Diagnosis of carpal tunnel syndrome using ultrasonography

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Background
The carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy. Therefore, this study aimed to determine the diagnostic efficacy of the gray-scale and Doppler sonography in the diagnosis and grading of patients with CTS.

Patients and methods
This is a prospective study conducted on 40 adult patients (28 women and 12 men; 76 wrists). Twenty were suffering from CTS, and the other 20 were healthy controls. All of them were examined using a 7–12 MHz linear transducer. Presence of median nerve edema, swelling, flattening ratio of the median nerve, and bowing of the flexor retinaculum were evaluated by gray-scale sonography while Doppler sonography evaluated intraneural hypervascularity. Sensitivity and specificity were calculated considering the nerve conduction studies as a gold standard.

Results
Cross-sectional area (CSA) inlet has the highest sensitivity and accuracy in the diagnosis of CTS (92 and 90%, respectively) in addition to subjective ultrasonography findings such as nerve edema and nerve mobility which had a100% specificity. Doppler examination findings also had a high specificity of 92%. Combined CSA inlet and the swelling ratio have a higher diagnostic accuracy of 95% in diagnosing CTS compared with CSA inlet alone. The CSA inlet used in the grading of CTS with cutoff values of 9–15 mm^2 for mild CTS, CSA more than 15 mm^2 for moderate CTS, and CSA more than or equal to 16 mm^2 for severe CTS.

Conclusion
A combination of CSA inlet and swelling ratio have the highest sensitivity and accuracy than CSA inlet alone in diagnosing CTS.

Keywords:
cross-sectional area, carpal tunnel syndrome, Doppler, grading, gray-scale ultrasound, nerve conduction studies

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Introduction

Carpal tunnel syndrome (CTS) or compression neuropathy of the median nerve (MN) at the wrist is the most common peripheral entrapment neuropathy [1].

Nerve conduction studies (NCS) provide essential information regarding MN function but does not give any morphologic information about the MN and local compressive causes. Both ultrasound (US) and MRI have been used successfully in the evaluation of CTS. By allowing direct visualization of the entrapped MN, these techniques can represent the causes of secondary CTS and describe anatomical variants, such as a bifid MN or a persistent median artery of the forearm as well as any space-occupying lesions including tenosynovitis and ganglion cysts. The use of US in the diagnosis of CTS has many advantages for both the physician and the patient. It is noninvasive and allows for improved patient comfort. The US evaluation for CTS is less time-consuming than electrodiagnostic studies [2].

The basis of US for CTS evaluation reflects the underlying pathologic mechanisms. The MN undergoes physiologic changes, including proximal swelling and edema as it undergoes compression within the carpal tunnel, which is seen in the US as an increase in the cross-sectional area (CSA) and hypoechogenicity. As the MN swells, it pushes outwardly against the flexor retinaculum, leading to bowing of the flexor retinaculum and flattening of the MN. In advanced CTS, inflammation of the MN leads to hypervascularization, which can be detected by color and power Doppler (PD) imaging [2].

The recent American Association of Neuromuscularand Electrodiagnostic Medicine practice guidelines for the diagnosis of CTS using US suggested measuring at the carpal tunnel inlet since here the MN CSA shows the highest rates of sensitivity and specificity in diagnosing CTS when compared with the carpal tunnel outlet and the midcarpal tunnel [3,4]. A recent meta-analysis reviewing studies comparing nerve conduction with US for the diagnosis of CTS suggested that the sensitivity of US diagnostics was overall less than that of nerve conduction [3].

However, controversies in the literature and studies regarding the best diagnostic value of criteria was used to improve the diagnostic sensitivity of US for diagnosing CTS. The objective of this study is to determine the diagnostic efficacy of the gray-scale and Doppler sonography in the diagnosis and grading of patients with CTS.

