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RESEARCH

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Diagnostic value of diffusion-weighted MRI using apparent diffusion coefficient (ADC) in evaluation of median nerve in carpal tunnel syndrome

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Abstract

Background The diagnosis of carpal tunnel syndrome is based on a combination of clinical history, clinical examination and frequent use of electrodiagnostics as nerve conduction study and electromyography which often do not provide the spatial and anatomical localizing information, especially with small nerves of the extremities. Conventional magnetic resonance imaging can reveal morphological changes in carpal tunnel syndrome patients.

Aim The purpose of our study was to assess the efficacy of diffusion magnetic resonance imaging as a functional imaging in evaluation of median nerve in carpal tunnel syndrome.

Patients and methods This prospective study included a group of 33 patients with carpal tunnel syndrome diagnosed by both clinical examination and electromyography; 40 writs were examined. A control group of 20 subjects of matched age group were also included. All the participants were subjected to conventional and diffusion magnetic resonance imaging studies.

Results Median nerve apparent diffusion coefficient values of patients are lower than those of controls. The sensitivity and diagnostic accuracy of diffusion conventional magnetic resonance imaging were 95% and 97.5%, respectively, versus 25% and 62.5% of conventional magnetic resonance imaging. A cut-off apparent diffusion coefficient value $\leq$ 0.99 obtained at distal radio-ulnar joint level and > 1.07 at pisiform level as well as apparent diffusion coefficient ratio at a cut-off $\leq$ 0.2 was significantly valid for diagnosing carpal tunnel syndrome.

Conclusions Diffusion magnetic resonance imaging provides functional evaluation of median nerve in patients with carpal tunnel syndrome.

Keywords Carpal tunnel syndrome, Diagnosis, Diffusion tensor imaging, Magnetic resonance imaging

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Background

Carpal tunnel syndrome (CTS) is the most common peripheral neuropathy of the upper limb caused by median nerve (MN) entrapment at the level of the carpal tunnel due to anatomical variation or increased contents such as ganglion cysts, tenosynovitis, hypertrophied tendons and ligaments, and dislocation of wrist bones. Excessive motion of the wrist and hand related to certain occupations is also considered an important factor [1, 2].

Peripheral neuropathy is diagnosed mainly clinically or by electrodiagnostics, but these methods are non-specific and give no information about any structural changes of nerves that may lead to neuropathies [3].

Conventional magnetic resonance imaging (cMRI) using standard sequences can be used to determine many peripheral nerve disorders. It can reveal morphological changes in CTS patients either causes of median nerve entrapment or changes in the nerve fibers. However, the effect of causative lesions on the nerve is more obvious on functional imaging [4].

Diffusion-weighted imaging (DWI) is an advanced MRI technicality that facilitates direct imaging of the nerves in most cases as tumors, trauma, and peripheral neuropathies. It depends on the diffusion of water molecules in generating contrast in MR images and mapping of the diffusion process of molecules giving microscopic details about tissue architecture using different parameters as apparent diffusion coefficient (ADC) values of the median nerves in CTS for quantitative assessment [5].

The aim of this study was to assess the diagnostic performance of diffusion MRI parameters in evaluation of median nerve (MN) in carpal tunnel syndrome (CTS).

Methods

Study population

The current prospective study included 33 patients diagnosed clinically to have carpal tunnel syndrome in 40 wrists; their ages ranged from 23 to 55 years with a mean of 40.7 ± 7.7 years. They were referred to MRI unit in Radio-diagnosis department from Rheumatology department over a period from September 2021 to October 2022. A control group of 20 individual without median nerve neuropathy were also included. Both groups correspond in terms of age and sex to avert bias.

Approval of Research Ethics Committee (REC) and informed consent were obtained from parents after explanation of the benefits and risks of the procedure. Privacy and confidentiality of all patients' data were guaranteed. All data provision were monitored and used for scientific purpose only.

The inclusion criteria for the patients group were: Symptomatic patients with clinically evident CTS as diagnosed by physicians, they had typical symptoms and signs of CTS such as intermittent (nightly) numbness, tingling, or burning sensations in the thumb, index finger, middle finger, and the lateral half of the ring finger, atrophy of the thenar muscles and positive provocative tests and had pathological nerve conduction tests. As regard the control group, the included subjects were completely asymptomatic and had no symptoms or signs of CTS. No gender predilection.

Exclusion criteria were any contraindications to MRI examination as any metallic prosthesis.

All included individuals were subjected to MRI

1.5 Tesla GE (General Electric) machine (closed magnet).

Data collection

- Full history: personal history, predisposing factors (as repetitive motion or flexion of the hands or wrists, or working with vibrating tools), onset, course, and duration of current symptoms, affected side, past history of previous wrist trauma, presence of predisposing systemic diseases as rheumatoid arthritis, diabetes, thyroid disorders, kidney failure, lymphedema or other neurological disorders, any medications, or previous operations.
- Check of all previous radiological examination or investigations.

Clinical examination

At Rheumatology Department including nerve conduction studies (NCS) and needle electromyography (EMG).

Patient preparation

No specific preparation of the patient before MRI.

Patient position

The studied subjects were in head first prone position with arm up like (superman/ swimmer's position). The wrist was in small flex coil with using cushions for immobilization. A cushion was used under the chest for extra comfort. The laser beam localizer was centered over the wrist joint.

MRI protocol

The following planes were used:

- Axial: Perpendicular to wrist joint (across carpal bones), the slice covers from above carpometacarpal joint up to three slices below distal radioulnar joint.
- Coronal: Parallel to anterior radial metaphysis at distal radioulnar joint, the slice covers from dorsal to palmar.
- Sagittal: Perpendicular to anterior radial metaphysis at distal radioulnar joint, the slice covers from medial to lateral.

The following MRI pulse sequences were included:-

1. Axial, sagittal, and coronal T1-weighted fast-spin-echo sequence (T1WFSE): TR/TE = 600/30, FOV:

14*14 cm, 3 mm thickness, NEX: 2 and matrix: 320*192.

