Usefulness of neuromuscular ultrasound in the diagnosis of idiopathic carpal tunnel syndrome

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Objective

The aim of the study was to assess the usefulness of neuromuscular ultrasound in the diagnosis of idiopathic carpal tunnel syndrome (CTS) and to determine the relationships of ultrasonographic measurements with the clinical severity and the electrophysiological grading scale.

Patients and methods

One hundred CTS diseased hands and 100 nondiseased hands were assessed clinically and by nerve conduction studies. We measured ultrasonographic cross-sectional area (CSA) of the median nerve at various levels of the carpal canal (inlet and outlet), flattening ratio (FR), palmar bowing of the flexor retinaculum, wrist/ forearm ratio, as well as median nerve mobility and power doppler signals. Data from patients and controls were compared to determine the diagnostic relations and the grade of severity.

Results

Measures of CSA of the median nerve at the inlet and at the outlet, palmer bowing and inlet/forearm ratio in the CTS group were significantly higher than the control group (P<0.05); 50% of diseased hands showed restriction of mobility of the median nerve, while 31% had doppler signals. Positive correlations of ultrasonographic measurements with patient-oriented measures, clinical severity scale and electrophysiological grade were observed.

Conclusion

Ultrasonographic measurements of CSA at the inlet and flexor retinaculum have a relatively higher diagnostic accuracy than FR for CTS. The correlation between clinical scores, historical-objective-distribution scale, electrophysiological grade and ultrasonographic measurements reflects the usefulness of neuromuscular ultrasound in the diagnosis of idiopathic CTS.

Keywords:

carpal tunnel syndrome, diagnosis, neuromuscular ultrasound

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Introduction

Carpal tunnel syndrome (CTS) is the most common neuropathy of the upper extremities and accounts for 90% of all entrapment neuropathies [1]. Characteristic symptoms and signs, and electrophysiological studies are the cornerstones in the diagnosis of CTS [2,3]. False-negative cases can be seen in about 10–20% of patients [4].

Neuromuscular ultrasound (NMUS) has been introduced into electrodiagnostic laboratories as a complement to nerve conduction studies and electromyography for the diagnosis of a variety of nerve and muscle conditions [5].

The electrophysiological studies usually show the level of the lesion, but do not provide anatomical information about the nerve or its surroundings [6,7]. In the last few years, NMUS, being inexpensive and noninvasive imaging modality, has been shown to be useful diagnostic tools in CTS,

providing information on the median nerve and surrounding structures [8–10].

There are a number of criteria used to diagnose CTS by ultrasonography in the literature, such as cross-sectional area (CSA) at the level of the pisiform bone, flattening ratio (FR), swelling ratio, bowing of the flexor retinaculum (PB) and median nerve wrist-to-forearm area ratio (WFR) [7,11,12].

One of the problems of studying CTS is the lack of consensus to establish a definitive diagnosis [13]. Our aim was to assess the usefulness of US in the diagnosis of idiopathic CTS by measuring CSA of the median nerve at various levels of the carpal canal (inlet and outlet), FR, palmar bowing of the PB, wrist/forearm

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ratio, as well as median nerve mobility and power doppler signals; and to analyze if these measures were correlated with the clinical severity of CTS (as assessed by validated clinical scale) and the electrophysiological grading scale or not.

Patients and methods

This was a prospective cross-sectional study. Between May 2015 and January 2016, patients with suspected CTS who have attended the Outpatient Rheumatology and Rehabilitation Clinic, Minia University Hospital, underwent nerve conduction studies and subsequent sonographic evaluation. The study was approved by the ethics committee of the Faculty of Medicine, Minia University. Consecutive patients with suspected CTS gave their verbal informed consent and were prospectively enrolled. Patients were excluded if they had a history of wrist/elbow trauma, local joint injection, fracture or surgery, clinical, electrophysiological or radiological evidence of proximal median neuropathy, cervical radiculopathy or polyneuropathy, history of underlying disorders that can be associated with CTS: physiological, e.g. pregnancy; drugs, e.g. hormonal contraception; neuropathic causes, e.g. diabetes mellitus, alcoholism; endocrinal, e.g. hypothyroidism, acromegaly; wrist arthritis due to any cause, e.g. rheumatoid arthritis, renal failure, congestive heart failure. Moreover, local structural abnormalities that may cause median nerve compression such as tenosynovitis, ganglions and accessory muscles inside the tunnel were excluded.