Patients and methods

A prospective case–control study conducted during the period from August 2016 to September 2017. In all 40 patients (76 wrists) were included in the study. They were referred to the Diagnostic Radiology Department from the Rheumatology, Rehabilitation and Physical Medicine Department for US examination of the carpal tunnel. The study protocol was approved by the Ethics Review Board of Faculty of Medicine, Assiut University, and informed consent was obtained from all participants according to the Declaration of Helsinki.

Patients were classified into two groups:

Group I includes 20 symptomatic patients with 38 wrists.

Group II includes 20 volunteers (38 wrists of asymptomatic persons) considered as the control group.

Inclusion criteria

Patients complaining of finger numbness (medial three and half fingers), pain (mostly nocturnal, radiating to the wrist and arm), and those clinically diagnosed as CTS or have undergone abnormal NCS.

Exclusion criteria

Patients with a history of previous wrist surgery or wrist trauma, clinical findings of any other neuropathies (e.g. cervical radiculopathy), and those with secondary causes of CTS such as rheumatoid arthritis were excluded from the study.

All patients were studied as follows:

(1) Clinical questionnaire for the diagnosis of CTS according to Kamath and Stothard [5]
(2) Motor and sensory NCSs were done for symptomatic patients to diagnose and grade CTS (controls were not subjected to NCSs as their clinical questionnaire were ≤3)
(3) Gray-scale (Gyeonggi-do, Korea) US combined with power and color Doppler (CD) examination using an US device (Logic p6 pro; GE) that is equipped with a 7–12 MHz linear array transducer for small parts and color/PD.

US images obtained were analyzed as follows:

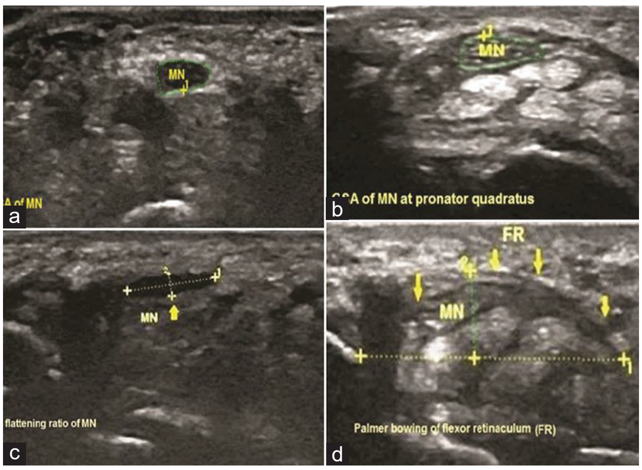
(1) Gray-scale US (according to Abdel Ghaffar *et al.* [6]; Fig. 1):
(a) The CSA of the MN at the inner hyperechoic rim of the MN at the carpal tunnel inlet (at the level of the pisiform and scaphoid bone)
(b) The CSA of the MN at the level of the distal third of the pronator quadratus (PQ) (CSA of PQ)
(c) Swelling ratio (also known as the wrist-to-forearm ratio) by dividing the CSA of the MN at the carpal tunnel inlet by CSA of the MN (at the level of the distal third of the PQ)
(d) Flattening ratio (defined as the ratio of the major axis of the MN to its minor axis) was calculated
(e) The bowing of the retinaculum (the ratio between a perpendicular line drawn from the retinaculum apex to the length of a straight line drawn from the hook of the hamate and the tubercle of trapezium).

(2) Doppler sonography:
(a) Both color and PD were used to detect intraneural blood flow.

Statistical analysis

Data obtained were analyzed using the Statistical Package for the Social Sciences program (SPSS, version 20; IBM Corp., Armonk, N.Y., USA).

Figure 1



Transverse images of the median nerve (MN) at carpal tunnel (a) showed CSA of the MN at inlet, (b) CSA of MN at the pronator quadratus (PQ), (c) flattening ratio of MN, and (d) palmar bowing of the flexor retinaculum (FR). CSA, cross-sectional area.

