Original Article

MRI Neurography Using DTI and Tractography as a Quantitative Tool in the Assessment of Median Nerve in Patients with Carpal Tunnel Syndrome

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ABSTRACT

Background: Carpal tunnel syndrome (CTS) is a typical medical problem, the affected patient can feel discomfort, tingling, and numbness in his hand. Ithappens when the nerve is compressed while passing through the wrist. It commonlyaffects obese / or pregnant patients and individualswith rheumatoid disease.

Results: In our study, we measured the cross-sectional area (CSA) (mm^2) of the nerve at the outlet and inlet of the carpal tunnel, the mean inlet and outlet were 21.92 ± 7.215, and 14.41 ± 5.051 (mm^2) respectively. Anegative correlation was reported between ADC and FA, FA was lower in CTS patients while ADC was higher in CTS patients. There was a significant difference in The FA and ADC valuesbetween Carpal tunnel patients and healthy patients. The mean FA and ADC valueswere 0.431± 0.064 and 1.237 ± 0.288 respectively. Our study recommends cut-off values for FA and ADC (0.412 and 1.049), so the sensitivity and specificity were noted to be 75% and 80% for FA and 80% and 60% for ADC respectively.

Conclusions: MRI neurography using DTI and tractography has a good diagnostic role in the evaluation of patients with CTS. It can be used as a quantitative tool together with changes in the morphology of the nerve by calculating different diffusion values (FA and ADC). Changes in the FA and ADC of the nerve along the carpal tunnel are the primary characteristics of CTS, indicating the level of nerve compression and clinical impairment.

Key Words: Carpal tunnel syndrome, diffusion tensor images, median nerve.

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INTRODUCTION

The carpal tunnel is a fibro-osseous tunnel through which the median nerve (MN) passes with the flexor tendons. The nerve is usually locatedjust ventral to the tendon of the (flexor digitorum superficialis). However, the position of the nerve may change with the movement of the wrist[1].

CTS involvesMedian nerve (MN) compression at the wrist due to microvascular compromise and MN structural changes. Compression usually occurs when the carpal tunnel is converted into a tight tunnel owing to the surroundingstiff tissue[2]. Diagnostic evaluation is based on clinical careful examination and electrophysiological testing, to determine the severity[3].

Initial studies have usedfunctional and morphological changes of MRI to evaluate MN disease not only radiological images but also Values. The Diffusion-weighted images (DWI) main purpose was to differentiate between benign and malignant lesions[4]. Recently, DTI was used as a technique depending on the initial principles of DWI, which has been used mainly for trackingfibercourses within the nervous system[5].

(DTI) helps as a good tool in the assessment of CTSby automatically estimating diffusion Measures of the nerve which can be used as a baseline value in initial diagnosis, andlaterin follow-up for evaluation of the nerve condition after treatment[6].

AIM OF THE WORK

This study aimed to evaluate the ability of Diffusion tensor images using quantitative values in the detection of entrapment of the Median nerve (MN)in cases of carpal tunnel disease.

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PATIENTS AND METHODS

In our study, (25) Twenty-fivehands of 25 patients were included; 19 females and 6 males aged from 31 to 67 years (the mean age was 53 years). Patients with All patients from the clinics of orthopedics neurology, physical medicine, and neurosurgery departments were directed to the radiology department. The study was conducted from April 2021 to May 2023. Our study included ethical approval from our institution's ethical committee with written informed consent of all patients. All the patients presented clinically with pain of thehand or wrist at the MN distribution, four of them showed wasting of the thenar muscles, while sixteen patients were suffering from hand paresthesia. History-taking, initial clinical diagnosis, and electrophysiological tests were applied to all patients. All patients with symptoms, signs, and nerve conduction studies suggestive of CTS were included in our study. Only patients with complain in one hand were included in our study. Patients with a history of hand or wrist surgery, traumatic nerve injury, fracture, or previoushistory of proximal neurologic disorders were excluded.

Caldwell Sierra Wave® (Cadwell Laboratories, Kennewick, WA, USA) was used for NCS. The nerve conduction velocity (NCV) of the MN was measured. The distal sensory latency (DSL) usedfor the median nerve (MN) was greater than 3.5 milliseconds (msec) as a cut-off point for NCSand was considered supportive of CTS.