The clinical diagnostic criterion of CTS is based on the American Academy of Neurology [14]: (a) paresthesia, pain, swelling, weakness or clumsiness of the hand provoked or worsened by sleep, sustained hand or arm position or repetitive action of the hand or wrist that is mitigated by a change in posture or by shaking of the hand; (b) sensory deficits in the median nerve-innervated regions of the hand; (c) motor deficit or hypotrophy of the median nerve-innervated thenar muscles; and (d) positive provocative clinical tests (positive Phalen's maneuvre and/or Tinel's sign). The clinical diagnosis of CTS was made when criterion 1 and one or more of criteria 2–4 were fulfilled.

Sixty-five patients (53 women and 12 men) with 100 CTS diseased hands and 100 healthy age-matched and sex-matched individuals with 100 nondiseased hands were included.

A modified Arabic version of the Boston Carpal Tunnel Questionnaire (BCTQ) was used to obtain a patient-oriented measurement [15]. The Arabic version of BCTQ evaluates two domains of CTS, namely 'severity score' (SYMPT score) assessed was designed to be self-administered and patients were asked to place a mark on a 0–10-point visual analog scale that they thought to be appropriate to their condition and 'functional status' was assessed with a six-item scale presented in a multiple-choice format, the functional (FUNCT) score was assigned from 1 point (mildest) to 5 points (most severe). No response to a certain question was given 0 points. Each score is calculated as the mean of the responses of individual items.

The historical-objective-distribution-based (Hi-Ob-Db) scale was also used to assess the condition regarding subjective symptoms as well as objective signs [16]. The clinical grade in the patient group was classified into six stages according to the Hi-Ob-Db clinical scale as follows [17]: stage 0 (no symptoms), stage 1 (paresthesia only at night), stage 2 (paresthesia even for a short time in the daytime), stage 3 (hypoesthesia in the finger of the median nerve distribution), stage 4 (accompanying weakness or thenar muscle atrophy), and stage 5 (thenar muscle complete atrophy or paralysis). The presence or absence of pain was obtained by the patients answering Yes/No. The Hi-Ob-Db score was indicated by the number 1–5.

Nerve conduction studies

All neurophysiological studies were done using Neuropack S1, MEB-9400K, 4 channels EMG/EP Measuring System (Nihon Kohden Corporation, Shinjuku, Tokyo, Japan).

Median sensory study

Recording from the index or middle finger (digit 2 or 3) using ring electrodes with G1 placed over the metacarpal-phalangeal joint and G2 placed 3–4 cm distally over the distal interphalangeal joint, by nerve stimulation at the middle of the wrist (between the tendons to the flexor carpi radialis and palmaris longus) and at a distance of 13 cm from G1. The ground electrode was attached between the stimulating and recording electrodes [18].

The peak latency was recorded and the conduction velocity was automatically calculated by the machine. Peak latency greater than or equal to 3.4 and/or conduction velocity across the wrist of less than or equal to 50 were considered abnormal [19].

For comparative studies, recording from the thumb using ring electrodes the superficial radial nerve was stimulated at the wrist along the lateral border of the radial bone. Using the same distance, the median nerve was also stimulated at the wrist in the usual location. Supramaximal responses were obtained at each stimulation site, and the peak latencies were compared [18] (the difference between the two peak latencies was manually calculated if ≥ 0.5 was considered abnormal) [19].

Median motor study

Recording from the abductor pollicis brevis (APB) muscle: G1 placed over the muscle belly and G2 placed over the first metacarpophalangeal joint. By stimulating the nerve at the wrist (between the tendons to the flexor carpi radialis and palmaris longus) at 7 cm proximal to G1 and then proximally at the antecubital fossa (over the brachial artery pulse) and the ground electrode was attached between the stimulating and recording electrodes. The distal motor latency, the amplitude and conduction velocity were automatically calculated by the machine. A distal motor latency of greater than or equal to 4.2 ms was considered abnormal [18,20]. A comparison study between median nerve by the above-mentioned method and the ulnar nerve stimulating at the wrist and recording from the hypothenar muscles is also used. A cut-off value of 1.6 ms was considered abnormal [21].

F-wave study recording from the abductor policies brevis and abductor digiti minimi and stimulating the median and ulnar nerves, respectively, was done. Abnormal F-wave results (decrease persistence and/ or chronodispersion) were excluded from the study. No needle electromyography study was done.