Different analytical equations were used to get sensitivity, specificity, negative predictive value, positive predictive value, and *P* value compared with NCS (the gold standard). The receiver-operating characteristic curve was also used showing the optimum cutoff value. Area under the curve (AUC) measured the test quality and accuracy: 0.5–0.6 indicated a failed test, 0.6–0.7 indicated a weak test, 0.7–0.8 indicated a fair test, and 0.8–0.9 indicated a good test, while 0.9–1 indicated an excellent test. *P* value was considered significant at less than 0.05. Continuous data were expressed in the form of mean ± SD and range while nominal data were represented in the form of frequency (percentage).

Results

The study included two groups of patients: the first group (the patients group) constituted 38 wrists of 20 patients with CTS (all patients were bilaterally affected except two patients with unilateral affection). Six (30%) patients were men and 14 (70%) were women with a female-to-male ratio of 2.33. The mean ± SD age of the studied patients was 41.40 ± 9.98 years with a range between 18 and 52 years (Table 1).

The second group (the control group) constituted 38 wrists of 20 healthy participants with clinical questionnaire less than or equal to 3. Five (25%) of them were men, while 15 (75%) were women. All controls were bilaterally examined except two patients who were unilaterally examined. The mean age of the control group was 39.5 ± 7.5 with a range between 24.5 and 45 years (Table 1).

Table 1 Demographic data of the studied groups

Variables	Patients group (*n*=20 patients)	Control group (*n*=20 healthy participants)	*P*
Age (years)	41.40±9.98	39.5±7.5	0.92
Range	18-52	24.5-45	
Sex			0.08
Male	6 (30)	6 (30)	
Female	14 (70)	14 (70)	

Continuous data were expressed in the form of mean±SD and range while nominal data were expressed in the form of *n* (%). *P* value was significant if less than 0.05.

Clinical evaluation of the patients showed that 24 (63%) and 20 (52.6%) wrists were positive for Phalen's test and Tinel's sign, respectively. The mean ± SD of clinical questionnaire score was 7.2 ± 0.83 with a range between 6 and 9.

Mild, moderate, and severe CTS were reported in 14 (37%), 14 (37%), and 10 (26%) patients, respectively ($P < 0.001$).

CSA at the carpal tunnel inlet (CSA inlet) had a sensitivity of 92%, specificity of 31%, and an accuracy of 90% for detection of CTS with an AUC being 0.87 and *P* value less than 0.001 at a cutoff point more than 9 mm^2.

CSA at the PQ muscle (CSA PQ) had a sensitivity of 84.21%, specificity of 78%, and an accuracy of 85% for the detection of CTS with an AUC of 0.82 and *P* value less than 0.001 at a cutoff point more than 8 mm^2.

A swelling ratio (CSA inlet/CSA PQ) showed a sensitivity of 71%, specificity of 64%, and an accuracy of 75% for the detection of CTS with an AUC of 0.76 and $P = 0.03$ at a cutoff point more than 1.22 (Fig. 2).

US parameters of the examined wrists with CTS based on the degree of CTS are summarized in Table 2. There are no significant differences between the degrees of CTS as regards the bowing of forearm (dynamic and at rest) and flattening of the MN (dynamic and at rest).