2. Axial, sagittal, and coronal T2-weighted fast-spin-echo sequence (T2WFSE): TR/TE = 2500/60, FOV: 14*14 cm, 3 mm thickness, NEX: 2 and matrix: 320*192.
3. Axial Fat suppressed axial turbo-spin echo (Spectral Attenuated Inversion Recovery) T2-SPAIR: TR/TE = 4498/70, FOV: 14*14 cm, 3 mm thickness, NEX: 2 and matrix: 320*192.
4. Proton density-weighted spin echo sequence (PD): TR/TE = 2000/30, FOV: 14*14 cm, 3 mm thickness, NEX: 2 and matrix: 320*192.
5. Short Tau inversion recovery (STIR): TR/TE = 3000/50, FOV: 14*14 cm, 3 mm thickness, NEX: 2 and matrix: 320*192.
6. Axial diffusion-weighted imaging (DWI):

    - Diffusion-weighted imaging was performed using different diffusion-sensitizing gradient strengths (denoted by b-values) that are selected by a radiologist (b-value 0, 250, 500 and 1000 s/mm^2).
    - The acquisition parameters were (TR/TE: 6000/80 ms), matrix 120 × 95, FOV as small as possible, slice thickness 4 mm, Interval 2 mm, scan time 3–6 min.
    - The acquired DW imaging data were post-processed to obtain apparent diffusion coefficient (ADC) map.

7. The apparent diffusion coefficient (ADC) maps:

    - An apparent diffusion coefficient map was generated automatically on a pixel-by-pixel or voxel-by-voxel basis using a monoexponential model on the work station.
    - The ADC values (typically expressed as $\times 10^{-3}$ mm^2/s) were calculated in an automated process on the work station.

Image analysis

- The MR images of patients and control subjects were analyzed by two radiologists with 21 and 12 years of MRI experience, blinded to the clinical data and laboratory indicators, in a standard clinical Picture Archiving and Diagnostic System workstation, and final decisions reached by consensus are reported.
- All conventional MRI sequences were analyzed for assessment of any MN signal intensity changes.
- Diffusion-weighted imaging data were analyzed using offline separate work station for assessment of any abnormal signal intensity.
- Quantitative analysis was performed to calculate apparent diffusion coefficient (ADC): two regions of interests (ROIs) were placed across the median nerve (at distal radio-ulnar joint (DRUJ) and at the level of pisiform). Apparent diffusion coefficient (ADC) of the average value was obtained.
- The data obtained from standard sequences, ADC map were compared in patients and control groups.

Statistical analysis

- Data were coded and entered using the SPSS (Statistical Package for Social Sciences) version 20 for Windows® (IBM SPSS Inc, Chicago, IL, USA).
- Data were tested for normal distribution using the Shapiro–Walk test. Qualitative data were expressed as frequencies (count) and relative frequencies (percentages). For comparing categorical data, Chi square test ($\chi 2$) was used. Quantitative data were presented as mean ± SD (Standard deviation) and range. For comparing between two independent groups of normally distributed variables (parametric data), Student's t-test (t) was used. Receiver operation characteristic (ROC) curves were constructed to assess the diagnostic sensitivity, specificity, and accuracy of ADC for CTS. Area under the curve (AUC) was used for evaluation of the diagnostic performance of the test for CTS.
- Probability (p value): p value < 0.05 was considered significant.

Results

This prospective study included 2 groups: a patients group of 33 patients with clinically diagnosed CTS and a control group of 20 healthy individuals. The ages of the patients ranged from 23 to 55 years with a mean of 40.7 ± 7.7; most of them were at the age group between 30 and 40 years (45%) and the ages of the control subjects ranged from 32 to 50 years with a mean of 39.3 ± 6.4, with no significant difference ($p = 0.624$). Sex distribution was comparable in the patients and control groups ($p = 0.770$), where females constituted 75% of the patients group and 70% of the control group.

After clinical assessment of all the studied patients ($n = 33$), unilateral affection was found in 26 patients representing 78.8%, and bilateral affection was detected in 7 patients representing 21.2%. The right side was the most frequently affected (84.8%), and the left side was affected in 36.36% of the patients. So, the examined wrists were 40 wrists in the patients group and 20 wrists in the control group.

Concerning frequency of clinical presentation in the studied patients, all of patients (100%) had pain, tingling, and numbness (unilaterally in 26 patients and bilaterally in 7 patients), while weakness of thumb abduction was present in 20 patients (60.6%), and swelling in 11 patients (33.3%). The duration of those symptoms was variable ranging from 2 to 16 months. More than one symptom was found in one patient.

In all the studied patients, nerve conduction study was performed on the affected 40 wrists. It revealed mild CTS in 2 wrists (5%), moderated CTS in 28 wrists (70%), and severe CTS in 10 wrists (25%), whereas all control subjects showed normal nerve conduction study, with a significant difference between 2 groups ($p < 0.001$) as illustrated in Table 1.

Conventional MRI explored CTS in only 10 wrists (25%). It was helpful in detecting the cause of median nerve affection in most of these cases; a ganglion cyst inside the carpal tunnel in 1 wrist, osteoarthritis in 3 wrists, postoperative fibrous soft tissue band compressing the MN in 2 wrists (Fig. 1) and wrist fracture in 1 wrist. The morphological changes detected was enlarged MN, flattening of MN, increased signal intensity of MN and flexor retinaculum bowing (Figs. 2 and 3).

Table 1 Nerve conduction study in the studied patients and control groups

	Groups				Test of significance
	Patients N = 40 wrists		Control N = 20 wrists		
	N	**%**	**N**	**%**	***p* value**
Nerve conduction study					
Mild	2	5.0	0	0.0	< 0.001*
Moderate	28	70.0	0	0.0	
Severe	10	25.0	0	0.0	
Normal	0	0.0	20	100.0	

p value: probability

*significant *p* value (< 0.05)

Other findings in the conventional MRI were as follows; Ganglion cyst in 9 wrists (22.5%), tenosynovitis and joint effusion (17.5%), autoimmune arthritis (7.5%), lipoma (5%), hematoma (2.5%), scapholunate diastasis and osteoarthritis (5%) (Fig. 4), avascular necrosis of lunate (Kienbock disease) (7.5%), triangular fibrocartilage injury (5%), and dorsal intercalated segment instability (DISI) deformity of lunate fracture (2.5%).

According to diffusion study, diffusion was restricted in median nerve in 28 wrists (70%), while it was free in 12 wrists (30%), with significant difference from control subjects ($p < 0.001$).

In the patients group, the mean ADC at the level of distal radio-ulnar joint (DRUJ) was significantly lower than that in the control group (0.93 ± 0.11 versus 1.12 ± 0.04, respectively, $p < 0.001$). At the level of pisiform, the mean ADC was higher in the patients (1.25 ± 0.15) compared to that in the controls (0.92 ± 0.07) with a significant difference ($p < 0.001$). ADC ratio also showed a significantly lower mean in the patients group than in the control group (0.76 ± 0.16 versus 1.22 ± 0.08, $p < 0.001$). Comparisons between the patients and control groups according to median nerve ADCs at the level of distal radio-ulnar joint and pisiform and ADC ratio are shown in Table 2.