An electrodiagnosis grading scale for CTS was used [22]. The scale is as follows: grade 0 then denotes no neurophysiological abnormality; grade 1, very mild CTS, detected only in two sensitive tests (e.g. inching, palm/wrist median/ulnar comparison, ring 'double peak'); grade 2, mild CTS finger (orthodromic sensory conduction velocity from index finger to wrist <40 m/s with motor terminal latency from wrist to APB <4.5 ms); grade 3, moderately severe CTS (motor terminal latency >4.5 and <6.5 ms with preserved index finger SNAP); grade 4, severe CTS (motor terminal latency >4.5 and <6.5 ms with absent SNAP); grade 5, very severe CTS (motor terminal latency >6.5 ms); and grade 6, extremely severe CTS (surface motor potential from APB <0.2 mV, peakto-peak).

Neuromuscular ultrasound

Musculoskeletal ultrasound (US) scans were performed using Siemens ACUSON P300 Ultrasound System (Siemens Healthcare, Boulevard, Malvern, USA) multifrequency 10–18 MHz linear transducer. All patients were assessed and examined by one medical staff who was blinded to the NCS results. All cases who were found during the scan to have a cause of CTS like arthritis, ganglion, tenosynovitis were excluded.

Participants were seated facing the examiner with arms extended and wrists resting on the examination couch, forearms supinated, and the fingers semiextended [23] as shown in Figs. 1 and 2. A dedicated protocol with optimization of the scanning parameters (depth, focal zone, frequency, and color-Doppler settings for low-flow vessels) had been preprogrammed for the purpose of this study to ensure consistency of the results obtained. The full course of the median nerve in the carpal tunnel was evaluated in transverse and sagittal planes. The weight of the probe was applied without additional pressure. All examinations were performed following the same protocol [24,25]. To obtain a sagittal view, the transducer was aligned with the thenar crease (which typically also aligns with the middle finger) and was placed at the wrist. To obtain a cross-sectional view, the transducer was rotated 90° and aligned with the distal wrist crease. Finally, to obtain a proximal CSA for comparison, the transducer was started at the wrist and the nerve was traced proximally to the midforearm [23].

Figure 1



Patient positioning during neuromuscular ultrasound of the median nerve at the wrist. MN, median nerve; FCR, flexor carpi radialis; FT, flexor tendons. 1=pisiform, 2=scaphoid, 3=FDS, 4=FDP, 5=FPL, 6=FCR, 7=flexor retinaculum, 8=ulnar artery, 9=ulnar nerve, D1=transverse diameter, D2=longitudinal diameter. 1=pisiform, 2=scaphoid, D1=transverse line between the two bones, D2=palmer bowing.

The CSA of the median nerve was measured by the tracing method at the tunnel inlet [26] and outlet [26,27]. The median nerve then imaged in the cross-section at midforearm, and then the WFR was calculated [10,28]. The median nerve FR (at the pisiform level) was calculated by dividing the major transverse axis of the nerve by its minor longitudinal axis [24]. PB bowing was defined as a measurement at 90° from a line drawn from the hook of the hamate





Transverse sonographic section of an enlarged median nerve at the level of the pisiform bone in a patient with carpal tunnel syndrome. (a) The cross-sectional area of the median nerve (direct method within the oval, dotted line); (b) the flattening ratio of the median nerve at the carpal tunnel inlet; (c) the palmar bowing of the right flexor retinaculum.

bone to the tubercle of the trapezium bone [29]. The median nerve mobility (transverse sliding) in the carpal tunnel was observed dynamically during flexion/ extension of the fingers and wrist. An imaginary, transverse line was drawn bisecting the levels of the pisiform and the hook of the hamate. The mobility of the median nerve was evaluated on the axial plane at this level [25], and finally blood flow in the median nerve sheath was then detected at around 2 cm above the carpal tunnel using color and power doppler sonography [30].

Statistical analysis

Analysis of data was done by a personal computer using statistical program for social science, version 16 (SPSS; SPSS Inc., Chicago, Illinois, USA). Data were expressed as mean±SD for parametric variables and as number and percentage for nonparametric variables. Comparison between groups for parametric data was done by independent samples *t*-test (unpaired *t*-test) and analysis of variance test. χ^2 -Test was used to compare qualitative variables. Sensitivity and specificity of US measurements in CTS patients were obtained by determining the cut-off point using the receiver operating characteristics (ROC) curve. Correlations were calculated using Pearson's correlation coefficient. The level of statistical significance was set at a *P* level less than 0.05.