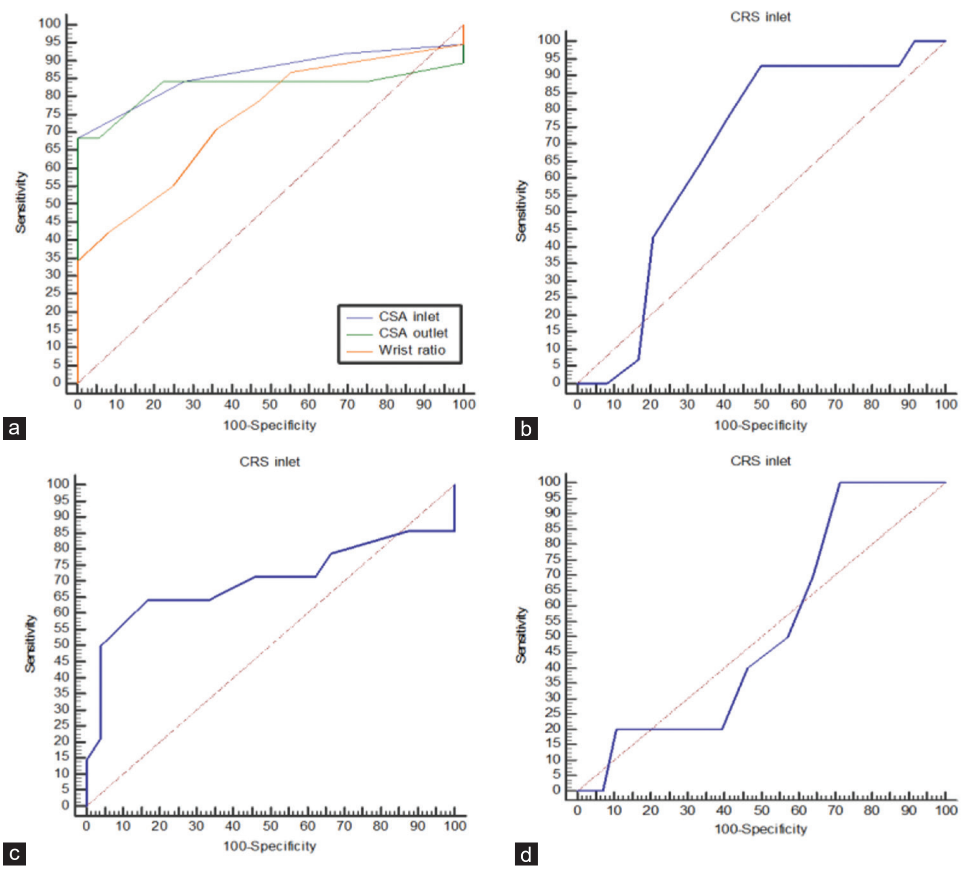
Patients with severe and moderate CTS had significantly higher CSA inlet and outlet ($P < 0.001$) compared with those with mild affection. Although patients with severe CTS had higher CSA inlet and outlet than those with mild CTS, only CSA inlet had a significant difference ($P < 0.001$) between moderate and severe CTS (Table 3 and Fig. 2).

Table 2 Ultrasound parameters based on the degree of carpal tunnel syndrome

US parameters	Degree of CTS based on nerve conduction			*P*1	*P*2	*P*3
	Mild (I) (*n*=14)	Moderate (II) (*n*=14)	Severe (III) (*n*=10)			
CSA inlet	10.57±2.34	12.50±2.99	14.34±1.56	**<0.001**	**<0.001**	**<0.001**
CSA outlet	9.01±2.01	11.09±1.91	11.11±2.87	**<0.001**	**<0.001**	0.98
Wrist ratio	1.19±0.67	1.18±0.94	1.21±0.92	0.55	0.65	0.99
Flattening of median nerve						
At rest	3.22±1.05	3.09±1.03	4.01±1.1	0.11	0.34	0.23
Dynamic	3.67±1.11	3.11±1.32	3.67±0.98	0.34	0.35	0.37
Palmar bowing						
At rest	5.1±1.32	4.9±1.21	5.5±1.08	0.27	0.09	0.82
Dynamic	5.33±1.23	5.52±2.01	5.55±1.56	0.34	0.19	0.07

Data were expressed in the form of mean±SD. CSA, cross-sectional area; CTS, carpal tunnel syndrome.; US, ultrasound. *P*1 compared between mild and moderate CTS; *P*2 compared between mild and severe CTS; *P*3 compared between moderate and severe CTS. *P* value was significant if less than 0.05 (by one-way analysis of variance), Bold: Highly significant **

Figure 2



(a) ROC curve of CSA inlet, CSA outlet, and wrist-to-forearm ratio for the prediction of CTS, (b) ROC curve of CSA inlet for the prediction of mild CTS, (c) ROC curve of CSA inlet for the prediction of moderate CTS, and (d) ROC curve of CSA inlet for the prediction of severe CTS. CSA, cross-sectional area; CTS, carpal tunnel syndrome; ROC, receiver-operating characteristic.