The individuals with CTS were separated into three distinct groups according to the severity of CTS: 1st The mild group: showeda (DSL) of greaterthan 3.5 (msec) up to 4.5 (msec). 2nd the moderate grouphad a (DSL) ofgreater than 4.5 (msec) up to 5.5 (msec) and finally the severe group: had (DSL)of greater than 5.5 (msec).MRI will be performed using a 1.5T (PHILIPS) Magnet at our department of radiology.

Technique of examination

The MRI examination was conducted using a 1.5T Philips Achieva MRI system equipped with a 16-channel sensitivity-encoding head coil. The patients were scanned while lying face down, with their arms positioned alongside their heads. The back of the hand will be aligned parallel to the coronal plane of the magnet. Additionally, a (C200) circular coil will be positioned over the wrist joint and secured in place using rubber bands.Initial scout localizers were done as detailed:axial plane l, coronal plane, and sagittalplane.The echo planner sequence of DTI: single-shot spin-echo has been used with parameters as follows:TR/TE: 4,600/90, Field of view: 140 mm, Flip angle: 90°, Signals no averaged: 3, Matrix size: 128 × 128.

Diffusion weighting was performed using a b-values of (1,000 s/mm^2) in 32 different orientations. The data was acquired from 35 axial slices, each with a thickness of 4mm and no interslice gap.The total sequence lasted approximately 7 minutes and 49 seconds on average. To provide anatomical reference, the AT1WI axial sequence was acquired using parameters as follows: TR/TE: 382/20, Flip angle: 90°, Signals no averaged: 2, Field of view: 140mm. A radiologist with 10 years of experience in neuroradiology evaluated the images.

After transferring the DTI data to a computer, the process of fiber tracking was carried out utilizing the software provided by the manufacturer (PRIDE, Philips Medical Systems). At first, color-coded maps were utilized in the coronal plane to precisely pinpoint the nerve's location. Subsequently, the Circular region of interest (ROI) was positioned in the anatomical site where the MN was anticipated to be, using data from color-coded maps in coronal and axial planes.The placement of ROI was carried out at two specific levels: the distal radioulnar joint (RUJ) and one of the closest slices proximally.The precise anatomical location found on T1-W images served as a reference to validate the coded fiber locations.The anisotropy threshold was 0.3. The ROI was bigger than the nerve, yet we excluded surrounding tendons, vessels, and fat, to avoid partial volume artifacts.

The software was utilized to calculate the mean FA value and mean ADC after confirming the anatomic location of the MN tract. Focal FA values were conducted by localizing three points along the nerve tract in both axial and coronal planes on our map. One measurement was taken at the flexor retinaculum level, while the remaining measurements were taken at the wrist level and forearm level. FA was measured at the wrist level by recording from the nerve at the junctions of the tendons of the palmaris longus and flexor digitorum. At the forearm level, the measurement was taken 5 cm proximal to the flexor retinaculum, specifically in the center of the muscle of the flexor digitorum. During the measurements, (ROIs) smaller than the nerve was chosen to avoid partial volume effects. The Statistical Analysis was conducted using the software SPSS 11.0.

Statistical Analysis

The information was collected, revised, encoded, and inputted into version 28 of the IBM Statistical Package

for the Social Sciences (SPSS). The data were described using the mean, median, standard deviations, interquartile range, and ranges. Likewise, qualitative characteristics were reported in numbers and percentages. The normality of the data was detected using the Shapiro–Wilk test. A one-sample t-test was employed to compare the study group with parametric distribution and quantitative data. The correlation between two normally distributed numerical variables was detected using Pearson Correlation the ROC curve analysis was used to detect the specificity and sensitivity.The confidence level was established at 95%, with a margin of error of 5% being deemed acceptable. Consequently, the *p-value* was deemed statistically significant: In statistical analysis, a *p-value* greater than 0.05 indicates non-significance, a *p-value* less than 0.05 indicates significance and a *p-value* less than 0.01 indicates high significance.

RESULTS

In our study Twenty-five hands of 25 patients were included; 19 females and 6 males with a range of ages starting from 31 to 67 years (mean 53 years). Only one hand of the patient was included in our study.In the studied patients, we found that there was pain, paresthesia, and wasting of the thenar muscles (in 100%,96%, and 12% respectively). Diabetics and rheumatic arthritis patients were found in 24% and 8% of cases respectively).

Regarding the severity of the symptoms by (NCS) in the studied patients, we found that symptoms were mild in 20 %, moderate in 64 %, and severe in 16 % of the cases.