Results

Characteristics of the studied population

The characteristics of the CTS and control groups are showed in Table 1.

Clinical assessment

One hundred wrists of 65 patients were included. Phalen's and Tinel's signs were positive in 69 and 76 wrists, respectively. Thirty-five (54%) patients have bilateral CTS and 30 (46%) patients have unilateral CTS. Most of the patients (77%) were housewives. Family history CTS was positive in 33 (51%) patients.

On the basis of the patient-oriented data of the Arabic version of BCTQ, the symptom severity (SYMPT) score ranged from 0.16 to 8.17 with a mean of $3.55\pm$ 1.99 and the functional (FUNCT) score ranged from 1 to 4.42 with a mean of 2.41 ± 0.91 .

According to the Hi-Ob-Db scale, the patients were graded into five stages: eight (8%) wrists were stage 1 (half of them had pain), 50 (50%) wrists were stage 2 (38 wrists of them had pain), 30 wrists fall in stage 3 (24 of them had pain) and 12 wrists were graded as

stage 4 (all of them suffered pain) while no wrist was fit for stage 5.

Results of the electrophysiological study

All patients underwent nerve conduction studies. On the basis of the results, wrists were divided into five groups: normal (20%), mild (13%), moderate (51%), severe (9%) and very severe (7%). No wrist was fulfilling the criteria of very mild or extremely severe CTS. There were significant differences between the groups according to electrophysiological severity scale in terms of Phalen's maneuvre, Tinel's test, severity and functional scores, and Hi-Ob-Db scale (P=0.004, 0.006, <0.001, <0.001, <0.001, respectively) as shown in Table 2.

Ultrasonographic assessment

NMUS evaluation was done on the same setting or the next day of NCS and showed: measures of CSA of the median nerve at the inlet and at the outlet; palmer bowing and inlet/forearm ratio in the CTS group were significantly higher than the control group (P<0.05) (Table 3). There was no significant difference between patients and control as regards CSA at midforearm (P=0.6). Fifty wrists showed restriction of mobility of the median nerve, while 31 had Doppler signals (these findings were not found in the control group).

Table 4 showed significant differences between the groups according to electrophysiological severity scale in terms of CSA at the inlet (P<0.001), CSA at the outlet (P<0.001), inlet/forearm ratio (P<0.001), median nerve FR (P<0.001), palmer bowing (P<0.001), restricted mobility of median nerve (P=0.003) and positive power Doppler (P=0.001). Noting that, patients with very severe CTS have the highest value of CSA at the inlet and at the outlet, and the highest inlet/forearm and median nerve FRs.

NMUS of 20 patients with normal NCS revealed that 17 (85%) wrists could be diagnosed as CTS when CSA at the inlet greater than or equal to 9.5 mm², and 19 (95%) wrists could be diagnosed as CTS when palmer bowing greater than or equal to 2.55 mm, despite normal values of NCS.

Table 1	Demographic	data of carpa	tunnel syndrome	and control groups
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	CTS group (N=65)	Control group (N=100)
Age (years)	35.86±9.74 (18–55)	34.28±8.81 (20-54)
Sex (female/male)	53/12	87/13
Weight (kg)	78.89±11.04 (60–107)	78.51±11.15 (56–105)
Height (cm)	161.29±4.85 (151–189)	163.31±5.58 (151–186)
BMI (kg/m ²)	30.30±3.88 (24.54-39.78)	29.45±3.29 (22.31–35.44)

All values except for sex are presented as mean±SD, followed by range; CTS, carpal tunnel syndrome.

Table 2 Evaluation of the clinical parameters across groups

	No CTS (<i>N</i> =20) [<i>n</i> (%)]	Mild CTS (<i>N</i> =13) [<i>n</i> (%)]	Moderate CTS (<i>N</i> =51) [<i>n</i> (%)]	Severe CTS (<i>N</i> =9) [<i>n</i> (%)]	Very severe CTS (N=7) [n (%)]	P value
Symptom severity score	2.11±1.21	2.30±1.57	3.91±1.78	5.07±2.19	5.37±2.19	<0.001*
Functional score	1.8±0.79	1.93±0.76	2.52±0.83	2.96±0.64	3.52±0.76	<0.001*
Positive Phalen's maneuver	8 (40)	7 (54)	39 (76)	8 (89)	7 (100)	0.004*
Positive Tinel's test	14 (70)	5 (38)	42 (82)	8 (89)	7 (100)	0.006*
Hi-Ob-Db scale						
Stage 1 (n=8)	1 (5)	6 (43)	1 (2)	0	0	< 0.001*
Stage 2 (n=50)	13 (65)	5 (34)	32 (63)	0	0	
Stage 3 (n=30)	5 (25)	2 (15)	16 (31)	5 (56)	2 (29)	
Stage 4 (n=12)	1 (5)	0	2 (4)	4 (44)	5 (71)	

