The Egyptian Journal of Radiology and Nuclear Medicine (2012) **43**, 581–587

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

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ORIGINAL ARTICLE

Gray scale and color Doppler sonography in the diagnosis of carpal tunnel syndrome

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Received 6 March 2012; accepted 3 August 2012
Available online 15 September 2012

KEYWORDS

Carpal tunnel syndrome;
Gray scale sonography;
Color Doppler sonography;
Electrodiagnostic tests

Abstract *Purpose:* To determine the diagnostic accuracy of gray scale and color Doppler sonography in the diagnosis of patients with carpal tunnel syndrome.
Patients and methods: A total of 53 wrists in 41 consecutive patients with clinical suspicion of carpal tunnel syndrome, referred from the Department of Physical medicine, Rheumatology & Rehabilitation were examined with ultrasonography using a 12 MHz linear array transducer. The presence of median nerve edema, swelling, and bowing of the flexor retinaculum was evaluated by gray scale sonography, while intraneural hypervascularity was evaluated by color Doppler sonography. Sensitivity and specificity were calculated for each sonographic feature and compared with electrodiagnostic test (EDT) results.
Results: Electrodiagnostic tests confirmed carpal tunnel syndrome in 48 wrists. A median nerve cross sectional area (CSA) of 11 mm^2 was calculated as a definition of median nerve swelling. In comparison with electrodiagnostic tests, median nerve swelling showed the highest accuracy (89%) among the gray scale sonographic criteria, and the presence of median nerve hypervascularization showed the highest accuracy (94%) among all sonographic criteria. Median nerve edema and bowing of the flexor retinaculum showed accuracies of 81% and 77% respectively.
Conclusion: Median nerve intraneural hypervascularity detected by color Doppler sonography is more accurate in detection of median nerve involvement than gray scale sonography criteria in patients with suspected carpal tunnel syndrome.

1. Introduction

Carpal tunnel syndrome (CTS) is the most common form of peripheral entrapment neuropathy and is one of the essential etiologies of hand morbidity particularly prevalent in middle aged women (1,2). An early diagnosis is essential to prevent permanent nerve damage and functional sequelae (3). Diagnosis of CTS is

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Peer review under the responsibility of the Egyptian Society of Radiology and Nuclear Medicine

Production and hosting by Elsevier

0378-603X http://dx.doi.org/10.1016/j.ejrnm.2012.08.002

usually based on the combination of clinical symptoms (burning pain, numbness, and nocturnal parasthesia in the median nerve distribution), and signs, such as Tinel sign (tapping over the median nerve producing dysesthesias) and Phalen sign (dysesthesias with wrist flexion), electrodiagnostic tests, and imaging techniques (4,5). The clinical signs are moderately sensitive and specific (6), and false negative and false positive results have been reported with electrodiagnostic tests (EDTs) (7,8).

Ultrasonography (US) has emerged as a feasible, simple, relatively low cost, rapid, accurate and noninvasive imaging method for evaluating the median nerve in the carpal tunnel (4,5,9,10) to detect changes in the nerve shape and exclude anatomic variants and space occupying alterations as ganglion cysts and tenosynovitis (4,5). US permits perception of nerve compression characteristics, including altered echogenicity, increased cross-sectional area, and bowing of the flexor retinaculum (11,12).

Entrapment of the median nerve within the carpal tunnel causes nerve ischemia and affects the microvasculature within the neural fascicles (13). Vascular factors have been suggested by some investigators to have a role in CTS pathogenesis (14). In CTS, it is reported that the intraneural microvasculature of the median nerve is prominent and dilated due to inflammation and ischemia within the median nerve (14). Hence, it can be hypothesized that the evaluation of intraneural vasculature with color Doppler US may be useful for detecting CTS.

The purpose of this study is to assess the accuracy of gray scale and color Doppler sonography findings in diagnosing carpal tunnel syndrome in comparison with electrodiagnostic studies.