Carpal tunnel syndrome was diagnosed with DWI MRI in 38 wrists; they were mild CTS (2 wrists; 5.3%), moderate CTS (26 wrists; 68.4%), or severe CTS (10 wrists; 26.3%) when correlated with the nerve conduction study.

So, out of the 40 examined wrists in the patients group, conventional MRI diagnosed 10 wrists (25%), whereas DWI MRI diagnosed 38 wrists (95%) with CTS. Regarding the final outcome of the studied patients depending on nerve conduction studies associated with positive clinical diagnosis which were accepted together as a standard reference, the sensitivity of the conventional MRI was 25% which is much lower than that of the DWI technique (95%), the specificity was 100% for both diagnostic modalities, and the accuracy of diagnosis was 62.5% for the conventional MRI compared to 97.50% and 100% for the DWI MRI and nerve conduction study, respectively, as shown in Table 3.

(See figure on next page.)

Fig. 1 **A–E** images: A 43-year-old female patient complained of right hand pain, tingling, numbness radiating to shoulder and weakness of thumb abduction. The patient underwent surgical release of flexor retinaculum 1 year ago. The complaints returned 3 months ago. By nerve conduction studies, there was severe partial axonal degeneration of right median nerve at the wrist. **A** Axial PD MR image shows soft tissue band (yellow arrow) seen at the operative bed causing flattening and compression of the median nerve at the level of carpometacarpal joint and head of metacarpal bone with subsequent proximal swelling, **B** T2-SPAIR image shows increased signal intensity of the MN (yellow arrow), **C** T2-weighted MR image shows flattening of the MN (yellow arrow) at the level of hamate, **D** ADC map shows low mean ADC value of MN at DRUJ (0.95×10^{-3} mm^2/s), and **E** ADC map shows increase of mean ADC value at pisiform (1.4×10^{-3} mm^2/s). These MRI features are consistent with recurrent carpal tunnel syndrome

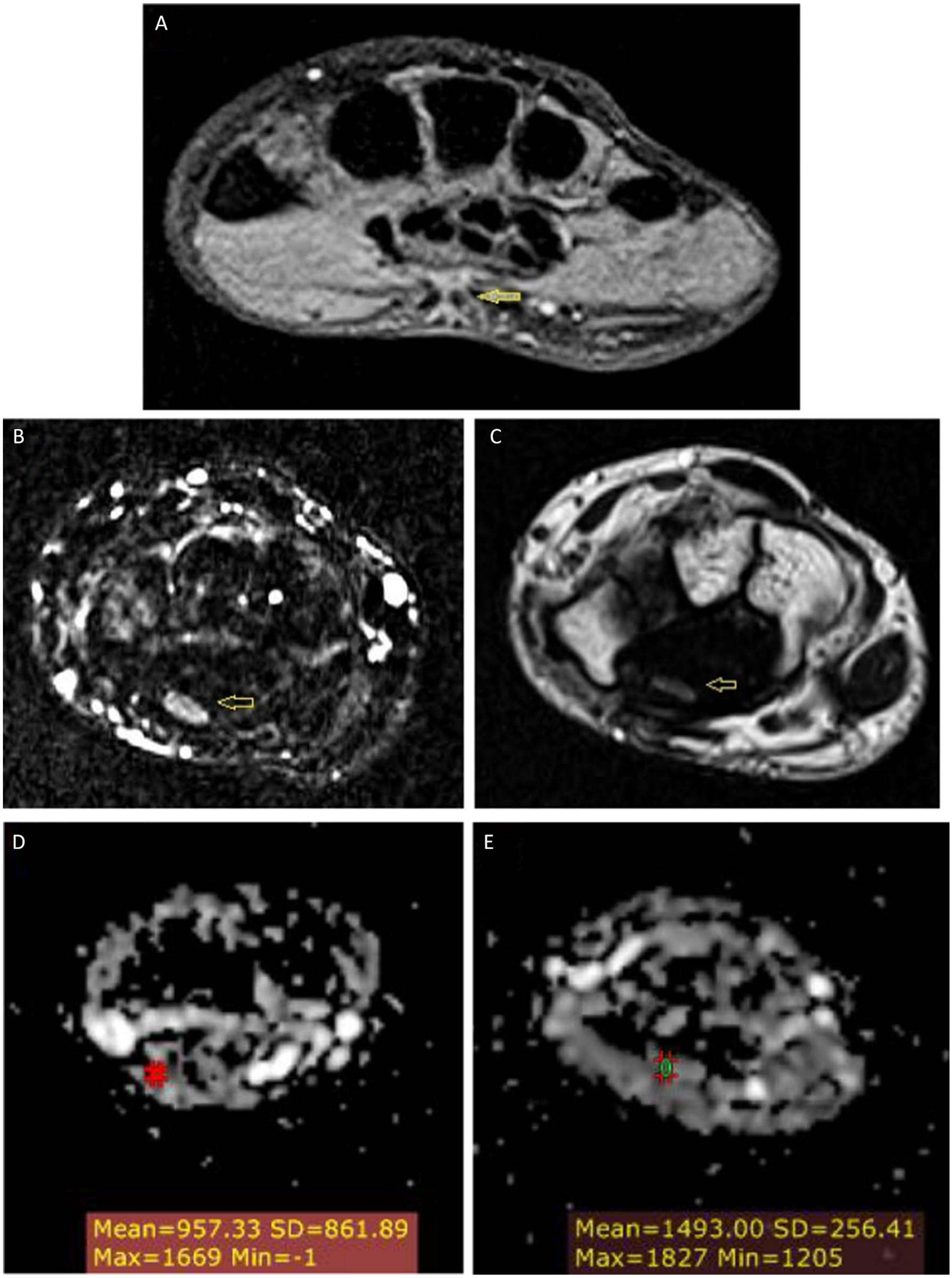

Fig. 1 (See legend on previous page.)