Regarding the Cross-sectional area (CSA) in(mm^2) in the studied patients, we found that the mean inlet and outlet CSA were 21.92 ± 7.215, and 14.41 ± 5.051 respectively (Table 1).

Table 1: Cross-sectional area (CSA) (mm^2).

inlet	Mean ± SD	21.92 ± 7.215
	Median (IQR)	22.30 (11.1)
	Range	8 – 34.6
outlet	Mean ± SD	14.41 ± 5.051
	Median (IQR)	14.0 (7.4)
	Range	7 – 25.6

Regarding the T2 Weighted images (MRI sequence) in the studied patients, we found that increased T2 signal, bowing of capsule, thickening at the inlet, and flattening at the outlet was noted in (100% for all), increased CS diameter was seen in (92%) and edema in (28%) of the cases (Table 2).

Table 2: T2 Weighted images (MRI sequence).

		Number	percentage
increased t2 signal	No	0	0%
	Yes	25	100.0%
increased CS diameter	No	2	8.0%
	Yes	23	92.0%
Bowing of capsule	No	0	0%
	Yes	25	100.0%
thickening at inlet	No	0	0%
	Yes	25	100.0%
flatening at outlet	No	0	0%
	Yes	25	100.0%
edema	No	18	72.0%
	Yes	7	28.0%

In our study, therecorded mean FA and mean ADC measurementswere 0.431± 0.064 and 1.237 ± 0.288respectively. (Table 3,4). (Figure 1,2,3,) In our study,we recommend cutoff values for FA and ADC to be (0.412 and 1.049), so the sensitivity and specificity were noted to be 75% and 80% for FA and 80% and 60% for ADC respectively. (Table 5, Figure 4). However using the cut-offthreshold of (0.47 for FA and 1.045 for ADC) the sensitivity and specificity of FA were (20%, and 70% respectively) and for ADC were (40%, and 25%/ respectively) (Table 6). Thenegative correlation between FA and ADC was not statistically significant according to (*P-value* 0.189). (Table7).

Table 3: Fractional anisotropy (FA) and apparent diffusion coefficient (ADC).

FA	Mean ± SD	0.431 ± 0.064
	Median (IQR)	0.433 (0.099)
	Range	0.305 – 0.553
ADC	Mean ± SD	1.237 ± 0.288
	Median (IQR)	1.274 (0.502)
	Range	0.664 – 1.735

Table 4: FA and ADC comparison.

	Mean ± SD	**Mean cutoff**	**Test value**	***P-value***	**Sig.**
FA	0.431 ± 0.064	0.47	-3.097**	0.005	HS
ADC	1.237 ± 0.288	1.054	3.169**	0.004	HS

P-value; *P-value*< 0.01: highly significant (HS)**; calculated by One-Sample t-test.

Table 5: FA and ADC ROC curve (the recommended cutoff).

	AUC	*P-value*	95% CI		cutoff	sensitivity	specificity
			Lower Bound	Upper Bound			
FA	0.710	0.154	0.396	1.000	0.412	75 %	80 %
ADC	0.700	0.174	0.453	0.947	1.049	80 %	60 %

AUC= area under the curve; CI= confidence interval; *P-value* calculated by ROC analysis.

Table 6: FA and ADC ROC curve.

	AUC	*P-value*	95% CI		cutoff	sensitivity	specificity
			Lower Bound	Upper Bound			
FA	0.710	0.154	0.396	1.000	0.470	30 %	80 %
ADC	0.700	0.174	0.453	0.947	1.054	75 %	60 %

AUC= area under the curve; CI= confidence interval; *P-value* calculated by ROC analysis.

Table 7: Correlation between FA and ADC.