2. Materials and methods

Fifty-three wrists of 41 patients with unilateral or bilateral symptoms of carpal tunnel syndrome, referred from the Physical medicine, Rheumatology & Rehabilitation department of Ain Shams University hospital, were included in this study between January and December 2011. Written and verbal consents were obtained from all patients. The carpal tunnel symptoms were bilateral in 12 cases and unilateral in 29 cases. All patients had characteristic clinical symptoms of CTS and their electrodiagnostic tests were performed within a week before the US examination was done

Patients with a history of previous wrist surgery or fracture, bifid median nerve seen on US, with conditions associated with neuropathy (e.g., hypothyroidism, diabetes mellitus, chronic renal failure, rheumatoid arthritis and pregnancy) and those with clinical findings of any other neuropathies (e.g., cervical radiculopathy) were excluded from the study.

All patients were subjected to the following:

A. Full history taking: Patients with symptoms suggestive of CTS were based on the presence of four clinical features. The four features are; predominantly nocturnal or early morning hand numbness, hand numbness provoked or worsened by sustained wrist position or manual activities, relief of hand symptoms with trick movements and a radial hand distribution of sensory symptoms (15).

B. Thorough clinical examination: including sensory examination of the hand to evaluate any paresthesia in median nerve distribution, motor examination to detect any weakness of thenar muscles and provocative tests for CTS (Tinel's sign, Phalen test and Reverse Phalen test).

C. Electrophysiological assessment: The following electrophysiological studies were done in the Physical medicine, Rheumatology & Rehabilitation department. The apparatus used was Tonnies version 1.59 in the EMG laboratory of Ain Shams University hospitals. The electrodiagnostic tests were performed within a week before the US examination was done. The nerve conduction studies (NCSs) performed were motor and sensory antidromic nerve conduction study of the median nerve to diagnose and grade CTS in all patients, motor and sensory antidromic nerve conduction studies of the ulnar nerve were done to exclude polyneuropathy and provide comparative data with median nerve NCS values especially in bilateral cases and F-response latency to the median nerve to exclude proximal root compression.

2.1. Methods of electrophysiological studies

Electrophysiological studies were performed in a quiet room with a constant temperature of 27 °C using thermostatic air conditioning. The patient was placed in a sitting position, with forearm supinated, and allowing maximum relaxation of the patient.

1-Motor nerve conduction study of the median nerve: Motor nerve conduction studies of the median nerve were performed using standard techniques of supramaximal cutaneous stimulation and surface recording electrodes. Motor amplitude, distal motor latency, and motor nerve conduction velocity (M-NCV) will be measured using the conventional methods. The recording active electrode to the median nerve is a surface electrode secured over abductor pollicis brevis muscle. The reference electrode is secured 3–4 cm distal to the active electrode on the palmer aspect of the thumb. The median nerve was stimulated supramaximally in two positions; at the wrist and at the elbow. Stimulation at wrist was between the palmaris longus and flexor carpi radialis tendons at the second wrist crease (approximately 1 cm proximal to the most distal crease). The second stimulation or elbow stimulation was done at the elbow crease medial to the biceps tendon and the brachial artery forming a segment over which nerve conduction can be calculated.

2-Sensory nerve conduction study of the median nerve: Sensory nerve conduction studies of the median nerve were obtained by producing antidromic stimulation (the cathode was placed distally) at the wrist to determine distal sensory latency. The latency was measured to the negative peak that is, peak latency. Electrode (E)-1 was placed proximally at the metacarpophalangeal joint of the 2nd digit while the E-2 electrode was placed 2 cm distal to E- 1 on the distal interphalangeal joint.