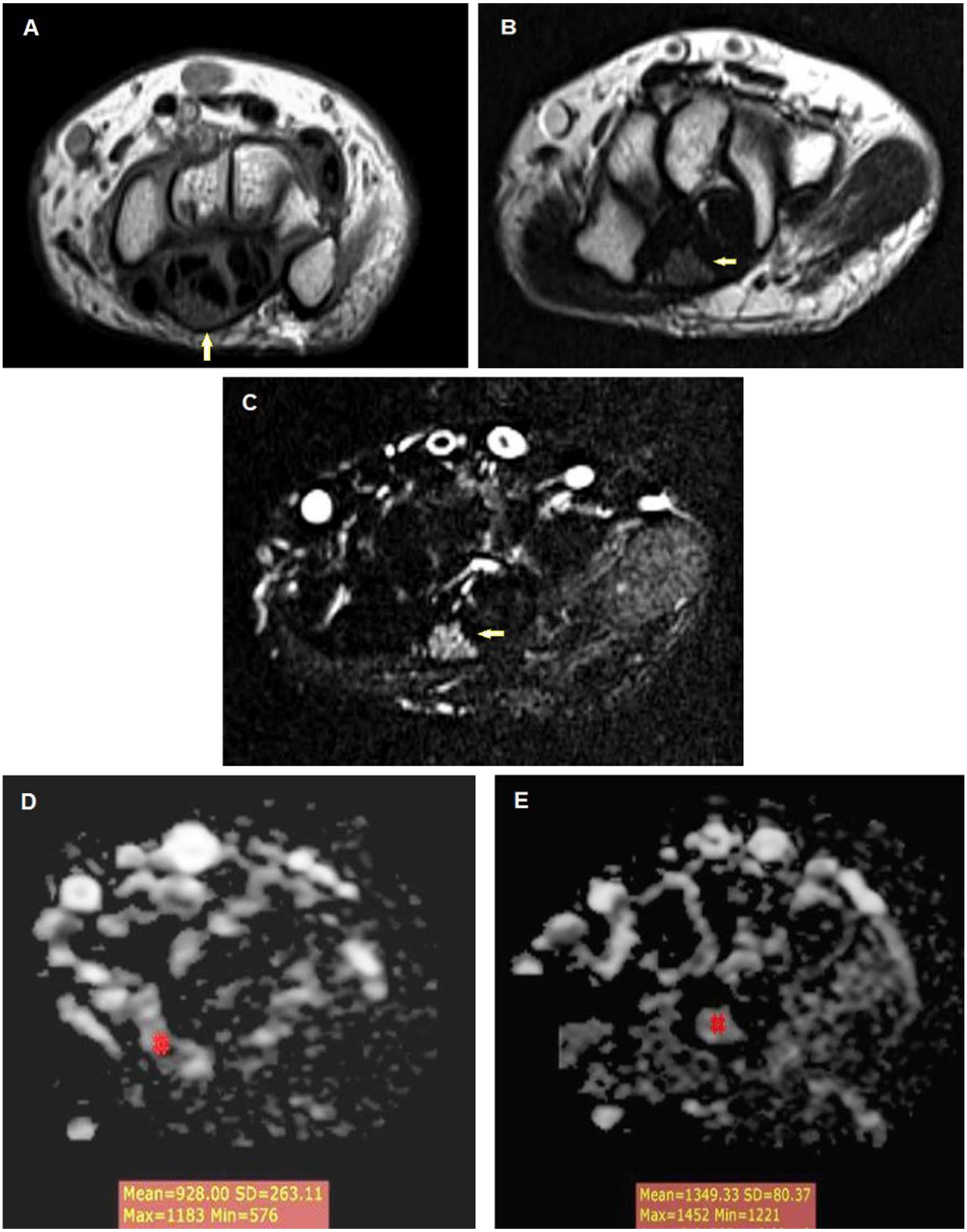

Fig. 2 **A–E** images: A 23-year-old female patient has presented with right hand pain, tingling, numbness mainly at the thumb, index and middle fingers, and radial half of the ring finger since 8 months. By nerve conduction studies, the case was diagnosed as severe carpal tunnel syndrome. **A** Axial T1, and **B** Axial T2-weighted MR images show manifest thickening of the examined median nerve with bowing of the flexor retinaculum (yellow arrows), **C** T2-SPAIR image shows increased signal intensity of the median nerve (yellow arrow), **D** ADC map showing low mean ADC value of MN at DRUJ (0.92×10^{-3} mm^2/s), and **E** ADC map showing increase of mean ADC value at pisiform (1.3×10^{-3} mm^2/s). These MRI features are consistent with carpal tunnel syndrome