CTS, carpal tunnel syndrome; Hi-Ob-Db, historical objective scale; *P<0.05, significant.

Table 3 Ultrasonographic findings in the carpal tunnel syndrome group versus control

	CTS diseased hands (n=100)	Nondiseased hands (n=100)	P value
CSA inlet (mm ²)	11.89±2.64 (8–25)	7.85±1.08 (5-9)	<0.001*
CSA outlet (mm ²)	10.34±2.36 (6-21)	6.76±1.29 (5-9)	< 0.001*
Inlet/forearm ratio	2.53±0.69 (1.28–5)	1.67±0.29 (1-2.25)	< 0.001*
Flattening ratio	3.10±0.83 (1.81–5)	2.88±0.48 (1.60-3.71)	0.02*
Palmer bowing (mm)	4.27±1.36 (1-8.1)	1.95±0.36 (0.80-2.60)	<0.001*

All values are presented as mean±SD, followed by range; CSA, cross-sectional area; CTS, carpal tunnel syndrome; *P<0.05, significant.

The accuracy of ultrasonographic measurements was evaluated by using cut-off points of ROC curve (Table 5). The area under the curve (AUC) of CSA at the inlet was 0.95, indicating a sensitivity and specificity of 84 and 100%, respectively, at a cut-off value of 9.5 mm². The AUC of the inlet/forearm ratio was 0.90 at a cut-off value of 2.08, indicating a sensitivity and specificity of 70 and 92%, respectively. The AUC of FR was 0.55 at a cut-off value of 3.7 indicating a sensitivity and specificity of 21 and 99%, respectively. The AUC of PB was 0.95 at a cut-off value of 2.55 mm, indicating a sensitivity and specificity of 91 and 95%, respectively.

Table 6 showed that CSA and palmer bowing were the most statistically significant parameters that had correlation with the clinical parameters. There was positive correlation between symptom severity score and US parameters as regards CSA at the inlet, inlet/ forearm ratio, palmer bowing and mobility (r=0.30, P=0.003; r=0.21, P=0.04; r=0.22, P=0.03; and

Table 4 Ultrasonographic parameters across groups

r=0.26, *P*=0.008, respectively); moreover; there was positive correlation between functional score and US parameters as regards CSA at the inlet, CSA at the outlet, inlet/forearm ratio, FR and palmer bowing (*r*=0.27, *P*=0.007; *r*=0.28, *P*=0.004; *r*=0.33, *P*=0.001; *r*=0.27, *P*=0.008; and *r*=0.20, *P*=0.04, respectively). The Hi-Ob-Db score showed positive correlation with US parameters as regards CSA at the inlet, CSA at the outlet, inlet/forearm ratio, palmer bowing, mobility and Doppler signals (*r*=0.29, *P*=0.003; *r*=0.20, *P*=0.04; *r*=0.31 *P*=0.002; *r*=0.29 *P*=0.004; *r*=0.28 *P*=0.005; and *r*=0.29, *P*=0.004, respectively).

Discussion

In most instances, the value of complementary testing should be determined by the extent to which it affects the probability of the patient having the diagnosis that had been established clinically. Clearly, there are diagnoses that cannot be well established on the