3-Motor nerve conduction study of the ulnar nerve: Motor nerve conduction studies of the ulnar nerve were performed using standard techniques of supra-maximal cutaneous stimulation and surface electrode recording. Motor amplitude, distal motor latency, and motor nerve conduction velocity will be measured using the conventional methods. The active electrode was placed and secured over abductor digiti minimi muscle and the reference electrode was placed 3–4 cm distal to the active electrode. The ulnar nerve was stimulated supramaximally with the elbow extended and forearm supinated. The stimulation at wrist was done at the distal wrist crease just lateral to the tendon of flexor carpi ulnaris, while the stimulation at elbow was posterior to the medial epicondyle of the humerus.

4-Sensory nerve conduction study of the ulnar nerve: Sensory nerve conduction studies of the ulnar nerve were obtained by producing antidromic stimulation at the wrist to determine distal sensory latency and peak latency. The E-l electrode was located on the fifth digit just distal to the metacarpophalangeal joint and the E-2 electrode was distal on the fifth digit.

5-F response latency of the median nerve: F-response latency to the median nerve was obtained by recording from the abductor pollicis brevis muscle (APB), and stimulation of the distal portion of the median nerve at wrist between palmaris longus and flexor carpi radialis tendons, with the cathode directed proximally, with providing a supra maximal stimulus. The active recording electrode is placed over APB muscle. The reference electrode is secured 3–4 cm distal to the active electrode. F-wave minimal and maximal latencies were obtained using 10 stimulations, at a rate of once every 2 s. F-wave was measured to exclude proximal root affection.

2.2. Electrophysiological diagnostic criteria

Patients with CTS were classified according to electrodiagnostic grading (16) into:

Grade 0: Normal: Normal standard and comparative tests.

Grade 1: Very mild CTS: Normal standard tests, abnormal comparative tests.

Grade 2: Mild CTS: Abnormal sensory with a normal motor response that is, prolonged antidromic distal sensory latency (DSL) $\geqslant$ 2.9 ms to the second digit.

Grade 3: Moderate CTS: Abnormal median sensory and motor response that is, prolonged distal motor latency (DML) to abductor pollicis brevis (APB) is $\geqslant$4.2 ms but $\leqslant$6.5 ms, and prolonged antidromic DSL with decreased amplitude sensory nerve action potential (SNAP).

Grade 4: Severe CTS: Absence of sensory response, abnormal distal motor latency to APB but still $<$6.5 ms with decreased amplitude of compound muscle action potential (CMAP) and abnormal EMG activity in APB.

Grade 5: Very severe CTS: Terminal latency to APB $>$6.5 ms.

Grade 6: Extremely severe CTS: Absence of median motor and sensory responses (surface motor potential from APB $<$0.2 mV amplitude).

2.3. US technique

A radiologist with 5 years of musculoskeletal US experience performed the US examination by using a 12 MHz linear array transducer (Philips, HD 10) at the Radiodiagnosis department at Ain Shams University hospital. The subjects were seated facing the radiologist with their arms extended on a flat surface in the supine position and their fingers semiextended. The median nerve was examined in the transverse and longitudinal planes along the carpal tunnel by gray scale to investigate the presence of median nerve compression criteria, including the measurement of cross sectional area (CSA) of the median nerve at the tunnel inlet using the ellipse method. The maximum height of the retinaculum was measured above a line subtended between its radial and ulnar carpal attachments. Color Doppler sonograms of the median nerve in the carpal tunnel were obtained in the longitudinal plane after adjusting the setting for investigating low flow vessels and sweeping the probe to determine the most vascular section of the nerve, which was usually the midsagittal plane of the nerve.

2.4. US image analysis

Each wrist was evaluated for the presence or absence of 4 sonographic criteria indicating carpal tunnel syndrome (Figs. 1–3):

1. Median nerve edema: The normal median nerve is a bundle of hypoechoic nerve fascicles surrounded by hyperechoic epineural connective tissue, all of which are encased in the hyperechoic nerve sheath (17). Nerve edema alters the signal of the nerve components resulting in increased hypoechoic signal of the nerve.
2. Median nerve swelling: Nerve swelling was defined as an enlargement of the cross sectional area of the nerve to 11 mm^2 or more within or proximal to the carpal tunnel. The CSA of the nerve was defined as the area of the nerve bundles in the perineural fibrous tissue.
3. Bowing of the flexor retinaculum: The presence of increased palmar bowing of the flexor retinaculum was determined by the displacement of the palmar apex of the retinaculum 2 mm or more from the straight line between the attachments to the trapezium tubercle and the hamate bone.
4. Nerve hypervascularization: It was determined on the color Doppler sonograms by the presence of any intraneural vascular structures.