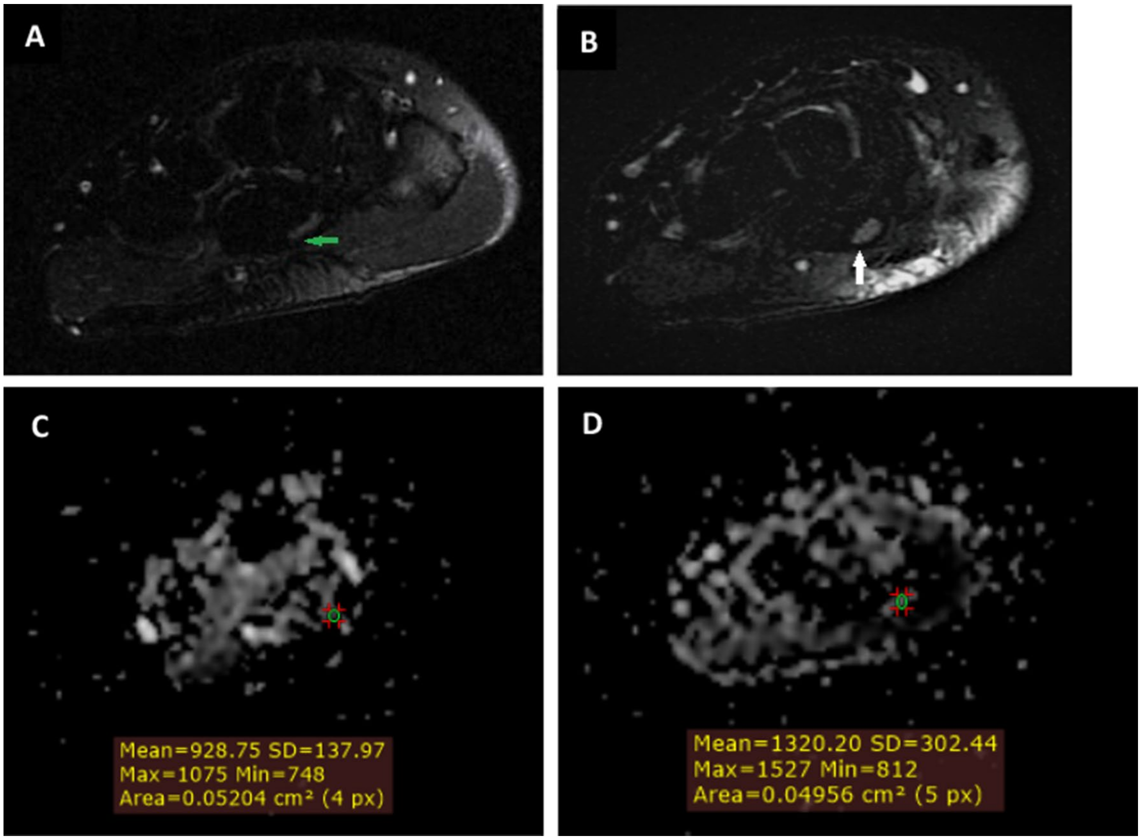

Fig. 3 **A**–**D** images: A 38-year-old female patient complained of left hand pain, tingling, numbness mainly at the thumb, index, middle finger, and radial half of the ring finger, and weakness of thumb abduction with history of wrist trauma 4 months ago. By nerve conduction studies, the case was diagnosed as severe carpal tunnel syndrome. **A**, **B** Axial T2SPAIR images showing increased signal intensity and flattening of the examined median nerve (green arrow) as well as bowing of the flexor retinaculum (white arrow), **C** ADC map showing low mean ADC value of MN at DRUJ (0.92×10^{-3} mm^2/s), and **D** ADC map showing increase of mean ADC value at pisiform (1.32×10^{-3} mm^2/s). These MRI and DWI features are consistent with carpal tunnel syndrome

According to the receiver operating characteristics (ROC) curve results for determining the diagnostic accuracy of DW-MRI for the CTS, at a cut-off ≤ 0.99, ADC obtained at DRUJ level was significantly valid for diagnosing CTS with excellent power of discrimination (AUC = 0.28) with 90% sensitivity, 100% specificity, and 93.3% accuracy. Pisiform ADC at a cut-off > 1.07 showed excellent diagnostic performance (AUC = 0.985), with 95% sensitivity, 100% specificity, and 93.3% accuracy. Moreover, ADC ratio at a cut-off ≤ 0.2 was significantly valid for CTS diagnosis with excellent power of discrimination (AUC = 1), 100% sensitivity, 100% specificity, and 100% accuracy as illustrated in Table 4 and Figs. 5, 6, 7.

Pairwise comparison of the AUCs of the three ADCs values revealed non-significant differences ($p > 0.05$) as shown in Fig. 8.

(See figure on next page.)

Fig. 4 **A**–**E** images: A 34-year-old female patient complained of right hand pain, tingling, numbness, and weakness of thumb abduction and swelling of the dorsal aspect of the wrist. By nerve conduction studies, the case was diagnosed as moderate carpal tunnel syndrome. **A** Coronal T2-weighted MR image, and **B** Coronal PD MR image show widening of scapholunate distance (green arrow) with suspected disrupted scapholunate ligament and altered signal intensity of distal segment of scaphoid bone with irregular contour with high signal in PD image denoting bone marrow edema (red arrow), **C** Axial T2-weighted MR image shows numerous separated bone fragments at intercarpal joints (yellow arrows), **D** ADC map shows low mean ADC value of MN at DRUJ (0.99×10^{-3} mm^2/s), and **E** ADC map shows increase of mean ADC value at pisiform (1.3×10^{-3} mm^2/s). Overall MRI picture is consistent with scapholunate diastasis with numerous separated bone fragments, osteoarthiritic changes of inter carpal joints. DWI features are consistent with carpal tunnel syndrome