There was a significant negative moderate correlation between CSA inlet and the sensory nerve conduction ($r = -0.59$; $P = 0.001$) while the correlation between CSA inlet and motor nerve conduction was weakly significant ($r = -0.23$; $P = 0.01$).

A nonsignificant weak positive correlation between Clinical Questionnaire Score and CSA at the level of the inlet and the level of PQ ($r = 0.21$, $P = 0.44$, $r = 0.22$, $P = 0.52$), respectively, was found.

Both nerve edema and mobility restriction, and an abnormality in Doppler sonography (subjective findings) was found to have a high specificity of 100 and 92%, respectively. A combination of data of CSA inlet and swelling ratio (objective findings) had the highest sensitivity of 99.6% in the diagnosis of CTS (Table 4 and Fig. 3).

CD of the MN showed that out of 36 wrists with CTS, six (15.7%) had detected intraneural abnormal hypervasculature and only three (7.8%) wrists had detected hypervasculature in PD. In case of the control group, only one wrist had abnormal intraneural hypervasculature in both color and PD.

Table 3 Diagnostic accuracy of cross-sectional area inlet in diagnosing mild, moderate, and severe carpal tunnel syndrome

Indices	Mild CTS (%)	Moderate CTS (%)	Severe CTS (%)
Sensitivity	92	64.29	100
Specificity	50	83.33	28.57
Positive predictive value	52	69.2	33.3
Negative predictive value	92	80	100
Optimal cutoff point (mm^2)	<15	>15	≥16
Area under the curve	0.63	0.69	0.52
P	<0.001	<0.001	<0.001

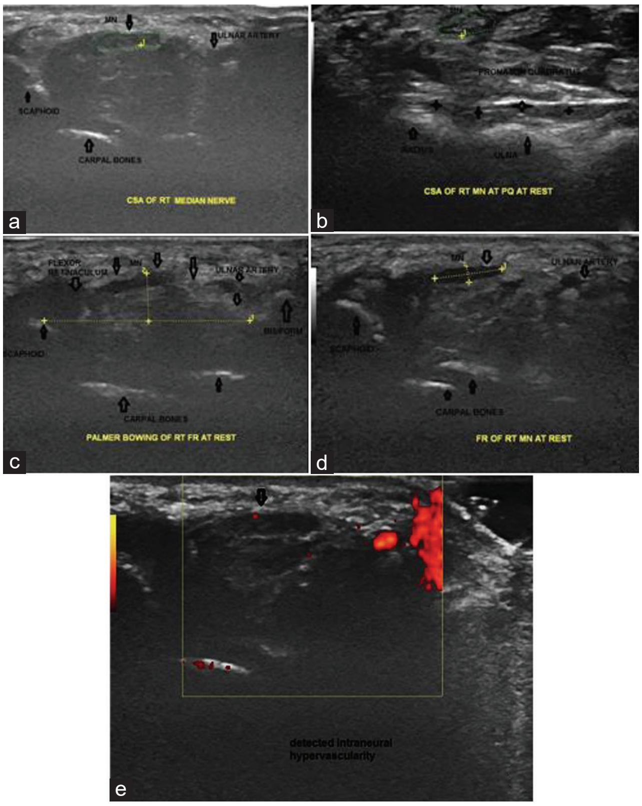
CTS, carpal tunnel syndrome.

Table 4 Diagnostic accuracy of combined cross-sectional area inlet, cross-sectional area pronator quadratus, and swelling ratio in detectingcarpal tunnel syndrome

Indices	CSA inlet/PQ (%)	CSA inlet/wrist ratio (%)	CSA PQ/wrist ratio (%)	All three (%)
Sensitivity	98	99.6	96	99
Specificity	24	20	50	15
Positive predictive value	57	56	66	55
Negative predictive value	92	98	92	93

CSA, cross-sectional area; PQ, pronator quadratus.