2.5. Statistical analysis

IBM SPSS statistics (V. 19.0, IBM Corp., USA, 2010) were used for data analysis. Data were expressed as Mean ± SD for quantitative parametric measures in addition to both number and percentage for categorized data. The diagnostic validity test was done for each of the 4 sonographic criteria indicating carpal tunnel syndrome. It included:

a. he diagnostic sensitivity: the percentage of diseased cases truly diagnosed (TP) among total diseased cases (TP + FN).
b. The diagnostic specificity: the percentage of non-diseased cases truly excluded by the test (TN) among total non-diseased cases (TN + FP).
c. The predictive value for a +ve test: the percentage of cases truly diagnosed among total positive cases.
d. The predictive value for a −ve test: the percentage of cases truly negative among total negative cases.
e. The efficacy or the diagnostic accuracy of the test: the percentage of cases truly diseased plus truly non-diseased among total cases.

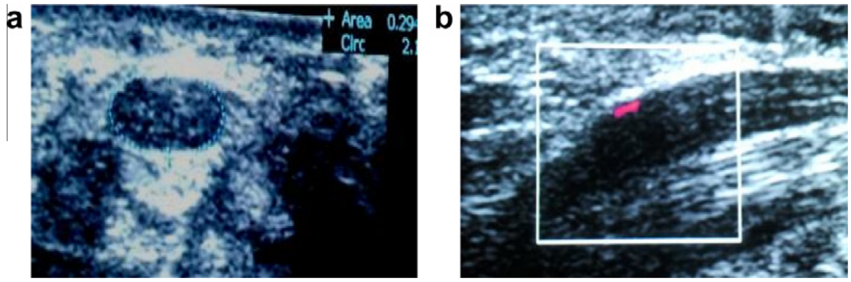

Fig. 1 (a) Transverse image of the median nerve at carpal tunnel showed nerve edema and swelling (CSA = 29 mm^2), as well as bowing of the flexor retinaculum. (b) Power Doppler showed +ve sign of intraneural hypervascularization.

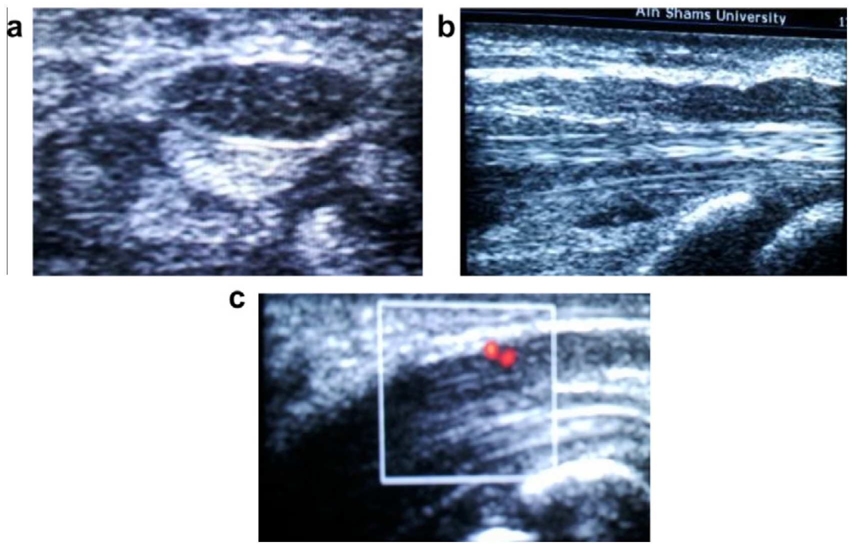

Fig. 2 (a & b) Transverse and longitudinal images of the median nerve at carpel tunnel showed nerve edema and significant swelling (CSA = 28 mm^2), as well as bowing of the flexor retinaculum. (c) Power Doppler showed +ve sign of intraneural hypervascularization.