	Pearson Correlation	*P-value*
FA	-0.271	0.189
ADC		

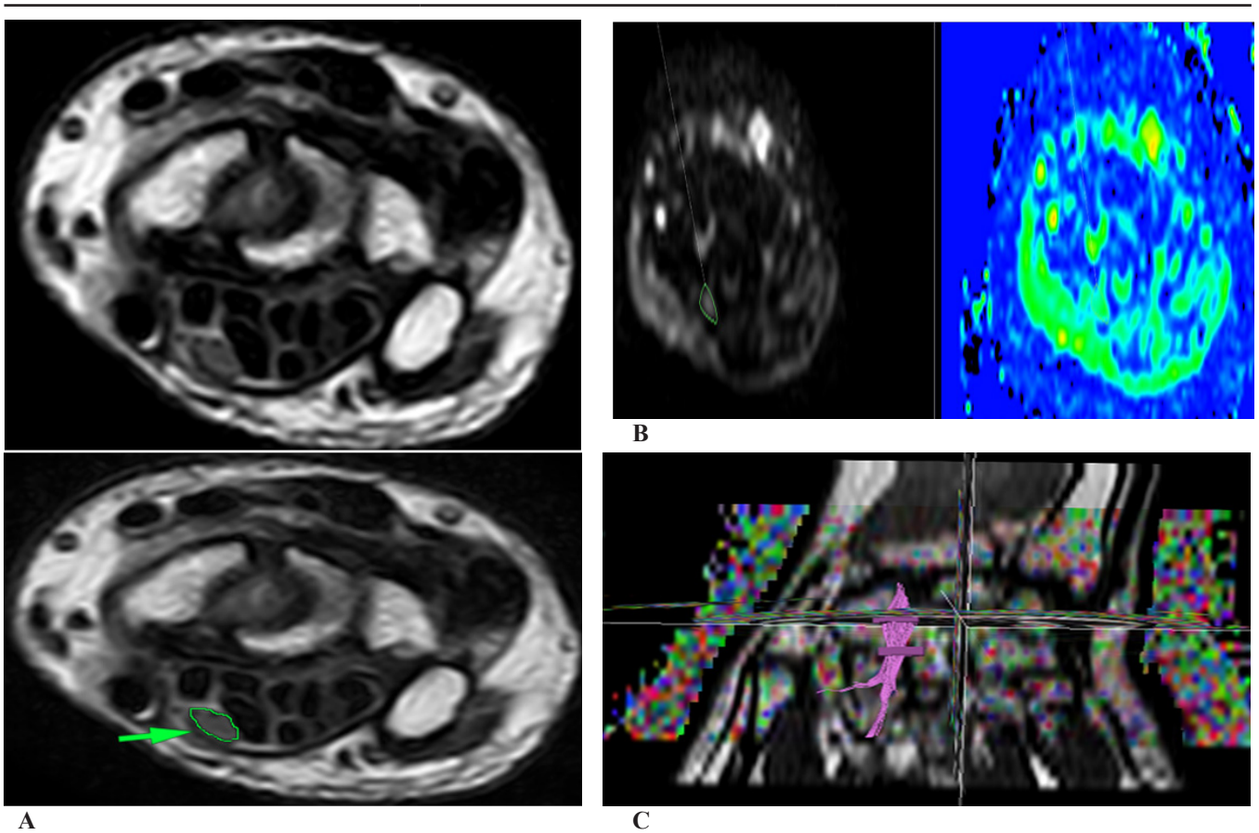

Fig. 1: A 65-year-old female with right-hand pain and paresthesia. The NCS showed right moderate CTS. The MRI examination showed: **A:** T2 axial weighted images revealed increased T2 signal, increased CS diameter, bowing of capsule, thickening at the inlet, flattening at the outlet, and mild surrounding edema. **B:** DWI and DTI revealed the right median nerve CSAof 22.3 mm2 at the pisiformlevel and 8.14 mm2 at the hook of the Hamate level. **C:** MRN revealed FA: 0.481 ± 0.156 and ADC: 1.055 ± 0.336.