Figure 3



A 45-year female patient presented with severe bilateral CTS. On gray-scale ultrasound it showed moderate right MN edema, (a) CSA of the right MN at the level of inlet (14 mm), (b) CSA of the right MN at the level of pronator quadratus (PQ) (14 mm), (c) palmar bowing of FR, (d) flattening ratio of right MN (4.3), and (e) power Doppler examination showed intraneural hypervascularity (black arrowed). CSA, cross-sectional area; CTS, carpal tunnel syndrome; MN, median nerve.

Discussion

CTS is a very common compression entrapment neuropathy of the peripheral nerve. The frequency of CTS may be higher in the industrial setting than in the general population, as illustrated by prevalence estimates of 5–15% in the workplace [1].

Therefore, we evaluated the role of gray-scale US and Doppler in the diagnosis and grading of CTS using neurophysiological findings as a gold standard.

The CSA inlet is the most commonly used parameter for diagnosing CTS. We found that measurements obtained at the level of the pisiform was the most remarkable, because of the increased diameter of the nerve as a result of edema, matching with Alfonso *et al.* [7].

Many studies have reported CSA inlet cutoff values for diagnosing CTS, ranging from 9 to 15 mm^2 with 57–98% sensitivity and 51–100% specificity [8–11]. In our study, the cutoff value of CSA (at the level of Pisiform) was more than 9 mm^2 with a sensitivity of 92% and specificity of 31%. This matched with Tai *et al.* [9], who reported that a CSA inlet more than or equal to 9 mm^2 is the best single diagnostic criterion, and the Zhang *et al.*[8] study showed a cutoff value of 9.05 mm^2 with a sensitivity of 85.7% and a specificity of 55%.

However, in some series, this value was found as high as 10 mm^2 such as the study done by Buchberger [10], and 11 mm^2 according to Sarría *et al.* [11]. This might be explained by the probability of including the hyperechoic rim. However, none of the investigators stated whether they included this rim during their measurements or not.

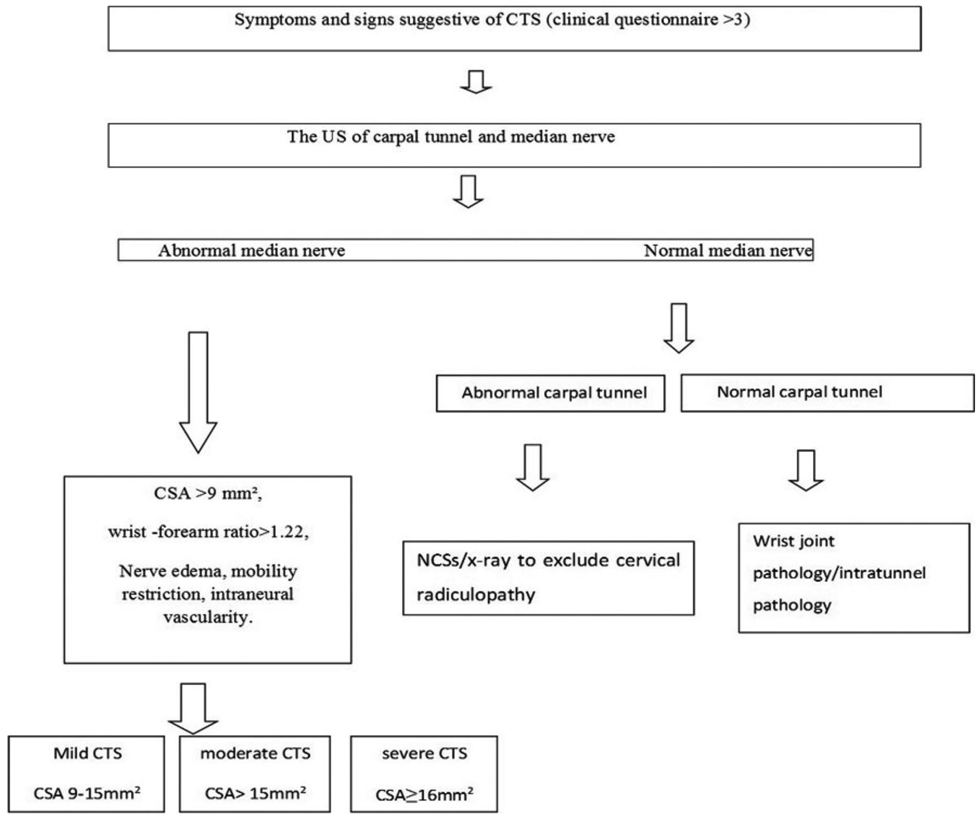
The swelling ratio of the MN (CSA inlet/CSA PQ) was considered one of the diagnostic criterion for CTS by many authors [8,12,13]. The cutoff value of the swelling ratio in our patient was more than 1.22 with low specificity and sensitivity, agreeing with that found by Zhang *et al.* [8], who reported a value of one. But this was different from what Hobson-Webb *et al.* [12]. Reported; the ratio more than or equal to 1.4 gave 100% sensitivity. Moreover, the current study showed no significant difference of the mean value of swelling ratio between patients and controls. This mismatched with Zhang *et al.*[8] and Hobson-Webb *et al.* [12], who reported a significant difference of the mean value of swelling ratio between patients and controls, which may be due to the small sample size and different US settings.