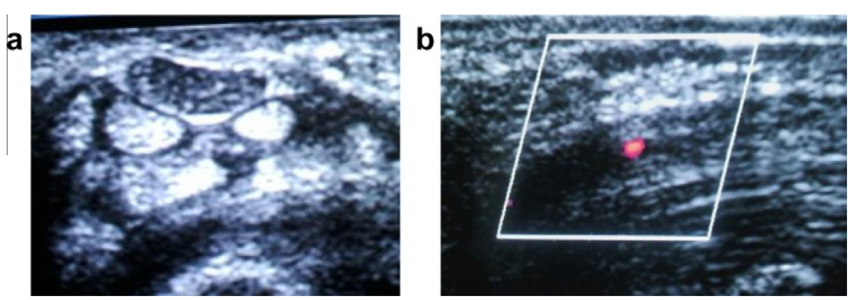

Fig. 3 (a) Transverse image of carpal tunnel revealed absent gray scale signs of CTS with normal median nerve CSA (10 mm^2), absent edema and absent bowing of the flexor retinaculum. (b) Power Doppler revealed +ve sign of intraneural hypervascularization.

3. Results

The patient cohort consisted of 31 women ranging in age between 35–59 years with a mean of 49.1 ± 6.5 years and 10 men ranging in age between 33–55 years with a mean of 47 ± 5.62. The duration of the symptoms suggestive of CTS among the patients ranged from 2 to 13 months with a mean of 6.9 ± 3.4 months.

Electrodiagnostic tests of 53 wrists in 41 patients with symptoms of carpal tunnel syndrome revealed positive results in 48 wrists (Tables 1 and 2). Gray scale sonography revealed at least one abnormal finding in 52 wrists. All gray scale sonography criteria were present in 39 wrists (74%) (Figs. 1 and 2). Color Doppler sonography detected intraneural hypervascularity in 49 wrists and correctly identified carpal tunnel syndrome in 47. Of 48 wrists with carpal tunnel syndrome, 3 wrists showed only one positive sonography criterion for CTS which was median nerve hypervascularity (Fig. 3), 5 wrists showed 2 positive sonography criteria which were nerve swelling and edema, and 3 wrists showed 3 positive criteria which were nerve swelling, edema and bowing of the flexor retinaculum in 1 wrist and

Table 1 Electrodiagnostic tests grading of Carpal tunnel syndrome in 53 patient wrists.

Electrodiagnostic tests grade	Number of wrists and percentage
Normal G0	5 (9.4%)
Mild G2	29 (54.7%)
Moderate G3	15 (28.3%)
Very severe G5	4 (7.5%)

Table 2 Results of electrodiagnostic tests among patients with CTS.

Results of EDTs	Patients (n = 48)
Median nerve distal sensory latency (ms)	3.4 ± 0.5
Median nerve distal motor latency (ms)	4.4 ± 0.9
Median nerve amplitude of compound muscle action potential (mv)	19.2 ± 9.4
Motor conduction velocity of median nerve (m/s)	59.2 ± 10.5

EDTs: electrodiagnostic tests, n: number.

nerve edema, swelling and hypervascularity in 2 wrists. In 44 wrists with CTS, both nerve swelling and hypervascularity were present, whereas 4 wrists showed either nerve swelling or nerve hypervascularization. In the case of disagreement between nerve hypervascularity and nerve swelling, the former correlated correctly with electrodiagnostic tests in 3 wrists (Fig. 3) and the latter in 1 wrist.