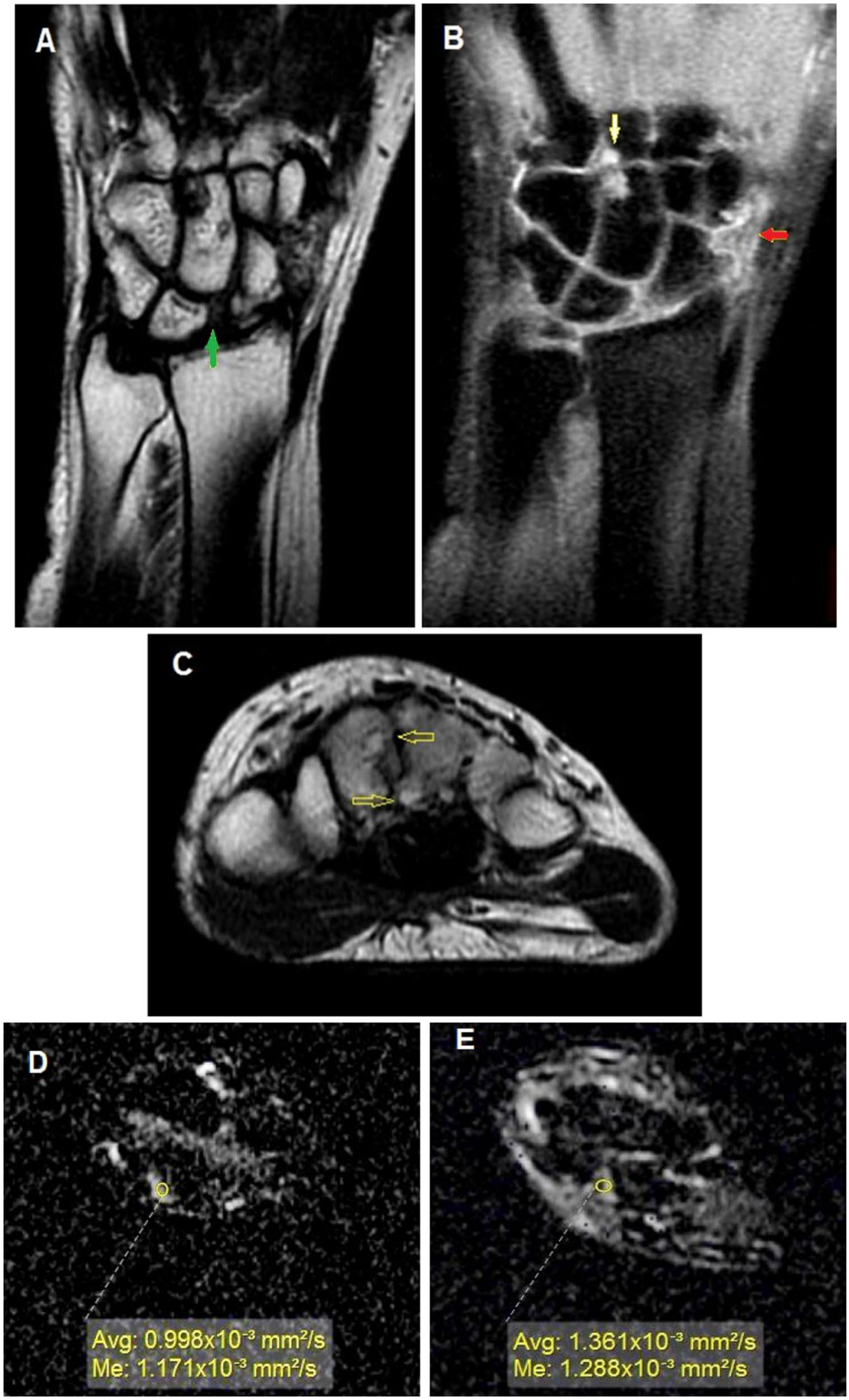

Fig. 4 (See legend on previous page.)

Table 2 Comparisons between the patients and control groups according to median nerve ADCs at the level of distal radio-ulnar joint and pisiform and ADC ratio

	Groups		*p* value
	Patients $N=40$ wrists	**Control $N=20$ wrists**	
ADC at DRUJ level			
Minimum	0.79	1.04	< 0.001*
Maximum	1.21	1.17	
Mean ± SD	0.93 ± .11	1.12 ± .04	
ADC at pisiform level			
Minimum	0.88	0.85	< 0.001*
Maximum	1.44	1.07	
Mean ± SD	1.25 ± .15	0.92 ± .07	
ADC ratio			
Minimum	0.61	1.07	< 0.001*
Maximum	1.36	1.30	
Mean ± SD	0.76 ± .16	1.22 ± .08	

DRUJ distal radio-ulnar joint

p value: probability

*significant *p* value (< 0.05)

Discussion

Carpal tunnel syndrome (CTS) occurs when the median nerve is entrapped at the level of the carpal tunnel. It is important to treat it early to avert its permanent damage; either by conservative treatment in mild stage or surgically in moderate and severe stages [6].

Diagnosis of CTS is based mainly on clinical evaluation and nerve conduction studies which lack anatomical localization. Also, musculoskeletal ultrasound results are operator dependent and discordant [7].

Magnetic Resonance Imaging (MRI) can only detect structural changes in CTS patients as median nerve enlargement, flattening, and increased signal intensity, and bowing of flexor retinaculum. However these results are inconstant, non-specific and of low sensitivity [8].

In contrary, DW-MRI is based on measurement of molecular diffusion along multiple directions in space in order to characterize micro architecture of biologic tissues. Apparent diffusion coefficient (ADC) index is used to quantify water diffusibility [9].

Table 3 Statistical analysis of diagnostic accuracy of diffusion-weighted MRI versus conventional MRI in differentiation between patients and control groups

		Patients $N=40$ wrists		**Control N = 20 wrists**		***p* value**	**Diagnostic performance**				
		N	**%**	**N**	**%**		**Sens.%**	**Spec. %**	**PPV**	**NPV**	**Accuracy %**
Conventional MRI	No	30	75.0	20	100.0	0.140	25.0	100.0	100.0	57.14	62.50
	Yes	10	25.0	0	0.0						
DWI-MRI	No	2	5.0	20	100	< 0.001*	95.0	100.0	100.0	95.24	97.50
	Yes	38	95.0	0	0.0						
Nerve conduction study	No	0	0	20	100	< 0.001*	100.0	100.0	100.0	100.0	100.0
	Yes	40	100.0	0	0.0						

Sens. sensitivity, *Spec.* specificity, *PPV* positive predictive value, *NPV* negative predictive value

p value: probability

* significant *p* value (< 0.05)

Table 4 Receiver operating characteristics (ROC) curve results for determining the diagnostic accuracy of DW-MRI using ADC values of median nerve in CTS patients

	Cut-off	**Sensitivity %**	**Specificity %**	**AUC**	**95% CI**	**Accuracy %**	***p* value**
ADC at DRUJ	≤ 0.99	89.47	100.0	0.25	0.796–0.995	93.3	< 0.001*
ADC at pisiform	> 1.07	89.47	100.0	0.983	0.854–1.00	93.3	< 0.001*
ADC ratio	≤ 0.89	100.0	100.0	1.0	0.884–1.0	100.0	< 0.001*

Pairwise comparison of AUCs of the three variables revealed non-significant differences ($p > 0.05$)

AUC area under the curve, *CI* confidence interval

p value: probability

* significant *p* value (< 0.05)