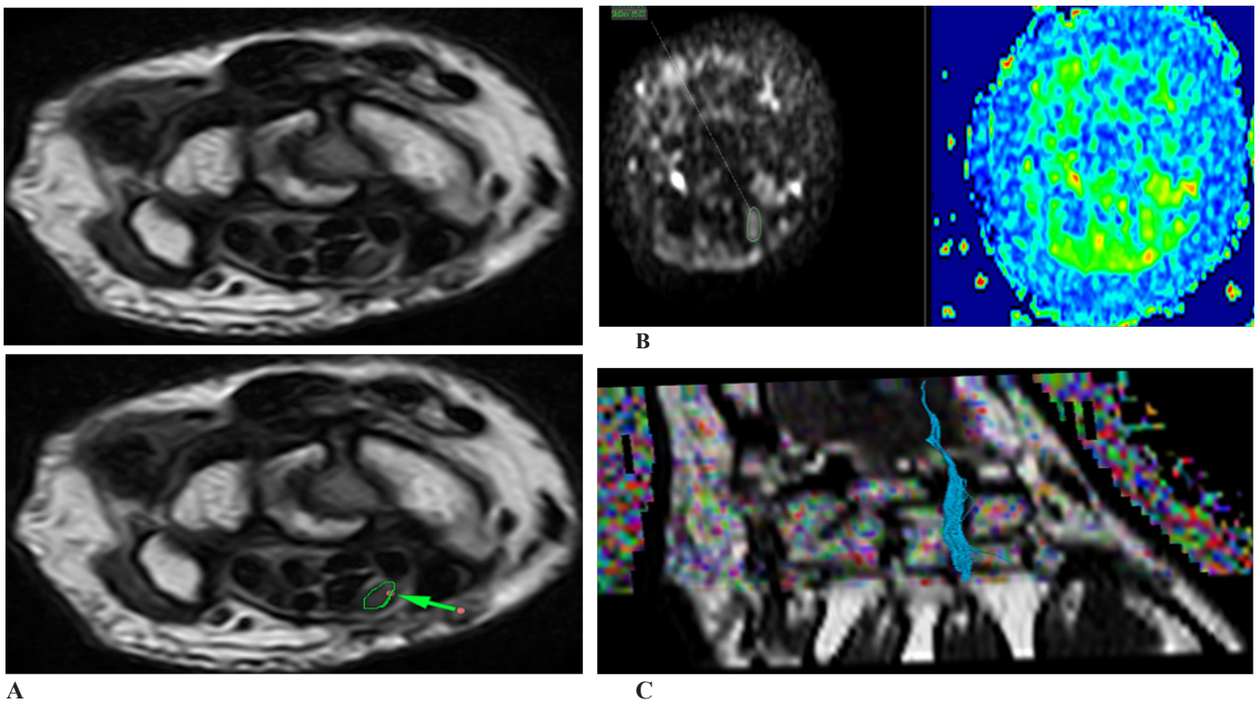

Fig. 2: A 65-year-old female with left hand pain, and paresthesia. The NCS showed left moderate CTS. MRI examination showed: **A:** T2 axial weighted images revealed increased T2 signal, increased CS diameter, bowing of capsule, thickening at the inlet, flattening at the outlet, and mild surrounding edema. **B:** DWI and DTI revealed a left MN (CSA) of 26.5mm2 atthe pisiform level and 21.8mm2 at the hook of Hamate. **C:** MRN revealed FA: 0.401± 0.165 and ADC: 1.057± 0.362.