Gray scale sonography detected median nerve swelling (CSA equal to or more than 11 mm^2) in 45 wrists of 48 patients with positive electrodiagnostic tests with CSA up to 29 mm^2 with an average CSA of 17.8 mm^2.

According to the sonographic criteria of carpal tunnel syndrome evaluated in this study (Tables 3 and 4) in 53 symptomatic wrists, nerve edema was present in 42 wrists with a sensitivity of 83%, a specificity of 62% and an accuracy of 81%. Median nerve swelling with a cross sectional area of 11 mm^2 or more was present in 48 wrists with sensitivity of 94%, specificity of 40% and accuracy of 89%. Bowing of the flexor retinaculum was found in 40 wrists with a sensitivity of 80%, a specificity of 60% and an accuracy of 77%. And finally color Doppler sonography detected median nerve intraneural hypervascularity in 49 wrists with a sensitivity of 98%, a specificity of 60% and with the highest accuracy

Table 4 Study results.

	True positive	True negative	False positive	False negative
Nerve edema	40	3	2	8
Nerve swelling	45	2	3	3
Bowing of flexor retinaculum	38	3	2	10
Nerve hypervascularization	47	3	2	1

among the sonographic criteria of 94% and positive predictive value of 96%.

Of the 5 wrists with clinical symptoms suggestive of CTS and negative electrodiagnostic tests, one showed isolated median nerve swelling, 2 showed nerve edema, swelling, bowing of the flexor retinaculum and nerve hypervascularization, and 2 showed no nerve abnormalities or retinaculum bowing on gray scale or color Doppler sonography.

4. Discussion

Accurate diagnosis of carpal tunnel syndrome and its differentiation from other causes of hand morbidity is essential, particularly if the patient is a candidate for surgery (18). The diagnosis of CTS usually is based on typical clinical signs and symptoms and can be confirmed with electrodiagnostic tests in most cases (3). Ultrasound has been advocated as a non-invasive, low cost technique for diagnosis of CTS. Electrodiagnostic tests are based on physiologic malfunctions of the median nerve, while ultrasound enables morphologic assessment including nerve swelling, edema, bowing of the flexor retinaculum, as well as evaluation of functional disturbance manifested by nerve hypervascularization (19,20).

Several authors have recommended the need for further studies about the role of imaging modalities in the diagnosis of CTS, considering that there are some drawbacks in the diagnostic accuracy of EDTs with sensitivity and specificity to be reported around 70% and 82% respectively failing to diagnose approximately 20–30% of CTS cases (21).

Prior studies to evaluate US imaging of CTS, with EDTs as a reference standard revealed a wide range of sensitivity and specificity values, ranging from 82% to 94% and 65% to 97% respectively (22,23).

Although a number of authors have reported discrepancies in the accuracy of sonography criteria of median nerve entrapment, almost all studies have agreed that nerve swelling is the

Table 3 Detectability of sonographic criteria indicating carpal tunnel syndrome in comparison with electrodiagnostic tests.

Criteria	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy
Nerve edema	83% (40/48)	60% (3/5)	95% (40/42)	27% (3/11)	81% (43/53)
Nerve swelling	94% (45/48)	40% (2/5)	94% (45/48)	40% (2/5)	89% (47/53)
Bowing of flexor retinaculum	80% (38/48)	60% (3/5)	95% (38/40)	23% (3/13)	77% (41/53)
Nerve hypervascularization	98% (47/48)	60% (3/5)	96% (47/49)	75% (3/4)	94% (50/53)

NB. Numbers in parentheses are number of wrists.

main sonographic criterion indicating CTS (1,2,5,12,18,22). The sensitivity of nerve swelling ranged from 57% to 89% and the nerve CSA indicating CTS ranged from 9 mm^2 to 15 mm^2 (1,5,20,22,24–27). The role of bowing of the retinaculum varied with sensitivities of 45–81%, while the sensitivity of nerve edema was 80% (20).

