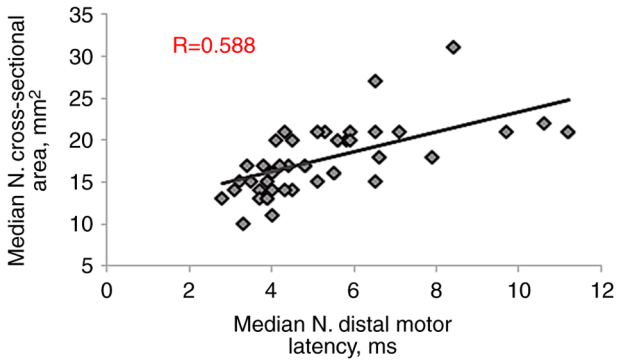

Figure 3. Scatter plot and regression line between median nerve cross-sectional area and distal motor latency in patients with carpal tunnel syndrome. Median N., median nerve.

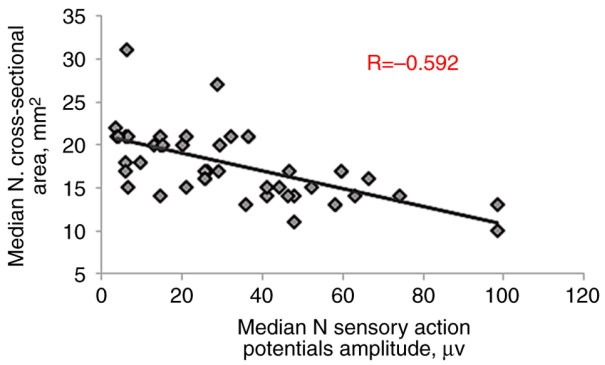

Figure 5. Scatter plot and regression line between median nerve cross-sectional area and sensory action potential amplitude in patients with carpal tunnel syndrome. Median N., median nerve.

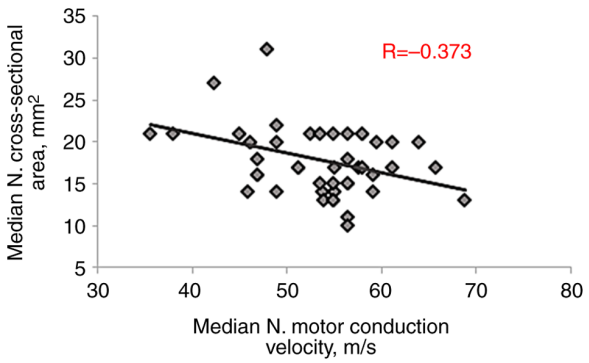

Figure 4. Scatter plot and regression line between median nerve cross-sectional area and motor velocity in patients with carpal tunnel syndrome. Median N., median nerve.

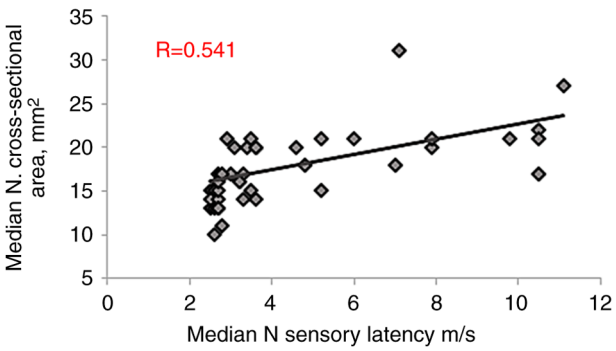

Figure 6. Scatter plot and regression line between median nerve cross-sectional area and sensory latency in patients with carpal tunnel syndrome. Median N., median nerve.

CSA cut-off value was 17.5 mm^2. The cutoff value of 17.5 mm^2 for distinguishing mild from severe CTS use in the present study is higher than the range of 9-14 mm^2 frequently reported in other populations (24-26). This disparity does not necessarily constitute a contradiction; rather, it draws attention to significant elements that have an impact on sonographic findings and the therapeutic application of these measurements. It is possible that this disparity is due to a variety of factors, such as: i) The characteristics of the population: The population in the present study comprised solely of Iraqi females who had a BMI that was defined as overweight, namely 28.58±3.1 kg/m^2. It is a well-established fact that demographic parameters, such as sex, race and body habitus have an effect on the size of the nerves. Studies have demonstrated that a higher BMI is associated with a larger median nerve CSA. This could potentially result in an upward shift of the ideal diagnostic cutoff in communities that have a higher prevalence of obesity in comparison to general populations in which lower cut-off values were established (27,28). ii) Measurement methodology: While the present study adhered to standard techniques, subtle differences in measurement protocols, such as the precise level

Table III. Pearson's correlation between MN cross sectional area at distal wrist with other parameters in patients with carpal tunnel syndrome.

