

*Original Article*

# MRI of wrist and diffusion tensor imaging of the median nerve in patients with carpal tunnel syndrome

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**Objectives:** Diagnosis of carpal tunnel syndrome (CTS) is based on the clinical symptoms and nerve conduction study. Magnetic resonance imaging (MRI) is non-invasive objective tool for assessing the median nerve and carpal tunnel. The purpose of this study was to evaluate MRI changes in patients with CTS, and compare them with healthy subjects.

**Materials and Methods:** Forty-three CTS patients and 43 age matched control were included and scanned in a 3T MRI scanner. Cross-sectional areas (CSA) of median nerve were measured at the level of distal radio-ulnar joint level (CSA1), proximal row of carpal bone (CSA2), and hook of hamate (CSA3). Flattening ratio (FR) of median nerve, thickness of flexor retinaculum, median nerve signal intensity, and thenar muscles were assessed. Fractional anisotropy (FA), average diffusion coefficient (ADC), and radial diffusivity (RD) of median nerve of CTS patients were obtained from diffusion tensor imaging (DTI) and compared with those of controls.

**Results:** Thirty-three patients (76.7%) were female. Mean duration of the pain was  $7.4 \pm 2.6$  months. The mean CSA1 ( $13.2 \pm 4.2$  mm<sup>2</sup>), CSA2 ( $12.5 \pm 3.5$  mm<sup>2</sup>), and CSA3 ( $9.2 \pm 1.5$  mm<sup>2</sup>) in CTS patients were significantly higher compared to control group: CSA1 ( $10.15 \pm 1.64$  mm<sup>2</sup>), CSA2 ( $9.38 \pm 1.37$  mm<sup>2</sup>), and CSA3 ( $8.4 \pm 0.9$  mm<sup>2</sup>), ( $P = 0.001$  in all). The mean FR of median nerve and thickness of flexor retinaculum were increased in CTS patients. The mean FA was reduced in CTS patients compared to control proximal to carpal tunnel and within the tunnel. Mean ADC and RD values were higher in CTS patients as compared to control for both levels.

**Conclusion:** MRI can detect subtle changes in the median nerve and thenar muscles in CTS and may be useful in equivocal cases and to exclude secondary causes of CTS. DTI shows reduced FA and increased ADC and RD in CTS patients.

**Keywords:** Median nerve, Carpal tunnel syndrome, Flattening ratio, Diffusion tensor imaging, Fractional anisotropy

**INTRODUCTION**

Carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy due to compression of median nerve within the carpal tunnel at the wrist. CTS is common in females with an estimated prevalence of 6.8%. Increased prevalence is also seen with advancing age, obesity, and occupation with strenuous physical and repetitive tasks. CTS commonly involves the dominant hand, but can be bilateral.<sup>[1-3]</sup>

Diagnosis is based on the clinical history and symptoms of pain, numbness, tingling, and burning sensation in the hand, exaggerated by sleep and repetitive movement of the wrist. Nerve conduction studies (NCSs) are highly specific but may not be confirmatory. It has also a substantial rate of false positives in normal asymptomatic individuals.<sup>[4]</sup> Imaging modalities as ultrasound and magnetic resonance imaging (MRI) are used as alternative screening as well as diagnostic tools. MRI with diffusion tensor imaging (DTI) serves as a

reliable, non-invasive and objective tool for assessing the median nerve and carpal tunnel.<sup>[5]</sup> MRI has high spatial resolution, can detect abnormality in the median nerve and adjacent structures and rule out secondary causes of CTS. The purpose of this study was to evaluate MRI changes in patients with CTS, and compare them with healthy subjects.

**MATERIALS AND METHODS**

This is a cross-sectional study carried out in a tertiary care center after getting approval from Institutional ethics committee. A total 43 patients who were diagnosed as CTS by clinical symptoms and electrophysiological study and 43 controls were included ( $Z = 1.96$  for 95% confidence interval, assuming power 80%). The electrophysiological tests used were palm-wrist latency difference  $>0.4$  ms (sensory) (sensitivity 96%) and 2<sup>nd</sup> lumbrical-interossei difference  $>0.6$  ms (motor) (specificity 96.4%); the affected hand was

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Received: 21 November 2022 Accepted: 25 February 2023 EPub Ahead of Print: 16 March 2023 Published: 03 May 2023 DOI: 10.25259/JNRP\_57\_2022

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diagnosed electrophysiologically CTS if both the tests are positive.<sup>[6]</sup> All the patients and controls underwent MRI in a 3T MRI scanner after obtaining written informed consent. Patients, less than 18 years, previous wrist surgery or injury, clinical suspicion of cervical spondylosis, brachial plexopathy, and tumoral causes, were excluded from the study.