A combination of CSA inlet and swelling ratio had the highest sensitivity of 99.6% and an accuracy of 95% than CSA inlet alone (sensitivity of 92% and accuracy of 90%). The current result supports Hobson-Webb *et al.* [12], who reported that a wrist-to-forearm ratio more than or equal to 1.4 gave 100% sensitivity for diagnosing CTS while using only the MN area at the wrist resulted in a sensitivity of 45–93%.

Concerning the correlation between CSA inlet and nerve conduction, it was logic to find a significant negative correlation between CSA and both sensory and motor nerve conduction, as the cross section of the nerve increases the conduction velocity decreases as a result of compression. This result was consistent with those found by El-Habashy *et al.* [14].

We also found a significant difference between grading of severity of CTS as regards CSA inlet. That was in agreement with that obtained by Karadağ *et al.* [15], who stated that the US was useful in grading the severity of CTS. Futhermore, it has been concluded that US measurement of CSA could give information about the severity of MN involvement and they set US cutoff points that discriminate between different grades of CTS severity.

Figure 4



A proposed algorithm for the diagnosis and grading of CTS based on US parameters. CTS, carpal tunnel syndrome; US, ultrasound.

So, we can be confident of determining the level of severity of CTS using US measurement of CSA of the MNs [16].

As regards the intraneural vascularization in CTS detected using Doppler US, PD US was considered superior to CD US in the demonstration of vascular flow due to its high sensitivity to slow flow, absence of angle dependency, and absence of aliasing. The power gain was optimized by reducing gain just enough to suppress the noise with the transverse image of MN [17]. We detected intraneural hypervascularity in six wrists of patients and one wrist of control with significant difference between patients and controls (P = 0.02), which is in agreement with the study of Ghasemi-Esfe *et al.* [18], who found that 10% of their healthy controls had intraneural vascularity and was initially considered a false positive finding of CD imaging.

From all the results, we proposed an algorithm for the diagnosis and grading of CTS based on US parameters (Fig. 4).

Our study carried some limitations. First, it was a single-center study and second, the small sample size in our study.

Conclusion

In conclusion, US of the MN are used in the diagnosis of CTS, but are not totally alternative to NCS. A combination of CSA inlet and swelling ratio have the highest sensitivity and accuracy than CSA inlet alone in diagnosing CTS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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