Variables	Coefficient	P-value
MN. distal motor latency, msec	0.588	<0.001
MN compound muscle action potential (msec)	-0.215	0.098
MN. motor conduction velocity, msec	-0.373	0.003
MN sensory action potentials amplitude, μv	-0.592	<0.001
MN sensory latency msec	0.541	<0.001
MN sensory conduction velocity, msec	-0.562	<0.001
Age, years	0.112	0.396
Height, cm	0.091	0.489
Weight, kg	0.099	0.453
Body mass index, kg/m^2	0.178	0.175

MN, median nerve.

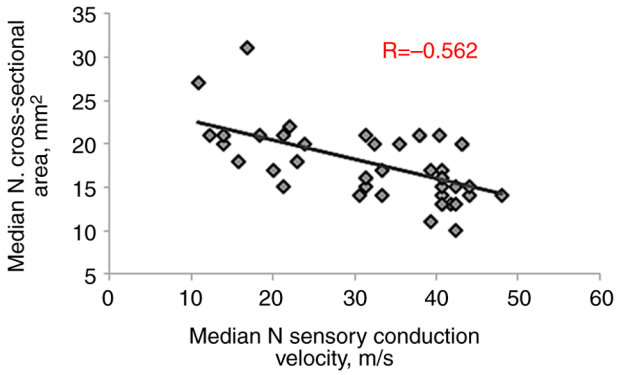

Figure 7. Scatter plot and regression line between median nerve cross-sectional area and sensory conduction velocity in patients with carpal tunnel syndrome. Median N., median nerve.

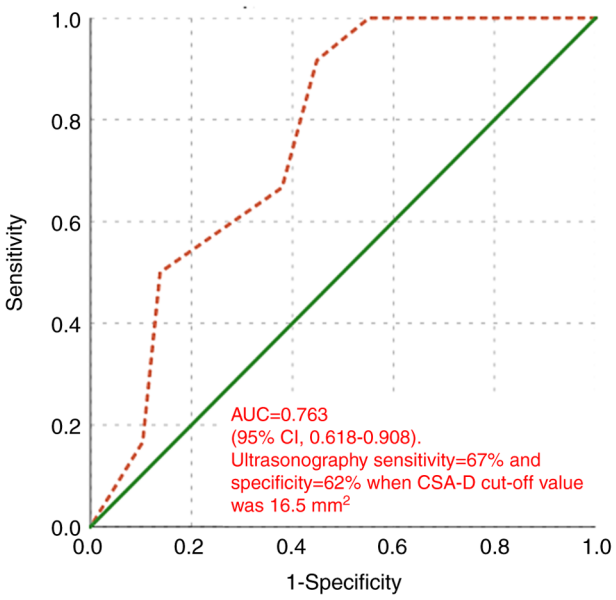

Figure 8. Receiver operating characteristic curve for ultrasound in the context of discrimination between mild and moderate carpal tunnel syndrome. The AUC was 0.763 (95% CI, 0.618-0.908; P=0.009). Ultrasonography exhibited a sensitivity of 67% and a specificity of 62% when the cut-off value of CSA-D was 16.5 mm^2.

of the pisiform bone, the use of the ellipse tracing function vs. manual trace and the pressure applied with the transducer can systematically influence the absolute CSA values obtained. The consistent application of the method used herein ensures internal validity; however, cross-study comparisons must account for these potential technical variations (29).

In the present study, US had a sensitivity of 95% and a specificity of 86%, suggesting that US is most effective in distinguishing mild from severe CTS. For differentiating mild from moderate CTS, the sensitivity and specificity at a cut-off value of 16.5 mm^2 were 67 and 62%, respectively. In the same manner, a cut-off value of 20.5 mm^2 for moderate to severe CTS yielded a sensitivity of 63% and a specificity of 83%.