(<i>N</i> :	No CTS =20) [<i>n</i> (%)]	Mild CTS (<i>N</i> =13) [<i>n</i> (%)]	Moderate CTS	Severe CTS	Very severe CTS	P value
			(11-01) [11 (70)]	(11=9) [11 (%)]	(N=7) [n (%)]	
CSA inlet (mm ²)	9.45±0.94	10.77±2.13	12.20±1.70	14.44±0.73	15.43±5.56	<0.001*
CSA outlet (mm ²) 8	3.50±1.40	9.54±2.30	10.65±1.83	11.44±1.67	13.43±4.12	< 0.001*
Inlet/forearm ratio	2.04±0.33	2.30±0.56	2.61±0.60	3.01±0.75	3.21±1.17	< 0.001*
Flattening ratio 2	2.92±0.59	2.80±0.68	3.14±0.78	2.72±0.68	4.36±1.07	< 0.001*
Palmar bowing (mm)	3.59±0.94	3.88±1.20	4.22±1.26	6.14±1.45	4.84±1.08	< 0.001*
Restricted mobility	5 (25%)	4 (31%)	27 (53%)	8 (89%)	6 (86%)	0.003*
Positive power doppler	6 (30%)	2 (15%)	11 (22%)	8 (89%)	4 (57%)	0.001*

CSA, cross-sectional area; CTS, carpal tunnel syndrome; **P*<0.05, significant.

Table 5 Sensitivity and specificity of ultrasonographic parameters in the carpal tunnel syndrome group

	AUC (%)	Sensitivity (%)	Specificity (%)	Cut-off value	P value
CSA inlet (mm ²)	95	84	100	9.5	<0.001*
CSA outlet (mm ²)	92	80	89	8.5	<0.001*
Inlet/forearm ratio	90	70	92	2.08	<0.001*
Flattening ratio	55	21	99	3.71	0.3
Palmar bowing (mm)	95	91	95	2.55	<0.001*
CSA at the inlet and mobility	97	66	97	0.85	<0.001*

AUC, area under the curve; CSA, cross-sectional Area; *P<0.05, significant.

Table 6 Correlation between ultrasonographic and clinical parameters in the carpal tunnel syndrome group

	Symptom severity score		Functional score		Hi-Ob-Db scale	
	r	P value	r	P value	r	P value
CSA inlet	0.30	0.003*	0.27	0.007*	0.29	0.003*
CSA outlet	0.14	0.16	0.28	0.004*	0.20	0.04*
Inlet/forearm ratio	0.21	0.04*	0.33	0.001*	0.31	0.002*
Flattening ratio	0.04	0.73	0.27	0.008*	0.18	0.07
Palmar bowing	0.22	0.03*	0.20	0.04*	0.29	0.004*
Restricted mobility	0.26	0.009*	0.12	0.23	0.28	0.005*
Positive power doppler	0.05	0.61	0.03	0.8	0.29	0.004*

CSA, cross-sectional area; Hi-Ob-Db, historical objective scale; *P<0.05, significant.

basis of clinical criteria alone and appropriate testing. Confirmation of CTS is usually evaluated by an electrophysiological study [31]. However, sometimes, it is difficult to diagnose CTS using only this modality, early cases and even severe CTS that show no response to the stimulation, elderly patients and associated peripheral polyneuropathy patients. US techniques came into advancement as a tool to complement the diagnosis of CTS [24].

In this study, the US measurements used in CTS diagnosis were the CSA of the median nerve at various levels of the carpal canal (inlet and outlet), the FR and the increased palmar bowing of the PB as well as the wrist/forearm ratio. Other parameters for US were also studied such as the median nerve mobility and power Doppler signals.

Mean normal values of median nerve CSA at the carpal tunnel inlet have varied among reports, ranging from 6.1 to 10.4 mm² [32–34]. In our healthy control group, median nerve CSA at the carpal tunnel inlet ranged from 5 to 9 mm² with a mean of 7.85±1.08 mm². Our results are consistent with previous studies of US in CTS in showing enlargement of the median nerve in CTS hands [32]. There were significant differences in the median nerve CSA between CTS and controls hands at all levels measured at the inlet and outlet, as well as in the FR and PB.

The efficacy of US for the assessment of CTS was evaluated in the present study. Electrodiagnostic studies were used as gold standard diagnostic procedures. The sensitivity of the CSAs for the diagnosis of CTS ranged from 48 to 89% [4,24] and the CSA cut-off at which the values were considered abnormal, varied from 9 to 15 mm² [4,7,24]. Our study showed 84% sensitivity and 100% specificity at a 9.5 mm² cut-off value for the mean CSA at the inlet. The study of Kim *et al.* [24] showed higher sensitivity (88.5%) probably due to the less number of their control (30vs. 100 wrists in our study) and higher sample size (246 wrists) and showed a higher specificity (90%) probably due to a higher cut-off value (10 mm²).