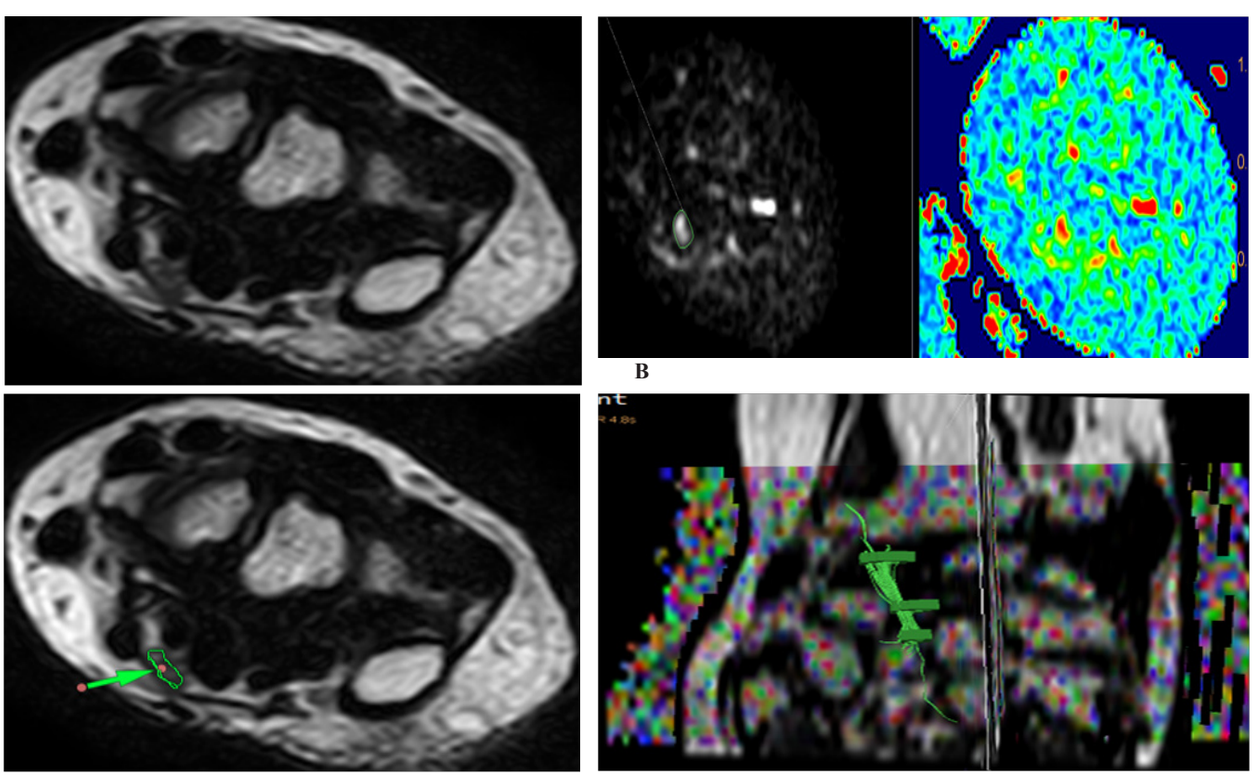

Fig. 3: A 40-year-old female patient withright-hand tingling and pain sensation at the distal end of fingers. The NCS showed right moderate CTS. MRI examination showed: **A:** T2 axial weighted images revealed increased T2 signal, increased CS diameter, bowing of capsule, thickening at the inlet, flattening at the outlet, and no surrounding edema. **B:** DWI and DTI revealed the right MN (CSA)of 28.4 mm2 at the level of the pisiform and 18.3 mm2 at the hook of the Hamate level. **C:** MRN revealed FA: 0.420 ± 0.188 and ADC: 0.943 ± 0.401.

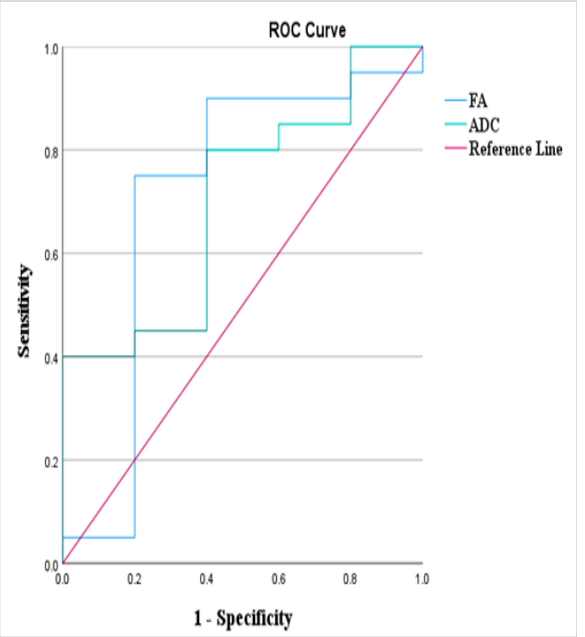

Fig. 4: ROC curve of FA and ADC variables.

DISCUSSION

Approximately 4% to 5% of the global populationare affected by carpal tunnel syndrome. The elderly, specifically those aged between 40 and 60 years, are the most susceptible group (2). Carpal tunnel syndrome accounts for 90% of all reported entrapment neuropathies[7].

Electrophysiological testing and clinical examination are the main methods to establish diagnosis. However,MR neurographygives important information about the different diffusion values (FA, ADC) of the nerve and makes the diagnosis of carpal tunnel disease of high confidence[8].

The research was conducted on a group of 25 individuals who had been diagnosed with CTSand referred from physical medicine, neurology, and orthopedic clinics at Ain Shams University. The mean age of patients was53.56± 10.92 which was supported by ***Yang et al***.[9] and ***Becker et al***. as well[10].

The female gender was more affected than males (76%, and 24% respectively).These findings were corroborated by the research conducted by. ***Kurtul et al***.[11], ***Yang et al***.[9], ***Kokubo et al***.[12] and ***Becker et al***. as well[10].