In this study, we evaluated the accuracy of 4 sonographic signs in predicting CTS- namely, the 3 gray scale sonography morphologic features and median nerve hypervascularization. The findings were compared with EDTs in all wrists to determine the accuracy of sonography in diagnosing CTS.

Previous US study investigators have proposed a range of median nerve CSA cutoff values at various measuring sites (5, 18, 20, 22, 24–27). Mohammadi et al. demonstrated in their study that there was no significant difference between the CSA of the median nerve at the tunnel inlet or outlet in different grades of CTS according to EDTs. Accordingly, in agreement with some investigators' (20) study design, we chose 11 mm^2 as the median nerve CSA threshold value measured at the carpal tunnel inlet to predict CTS. Previous studies (20,27) have included median nerve flattening as a sonographic predictor of CTS, however, its role varied among studies with sensitivities of 38–65%, therefore it was not included in our sonographic criteria.

Comparing the sonography findings and electrodiagnostic test results, demonstrated that nerve hypervascularization and nerve swelling yielded the best detectability of CTS with nerve hypervascularization showing higher accuracy (94%), and increase in positive and negative predictive values (96% and 75% respectively) compared to 89% accuracy, 94% positive predictive value and 40% negative predictive value of nerve swelling. Our results are in accordance with Mallouhi et al. whose study demonstrated nerve hypervascularization accuracy of 91% and Joy et al. who demonstrated a positive predictive value of 96%. In the current study, color Doppler sonography findings were true negative in one wrist with a CSA of 11 mm^2 and negative EDTs, and were true positive in 3 CTS patients with CSA of less than 11 mm^2.Bowing of the flexor retinaculum in the detection of CTS in our study yielded a sensitivity of 80% which is higher than results of previous studies (20). Our results indicate that color Doppler sonography allows more reliable assessment of median nerve entrapment and helps to select candidates for treatment.

Although compression of the median nerve beneath the flexor retinaculum is the primary basis of CTS, many of the early symptoms are thought to be due to altered intraneural hemodynamics. Sugimoto et al. (28) used dynamic MRI studies and concluded that CTS is more due to a circulatory disturbance than due to median nerve deformation or compression. Color Doppler sonography is a convenient integral adjunct to gray scale sonography which demonstrates the pathologic intraneural vasculature, thus permitting recognition of hypervascularization in the median nerve before the development of nerve swelling and edema and consequently allowing early detection of median nerve involvement in CTS.

There are only limited reports comparing sonography with EDTs, using clinical criteria as a gold standard. Some authors (29) have shown that sonography was as good as EDTs in confirming clinically diagnosed CTS, while others (30) reported higher sensitivity of EDTs when compared with sonographic studies.

According to Mondelli et al. mild CTS could be detected neither by sonography nor by EDTs in 23.5% of cases. Doppler studies may be of particular value in CTS with negative EDTs, since around 25% of patients with CTS have normal EDTs. Koyuncuoglu et al. (31) revealed positive US findings in patients who had CTS- positive clinical results, with negative EDTs in 30.5% of these patients, suggesting an advantage to using US, especially during the early stages of CTS, when the median nerve shows no functional abnormality in EDTs. It is notable that in a study by Ghasemi-Esfe et al. about 10% of their healthy control subjects had intraneural vascularity, which was initially considered a false positive finding of color Doppler imaging, however, when they demonstrated positive results at EDTs, it was suggested that these subjects might have occult or early stage CTS. In the same study, the authors attributed the positive results of color Doppler US in patients with clinical evidence of CTS and negative findings at EDT to the sensitivity of color Doppler imaging, however, possible alternative causes were not totally excluded.

In summary, our study revealed a high degree of accuracy of color Doppler US as a non-invasive and accurate technique for diagnosing CTS enabling the detection of functional intraneural circulatory disturbance allowing early diagnosis and treatment.

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