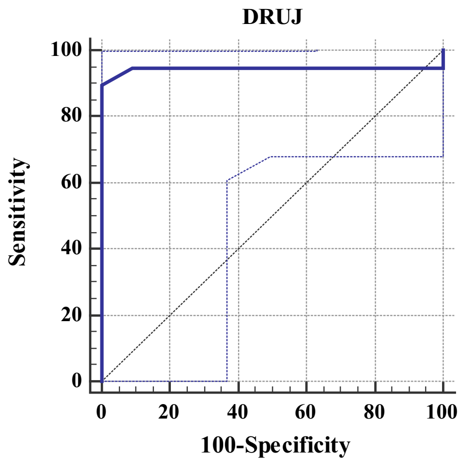

Fig. 5 ROC curve for the diagnostic performance of ADC at DRJU level

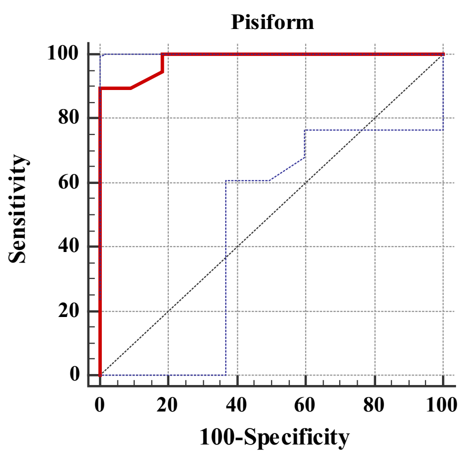

Fig. 6 ROC curve for the diagnostic performance of ADC value at pisiform level

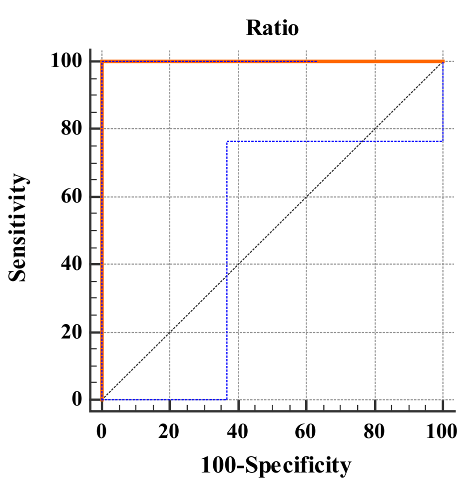

Fig. 7 ROC curve for the diagnostic performance of ADC ratio

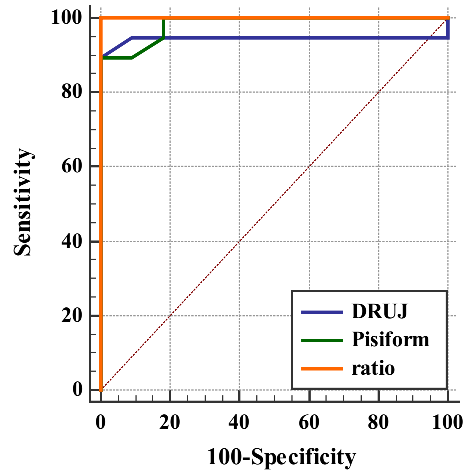

Fig. 8 Pairwise comparison of the area under the curves for DRUJ and pisiform ADCs and the ADC ratio

The aim of this work was to assess the efficacy of diffusion MRI parameters as apparent diffusion coefficient (ADC) in evaluation of median nerve (MN) in carpal tunnel syndrome (CTS).

The current study was conducted on 33 patients (40 wrists) subjected to functional diffusion MRI to assess its diagnostic accuracy in CTS. Most of the patients were at the age group (30–40) years and (40–50) years, this result matches with the fact that CTS is common at ages 45–54 years in females and 75–84 years in males [10].

Regarding sex distribution, 75% of the studied patients were females. Vo et al. [7] reported that the most common occupations of CTS patients were farmer, merchant, housewife, and teacher. Most patients were female. This result is also consistent with the observations of Dale et al. [11] who stated that CTS was predominant in women likely due to different working habits.

Matching our results, Allam et al. [2] showed that there were 14 females and 6 males in the study group, their mean age was 43.4 ± 2.95 years (range 40–47 years). Also, Wafaie et al. [1] reported in their study that 83.87% of the studied patients were females and 16.12% of them were males, and their ages ranged between 19 and 84 years with mean age of 46 years and SD of 13.65.

In the present study, we found that after clinical assessment of all the studied patients, the right side was the most frequently affected; unilaterally (63.6%) and in seat of bilateral affection (21.2%). This may be attributed to the frequent use of right hand in daily works.

Zyluk, et al. [12] reported that CTS is more strongly expressed in the dominant hand. Lewanska, et al. [13]

reported that the studied patients were diagnosed as idiopathic CTS where the right hand was affected in 20.3% of the patients, the left hand in 5.4% of them, and both hands in 74.3% of them.

The median nerve originates from the brachial plexus and is innervated by the C6, C7, C8 and T1 nerve roots**,** it enters the palm of the hand through the carpal tunnel deep to the flexor retinaculum and gives off a muscular branches to the thenar muscles and the lateral two lumbricals, then terminates by dividing into three common palmar digital nerves, which then divide into the palmar digital branches innervating the skin of the lateral side of the palm, and the palmar side of the index finger, middle finger, and one-half of the ring finger. A pressed median nerve leads to CTS causing wrist pain and problems in grasping and holding matters [14, 15]**.**

All the patients in this study had pain, tingling, and numbness, Hiltunen et al. [16] also stated that all studied patients had typical CTS symptoms such as pain, numbness and weakness, and abnormally low conduction velocities of median nerve. Klauser et al. [17] reported that all patients in their study were diagnosed as CTS clinically and by nerve conduction studies (NCS). They had the characteristic clinical symptoms of CTS as localized pain and complaint at the palmar aspect of the hand localized to the medial three and a half fingers with pain aggravation at night-time and associated numbness and tingling.

Nerve conduction studies evaluation for CTS comprises measurement of the conduction velocity across the carpal tunnel, and detection of the amplitude of sensory and motor responses. Mild CTS may not produce any nerve conduction abnormalities. Focal demyelination of the nerve occurs with increased compression resulting in local conduction block and/or slowing of motor and sensory conduction across the wrist. With more compression, the axons of the MN can be damaged, causing reduced amplitudes [18]**.**

Hiltunen et al. [16] stated that the degree of the entrapment ranged from mild to severe according to the American Association of Electrodiagnostic Medicine ratings: mild = slowing of sensory conduction velocity (< 50 m/s), moderate = slowing of sensory conduction velocity (< 50 m/s) and delayed motor distal latency (> 4 ms), and severe = absence of sensory response. In their study on 12 patients, 24 wrists were examined: 1 with severe CTS, 9 moderate, 6 mild, 4 previously operated CTS wrists, and 1 healthy wrist. Three of the 24 wrists were not analyzed due to motion artifacts.

In this study, we also classified the examined wrists according to the severity of CTS depending on NCS into mild, moderated, and severe a significant difference between two studied groups ($p < 0.001$).

There are no clinical or electrophysiological tests that could detect anatomical nerve variation in CTS which is important for operative intervention **(115)**. In our study, cMRI explored CTS in only 25% of the examined wrists by detecting the cause of MN affection as well as the morphological changes in the nerve itself.

Wafaie et al. [1] reported that MR imaging is also beneficial in demonstrating the cause of nerve compression and identification of space occupying lesions, and they found one patient with intracarpal tunnel ganglion cyst claimed to be the cause of MN entrapment. Chen et al. [19] also found 2 cases in their study with ganglion cysts causing MN entrapment.

Compared to conventional MRI, diffusion-weighted imaging (DWI) focusing on the intracellular, transcellular and extracellular molecular Brownian motion of water molecules facilitates detection of nerve microstructural and functional changes as in peripheral neuropathies. Tissues with higher cellularity, intact cell membranes, or excessive fluid distension cause decreased Brownian motion, or restricted diffusion and will display high signal, while tissues with decreased cellularity have unrestricted or increased diffusion [20]**.** In our study, diffusion study revealed restricted diffusion in 70% of the examined wrists with significant difference from control subjects ($p < 0.001$).