Probably distinct aspects of the process of the condition are being investigated by ultrasonography and nerve conduction investigations individually. US is used to examine the structural reaction of the nerve to external compression, whereas nerve conduction investigations are used to evaluate the functional capacity of the nerve to convey information. Rather than being considered contradictory with one another, these diagnostic tools ought to be regarded as complementary.

It is possible that the distinct pathological processes that are present at different phases of the disease are responsible for the greater efficacy of ultrasonography in separating mild from severe cases of CTS. On the other hand, the effectiveness of US in discriminating between mild and moderate cases is restricted.

The major pathophysiology of CTS is typically localized demyelination, which is caused by compression and ischemia in the early (mild) phases of the condition. Despite the fact that this functional deficit manifests electrophysiologically as longer sensory and motor latencies, it is possible that it did not cause a significant and long-lasting structural expansion of the nerve (9).

There is a possibility that the nerve will exhibit transitory swelling that is influenced by the symptoms; however, the

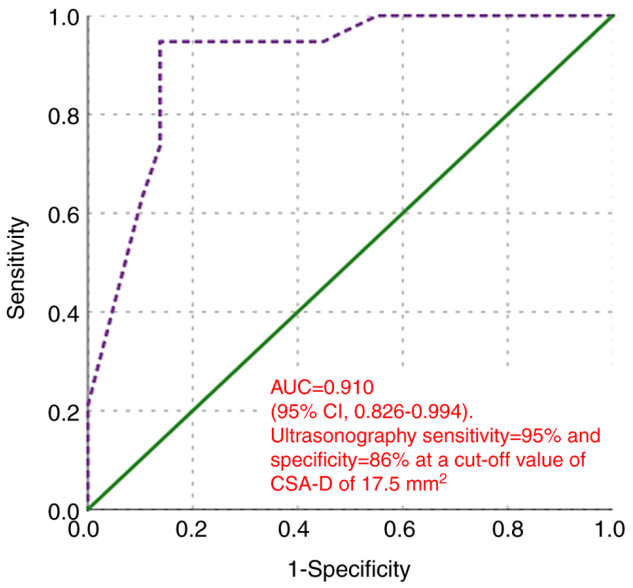

Figure 9. Receiver operating characteristic curve for ultrasound in the context of differentiating between mild and severe carpal tunnel syndrome. The AUC was 0.910 (95% CI, 0.826-0.994; P<0.001). At a cut-off value of CSA-D of 17.5 mm^2, ultrasonography exhibited a sensitivity of 95% and a specificity of 86%.

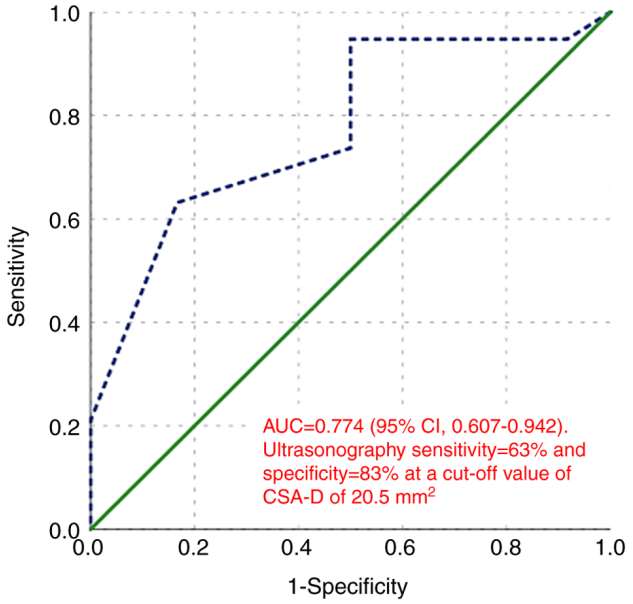

Figure 10. Receiver operating characteristic curve for ultrasound in the context of differentiating between moderate and severe carpal tunnel syndrome. The AUC was 0.774 (95% CI, 0.607-0.942, P=0.011). At a cut-off value of CSA-D of 20.5 mm^2, ultrasonography demonstrated a sensitivity of 63% and a specificity of 83%.

average CSA-D in the group with mild CTS in the present study was only slightly higher than the typical upper limits, which range from 9-14 mm^2. This results in a threshold that is less sensitive and specific in terms of differentiating between mild and moderate instances, as the CSA differences between the two types of cases become less distinct. By contrast, prolonged compression induces increasingly severe structural alterations as the severity of CTS increases, including the persistent endoneurial edema, the disturbance of the blood-nerve barrier, fibrosis, and ultimately, axonal degeneration (30).