Regarding the clinical picture in the studied patients, we found that there was pain, paresthesia, and wasting of the thenar muscles (in 100%,96%, and 12% respectively). Diabetics and rheumatic arthritis patients were found in 24% and 8% respectively). In contrast, ***Yang et al***.[9], reported that CTS was found to be mostly linked with old wrist injuries, gout, and rheumatoid arthritis. ***Becker et al***., as well, reported that DM was more frequent in patients with CTS[10].

In our research, we documented that the manifestations of NCS were mild in 20 % of cases, moderate in 64 %, and severe in 16 %. However, according to the findings of ***Kurtul et al***., the symptoms were categorized as mild in 43% of cases, moderate in 24.5% of cases, severe in 5.3% of cases, and very severe in 1.3% of cases., yet this study included much more casesas the included cases were (151 people)[11].

We reported that the mean inlet and outlet (CSA) of the MN was 21.92 ± 7.215(mm^2), and 14.41 ± 5.051 (mm^2) respectively. ***Saglam et al***.[13], as well, reported that the mean values of CSA measured proximally were 16.4 ± 4.5 mm^2 and the mean values of CSA measured distally were 13.6 ± 3.7 mm^2 respectively. A comparable result was reported by ***Klauser et al***. With mean CSA (19.9 mm^2) measured through the whole nerve segment[15].

To our knowledge DTI for carpal tunnel disease is still under research and few studies we conducted, most of them were done for pre and postoperative evaluation.We reported that the meanvalue of FA and the mean value of ADC were 0.431± 0.064 and 1.237± 0.288 respectively. ***Cingozet al***.[16], showed comparable resultswith mean FA value (0.382; IQR 0.330-0.495) and higher ADC values (1.509 mm^2/s; IQR 1.374-1.733 mm^2/s). In a study conducted by ***Guggenberger et al***.[17]: it was found that the mean value of (FA) value was 0.63 with (SD ± 0.1), while the mean value of (ADC) value was lower at 0.999 × 10(-3) mm (2)/s with (SD ± 0.134 × 10(-3)), yet the study was done on 3T MRI machine.Also,A higher mean FA (0.524) was reported by ***Klauser et al***.[14].

Wereportedthat the FA cutoffpointof (0.47) demonstrated asensitivity of 30 % with a specificity of 80% andusing ADC with a cutoff point (of 1.054) revealed a sensitivity of 75 % with a specificity of 60%. However, using cutoff values (0.412 and 1.049) for FA and ADC, the estimated sensitivity and later specificity werenoted to be 75% and 80% for FA and 80% and 60% respectively for ADC. These findings closely resembled the research conducted by ***Razek et al***. in 2017, in which the thresholds for distinguishing mild from moderate CTS were 0.42 and 1.35 × 10-3 mm^2/s, respectively. ***Vo et al***.[18] found similar outcomes in their research, where they observed that patients with CTS exhibited significantly reduced

FA values, with a threshold of 0.45, and ADC values of 1.31 × 10-3 mm^2/s. These measurements were taken at the carpal outlet and demonstrated a sensitivity of 90%, specificity of 84.6%, and accuracy of 92.1%[19].

In their study, ***Bulut et al***.[20] employed a higher threshold of 0.532 for FA, resulting in a greater sensitivity value of 94.4% and higher specificity of 70.8%, while ***Guggenberger et al***.[21] reported a comparablecut-off value to our studyfor FA (0.47)with highersensitivity (83.0%) but lower specificity (67.0%). ***Koh et al***. 2014 Also reported a highercut-offpoint for FA (0.536) with lower sensitivity and lower specificity (73.8% and 76.2 %respectively). ***Kwon et al***.[22] reported a comparablecut-offpoint for FA (0.44) witha lessersensitivity value of 72.0% buta higherspecificity value of 82.0%.1[23].

Limitations: The limited sample size and prospective study design were the primary limitations of the current study. To enhance the understanding of the potential benefits of these indices in evaluating CTS, it is advisable to conduct a larger study with an extended observation period, particularly including postoperative follow-up. Another limitation was using a 1.5 T MRI.Moreover, diffusion tensor imaging has technical challenges, and the quality depends on variable factors such as the homogeneity of the used field, the used coil, and the applied gradient systems.Lastly, the accurate calculation of FA and ADC values relies on the precise placement of the (ROI) within the median nerve by the operator, which may be subject to variability between different observers and even within the same observer.