The sensitivities of increased palmer bowing of the PB varied from 40 to 87.2% [7,24] and sensitivities of FR ranged from 37 to 100% [24,35]. Our results showed a sensitivity of 91 and 95% specificity at a cut-off value of 2.55 mm for the PB. These data of sensitivities correspond with the findings reported in earlier studies. Sensitivity of FR was found to be 21% at a cut-off value of 3.7 mm, which is less than the previous

data by Kim *et al.* [24] (77.8 vs. 21% in this study) due to a higher cut-off value (3.4 vs. 3.7, respectively). FR had a poor predictive value as observed by Wong *et al.* [36].

In our study, CSA of median nerve, FR and PB were significantly increased in the CTS group than the control group. Among them, CSA at the inlet and PB were found to have a relatively higher accuracy than FR according to the ROC curve. Therefore, the measurement of CSA at the inlet and/or PB can be considered as an alternative modality to distinguish CTS patients from asymptomatic controls. These data were found to be in concordance with previous data [7,24,37].

The WFR offers a novel approach in the ultrasonographic diagnosis of CTS. The WFR enhances ultrasonographic examination. The technique does not add significant time to the ultrasonographic examination and is easily reproduced. The ratio also helps to eliminate issues of variability between populations, as the patient becomes his own internal control and can facilitate standardization of values [11]. In this study, we compared the WFR of median nerve area between patients with electrodiagnostic evidence of CTS and controls. The WFR difference between the two groups (2.53±0.69 vs. 1.67±0.29) was of equal significance to CSA at the inlet and PB. These findings are in concordance with the data from Hobson-Webb et al. [11] (2.1±0.5 vs. 1.0±0.1) and Mhoon et al. [28].

Median nerve mobilities could be a reliable and specific criterion for the diagnosis of CTS. The restriction of the Median nerve (MN) mobility is a late finding in the disease progression, that is why this parameter has low sensitivity; however, a combination of MN mobility and CSA measurements improve the specificity and accuracy of US in defining a correct diagnosis of CTS [25]. In the present study, a combination of MN mobility and CSA at the inlet gives good specificity (97%), but with low sensitivity (66%).

In 1991, Hunter [38] observed that the mobility of the MN in CTS patients showed a significant decrease in the carpal canal in all planes of movement either actively or passively compared with the control group, and he referred this observation to fibrosis and adhesions of the nerve in the canal contents. This observation is in agreement with previous works by Nakamichi and Tachibana [39], Korstanje *et al.* [40] and Ooi *et al.* [25], who proposed that in the presence of median nerve adhesions, motion of the

wrist and flexor tendons may cause anatomical changes of the median nerve and may have participated in the pathophysiology of CTS. This observation can support the diagnosis of CTS especially if the gray-scale measurements (CSA, FR, and PB) are equivocal. However, we did not quantify transverse sliding of the median nerve as previously done by Nakamichi and Tachibana [39]. Our results were dependent on subjective analysis and further future trials are needed.

On assessing the correlation among the modalities used, positive correlations were observed between US parameters and patient-oriented measures (both the symptom and functional severity scales) and clinical severity scale as assessed by the Hi-Ob-Db scale, which was reported previously by Rao et al. [16] and Kim et al. [24]. Moreover, we found a positive correlation between US parameters and electrophysiological grade. Many other studies have shown good correlation between the Hi-Ob-Db scale and US, and between electrophysiological grade and US, indicating that the nerve swelling detected by the calculation of US reflects in itself the degree of nerve damage: the greater the severity of electrophysiological findings or clinical severity, the greater the CSA of median nerve [24,41,42].

Some of the previous studies have reported that mild CTS cannot show abnormal findings on US [7,24]. However, in the present study NMUS could detect abnormalities in mild CTS which were in concordance with Mhoon *et al.* [28].

One of limitations of the present study is the sonographer assess the mobility of median nerve subjectively, and no test for intrarater reliability was done.

In conclusion, this study confirms previous studies in demonstrating the usefulness of ultrasonography in diagnosing idiopathic CTS. Ultrasonographic measurements of the CSA at the inlet and PB of the median nerve have a relatively higher diagnostic accuracy than FR for CTS. NMUS could be considered as a feasible, noninvasive, and complementary diagnostic modality for the evaluation of CTS. It can be a very good objective alternative tool in situations, where EDX is not available or intolerable by the patient or inconclusive or does not match an evident clinical picture and to exclude structural causes of CTS, and to search for any anatomical variations.

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Conflicts of interest

There are no conflicts of interest.

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