The fact that in the present study, the group with severe CTS had a significantly higher mean CSA-D (21.37 mm^2) provides evidence that the accumulated structural damage induces nerve swelling that is both chronic and considerable. Ultrasonography is a powerful instrument that can differentiate between moderate and severe manifestations of disease due to the exceptional clarity it possesses.

US is sensitive to the significant nerve damage that is associated with advanced illness, as evidenced by the fact that it is able to differentiate between moderate and severe cases of CTS. It is possible that functional electrophysiological changes, which NCS is able to detect, may occur prior to lasting morphological alterations. This is suggested by the observation that US is not very effective at identifying the early phases of the condition.

The fact that NCS exposes structural compromise, while US indicates functional integrity adds validity to the hypothesis that functional integrity and structural compromise are two different sorts of information that they provide. As a result of this, combining the two methods may possibly provide a more realistic portrayal of the severity of the condition.

The results of the present study demonstrate a robust correlation between MN CSA and electrophysiologically assessed disease severity. Nevertheless, additional studies are required to investigate the impact of sonographic parameters on patient-reported clinical outcomes. For the purpose of clinical decision-making, it is essential to use a validated instrument such as the Boston Carpal Tunnel Questionnaire (BCTQ) (31) to determine whether nerve enlargement, as shown through ultrasonography, correlates with the severity of symptoms and functional impairment.

The authors acknowledge that the study population may not fully represent the complexity of all patients presenting with CTS-like symptoms in general practice due to the exclusion of patients with comorbidities, such thyroid disease, polyneuropathy and cervical radiculopathy. The primary objective of these criteria was to isolate the association between the morphology of the MN and its electrical activity in cases of CTS, excluding other disorders that may mimic or exacerbate CTS symptoms. Cervical radiculopathy may present with overlapping sensory symptoms (32), whereas polyneuropathy may cause aberrant nerve conduction tests and widespread nerve enlargement (33).

The present study had certain limitations which should be mentioned. First, the sample size was relatively small. Further multicenter studies with larger cohorts are thus warranted to validate the proposed cut-off values and improve the generalizability of the findings. Second, the present study employed a cross sectional design by selectively enlisting patients with a clinical suspicion of CTS. This may render the test to appear more precise than it actually is due to a high pre-test probability, a phenomenon known as spectrum bias. Third, the present study only demonstrated a link between the MN sonography tests and the electrodiagnostic examination. The present study does not indicate whether NCS or ultrasonography appropriately captures the clinical manifestations of CTS. Finally, the present study did not incorporate a correlation

with standardized clinical symptom scores, such as the BCTQ. Therefore, while CSA may be related to electrophysiological severity, its direct association with the subjective experiences of patients, such as pain, numbness and functional limitations remains a key area for future investigations.

In conclusion, the present study demonstrates that CSA-D and NCS are positively correlated, and the CSA-D is more sensitive in differentiating between mild and severe CTS, than between mild and moderate CTS. As regards the evaluation of structural and functional integrity, US and NCS provide complimentary information. When used in conjunction, they provide a more comprehensive evaluation of the nerve, which may be useful in clinical therapy and in the stratification of prognostic factors. Future research is required to focus on correlating these objective measures with clinical symptom scores in order to fully integrate ultrasonography into patient-centered care pathways.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JMK was involved in the conception and design of the study, in the literature search, in clinical analyses, in data analysis and in statistical analysis, as well as in manuscript preparation and in the reviewing of the manuscript. AMJAM was involved in the conception and design of the study and in data analysis, as well as in manuscript preparation and in the reviewing of the manuscript. IAM and AKA were involved in the conception and design of the study, manuscript preparation and in the reviewing of the manuscript. All authors have read and approved the final manuscript. All authors confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Research approval was obtained from the institutional Review Board of Al-Khadimain Teaching Hospital (Reference no. 5563 on April 24, 2023). A written informed consent to participate in the study as specified in the Declaration of Helsinki was obtained from each patient.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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