Bulut et al. [21] reported that there was a statistically significant difference in ADC values between the normal and mild, mild and moderate, and moderate and severe subgroups. There was significant moderate correlation between DWI parameters and CTS grades reflecting the degree of nerve compression in various grades of CTS.

We found that the mean DRJU ADC was significantly lower in the patients than in the controls. At pisiform, the mean ADC was higher in the patients than in the controls with a significant difference ($p < 0.001$). ADC ratio also was significantly lower in the patients than in controls ($p < 0.001$).

Allam et al. [2] illustrated that the mean DRJU ADC was significantly lower in the patients than in the control group (1.043 ± 0.14 versus 1.07 ± 0.04, respectively, $p = 0.29$). At pisiform, the mean ADC was higher (1.186 ± 0.1) in the patients compared to that in the control (0.982 ± 0.07), with a significant difference ($p < 0.001$). ADC ratio also showed a significantly lower mean in the patients than that in the control (0.87 ± 0.06 versus 1.1 ± 0.07, $p < 0.001$).

In a meta-analysis by Wang et al. [22], it showed that ADC was significantly higher in CTS patients ($p = 0.02$). Overall sensitivity of ADC-based diagnosis was 82.82%, and specificity was 77.83%. Taşdelen et al. [23] reported that CTS patients showed no significant difference between ADC measurements.

In Abdel Razek et al. [24] study, the mean ADC value of the median nerve in patients with CTS was more than that of controls. This may be attributed to free diffusion within the median nerve caused by occurring edema. Guggenberger et al. [25] reported that there is increased ADC significantly with age ($p = 0.001$). There was a significant difference in ADC between healthy volunteers and patients with carpal tunnel syndrome ($p = 0.001$). An ADC threshold of 1.054×10^{-3} mm^2/s might be used in the diagnosis of carpal tunnel syndrome.

Regarding the final outcome of the studied patients depending on nerve conduction studies associated with clinical presentation as a standard reference, the sensitivity of the conventional MRI was 25% which was much lower than that of the DWI technique (95%). Also, the accuracy of diagnosis was 62.5% for the conventional MRI compared to 97.50% for the DWI MRI.

Abdel Razek et al. [24], Kwon et al. [26] and Brienza et al. [27] noted a good correlation between ADC value of MN in CTS and nerve conduction study parameters. Yildirim et al. [28] added that diffusion tensor imaging parameters provide helpful information that complements clinical and electrophysiological assessments for evaluating the efficacy of non-surgical treatment of patients with CTS.

In the present study, we detected a significantly valid DRUJ ADC cut-off ≤ 0.99 for diagnosing CTS with 90% sensitivity. Pisiform ADC at a cut-off > 1.07 showed excellent diagnostic performance with 95% sensitivity. Moreover, ADC ratio at a cut-off ≤ 0.2 was significantly valid for CTS diagnosis with 100% sensitivity.

Allam et al. [2] reported an increase in the mean ADC value of the MN in CTS patients when moving from proximal to distal locations, in contrast to normal subjects, in whom the reverse occurred, and when dividing proximal value of ADC on distal value to get an ADC ratio, a cutoff value of 1 showed 100% accuracy in diagnosing CTS. They suggested a mean ADC value of 1.08×10^3 mm^2/s at the pisiform, as an optimal cutoff value to diagnose CTS with overall accuracy 86.7%. Stein et al. [29] studied the normative and pathologic diffusion values in CTS using 3 T MRI and found that ADC increased when moving from proximal to distal locations with $P = 0.001$.

Wafaie et al. [1] performed ROC curves for diffusion values between both groups to calculate their cut-off values. The threshold for mean focal ADC values was 1.19×10^{-3} mm^2/s, and for whole MN ADC were 1.23×10^{-3} mm^2/s.

On the other hand, Guggenberger et al. [25] stated that the threshold for mean focal ADC value was 1.05×10^{-3} mm^2/s. In a latter study by Kwon et al. [26], they documented that the optimal cutoff for ADC was 1.31×10^{-3} mm^2/s.

There were several limitations to our study: first, the field strength was only 1.5 T which limits signal-to-noise ratio and thus hinder acquisition of accurate data from smaller nerves. Second, only a small number of subjects were investigated in our study. A further study with a larger number of CTS patients should be conducted in the future. Another limitation was the uncomfortable patient position optimized to assess the median nerve. Finally, the use of peripheral nerve DWI was technically challenging because of susceptibility, chemical shift, and motion artifacts.

Conclusions

This study realized that diffusion-weighted MRI is a beneficial diagnostic tool in assessment of MN in cases of carpal tunnel syndrome when compared to conventional MRI. The increase in ADC value of the MN from proximal to distal locations is the most accurate feature in the diagnosis of CTS.

We recommend increasing the sample size with longer observation, and postoperative follow-up, for further inspecting the significance of diffusion indices in evaluating CTS. Other parameters should be considered, such as signal intensity ratio (SIR) and calculation of maximum cross-sectional area (CSA) for grading of its severity.

Abbreviations

ADC	Apparent diffusion coefficient
CTS	Carpal tunnel syndrome
cMRI	Conventional magnetic resonance imaging
CSA	Cross sectional area
DWI	Diffusion-weighted image
DRUJ	Distal radio-ulnar joint
EMG	Electromyography
MN	Median nerve
NCS	Nerve conduction studies
ROI	Region of interest
SIR	Signal intensity ratio

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Author contributions
All authors read and approved the final manuscript for submission. MFAA suggested the research idea, ensured the original figures and data in the work, minimized the obstacles to the team of work, correlated the study concept and design and had the major role in analysis, SE collected data in all stages of manuscript and performed data analysis. HA supervised the study with significant contribution to design the methodology, manuscript revision and preparation. MA correlated the clinical data of patient and matched it with the findings, drafted and revised the work.

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Availability of data and materials
The author's confirm that all data supporting the finding of the study are available within the article and the raw data ad data supporting the findings were generated and available at the corresponding author on request.

Declarations

Ethics approval and consent to participate
Informed written consents were taken from the patients and healthy volunteers, and the study was approved by ethical committee of Tanta university hospital, faculty of medicine. Committee's reference number: 33346/09/19.

Consent for publication
All participants included in the research gave written consent to publish the data included in the study.

Competing interests
The authors declare that they have no competing of interests.

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