CONCLUSIONS

In conclusion, DTI using FA and ADC can be used as a quantitative rolein the assessment of median nerve entrapment with high sensitivity and specificity.Changes in the FA and ADC of the nerve along the carpal tunnel are the primary characteristics of CTS, indicating the level of nerve compression and clinical impairment. Further studies are recommended for the evaluation of the median nerve after treatment using initial DTI values as the baseline for evaluation.

LIST OF ABBREVIATIONS

CTS: Carpal tunnel syndrome.

MN: median nerve.

AUC: Area under the curve.

MRI: Magnetic resonance imaging.

ROC: Receiver operating curve.

DTI: Diffusion tensor imaging.

NCS: Nerve conduction studies.

ROIs: regions of interest.

NCV: Nerve conduction velocity.

CSA: Cross-sectional area.

MRN: magnetic resonance neurography.

FA: fractional anisotropy.

DSL: distal sensory latency.

ADC: and apparent diffusion coefficient.

DECLARATIONS

Ethics approval and consent to participate

This study wasapproved by the Research Ethics Committee of the Faculty of Medicine at Ain Shams University in Egypt inApril 2021; Reference Number of approval: FMASU M S 204/2021., FWA 000017585. All participants included in this study gave written informed consent in this research. If any patient was unconscious at the study time, written consent for their participation was given by their own legal guardian.

CONSENT FOR PUBLICATION

All individuals involved in this study have provided written informed consent to publish all the data encompassed within this research. In cases where the patient was unable to provide consent due to unconsciousness, their legal guardian granted written informed consent for the publication of all the data.

Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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AUTHORS CONTRIBUTIONS

- Suggest and develop the research idea, Data collection, and analysis, share in statistical analysis, share in manuscript writing, revise and editing, Prepare MRI cases and perform required measurements, prepare figures and tables.
- SB,KS: Data collection and analysis, reviewing the literature, performing statistical analysis, sharing in manuscript writing, Preparing MRI cases.

All authors read and approved the final manuscript.

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Not applicable.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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التصوير العصبي بالرنين المغناطيسي باستخدام DTI وتصوير المسار كأداة كمية في تقييم العصب المتوسط لدى المرضى الذين يعانون من متلازمة النفق الرسغي

مى مختار كمال محمود بركات، سوزان بهيج و كارين نسيم

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الخلفية: متلازمة النفق الرسغي (CTS) هي مشكلة طبية نموذجية، يمكن للمريض المصاب أن يشعر بعدم الراحة، والوخز، والخدر في يده. ويحدث ذلك عندما يتم ضغط العصب أثناء مروره عبر الرسغ. وهو يؤثر عادة على المرضى الذين يعانون من السمنة المفرطة والمرضى الذين يعانون من أمراض الحمل والروماتويد.

النتائج: في دراستنا، قمنا بقياس مساحة المقطع العرضي (CSA) (مم^٢) للعصب عند مخرج ومدخل النفق الرسغي، وكان متوسط المدخلوالمخرج ٢١,٩٢ ± ٧,٢١٥، و١٤,٤١ ± ٥,٠٥١ (مم) ^ ٢) على التوالي. تم الإبلاغ عن وجودعلاقة سلبية بين ADC و FA، وكان FA أقل في مرضى CTS بينما كان ADC أعلى في مرضى CTS. كان هناك اختلاف كبير في قيم FA وADC بين مرضى النفق الرسغي والمرضى الأصحاء. كان متوسط قيمFAو ADC ٠,٤٣١ ± ٠,٠٦٤ و ٠,٤٣١ ± ٠,٠٦٤ على التوالي. توصي دراستنا بقيم قطعية لـ FA وADC (٠,٤١٢ و١,٠٤٩)، لذلك لوحظ أن الحساسية والنوعية تبلغ ٧٥٪ و٨٠٪ لـ FA و٨٠٪ و٦٠٪ لـ ADC على التوالي.

الاستنتاجات: التصوير العصبي بالرنين المغناطيسي باستخدام DTI وتصوير المسار له دور تشخيصي كبير في تقييم المرضى الذين يعانون من CTS. ويمكن استخدامه كأداة كمية جنبا إلى جنب مع التغيرات في مورفولوجيا العصب عن طريق حساب قيم الانتشار المختلفة (FA وADC). تعد التغيرات في FA وADC للعصب على طول النفق الرسغي هي الخصائص الأساسية لمتلازمة النفق الرسغي، مما يشير إلى مستوى ضغط العصب والضعف السريري.