### MRI protocol

MRI of wrist was done in 3T MRI (Discovery 750 w, GE Healthcare) using a 16-channel flex coil with the following parameters. Axial T1W (TR-633.0, TE-9.4, NEX-2), axial T2WI (TR-4322.0, TE-85.0, NEX-1), coronal and axial proton density fat suppressed (PDFS) (TR-4847, TE-30, NEX-2), and short tau inversion recovery coronal (TR-4886, TE-50 ms, NEX-2) were acquired with 3 mm slice thickness and 0.5 interslice gap. 3D T1WI MR sequence of the wrist was also acquired. A single-shot spin-echo echo-planar DTI sequence was done in axial plane with TR-8993 and TE-9.4 ms, slice thickness: 4 mm with no gap, "b" value of 0 and 1000 s/mm<sup>2</sup> applied in 30 directions.

### Image interpretation

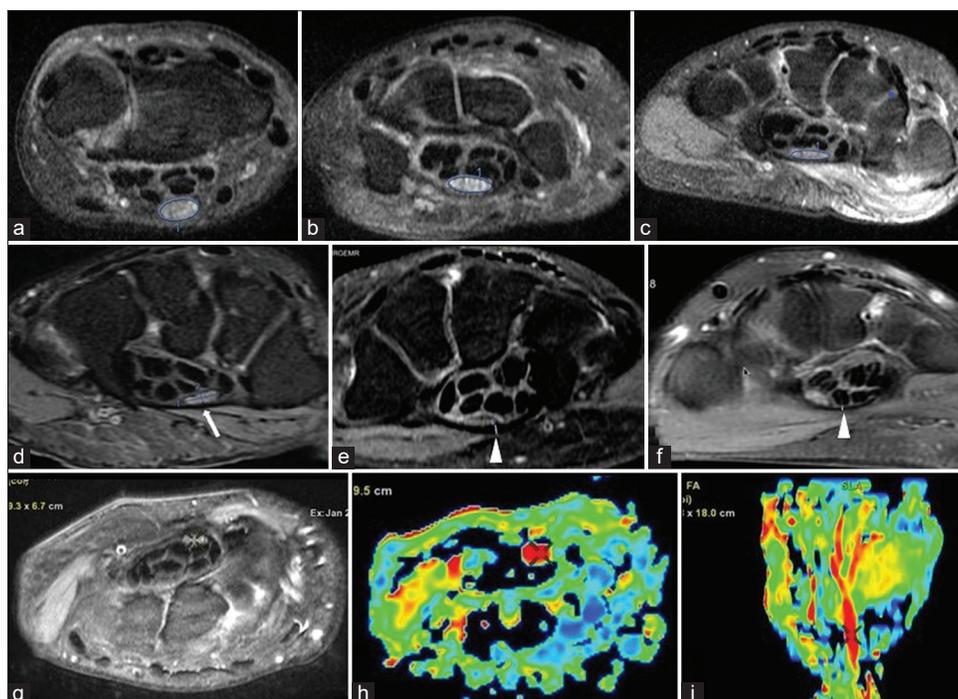
Image analysis and post processing were done in AWS system. Two radiologists of more than 12 years' experience

interpreted the MRI findings. In case of interobserver variation, conclusion was taken in consensus. Structural changes of the median nerve were assessed in T1W, T2W, and PDFS sequences, median nerve measurements were taken from axial PDFS images. Fractional anisotropy (FA), Average diffusion coefficient (ADC), and Radial diffusivity (RD) were obtained from the DTI images after post processing. Median nerve signal intensity was assessed by visual inspection, in comparison with the adjacent muscles.

Cross-sectional areas (CSA) of median nerve were measured at three different anatomical levels in axial PDFS sequence. CSA proximal to the tunnel (CSA1) was measured at distal radio-ulnar joint level. CSA at tunnel inlet (CSA2) was measured at the level of proximal row of carpal bone. CSA at tunnel outlet (CSA3) was measured at the level of hook of hamate bone [Figure 1].

Long axis and short axis of median nerve were measured at the level of tunnel outlet, and flattening ratio (FR) was obtained by dividing long axis diameter by the short axis diameter [Figure 1].

Thenar muscles bulk and signal intensity were assessed. Thickness of flexor retinaculum was measured at the level of hook of hamate in axial images.



**Figure 1:** Axial PDFS image of wrist showing CSA of median nerve in a 52-year-old female proximal to carpal tunnel (a), within the tunnel (b), and at the outlet (c). Note the nerve appears enlarged proximal to carpal tunnel and flattened at the outlet. Axial PDFS in another CTS patient having flattening ratio of median nerve 3.17, obtained by dividing long axis to short axis at the level of hook of hamate (d). Axial PDFS of wrist showing thicker flexor retinaculum (arrowheads) in a CTS patient (e), compared to control (f). Axial PDFS image (g), axial, (h) and coronal colored FA map derived from DTI (i) showing cursor in median nerve. CSA: Cross-sectional areas, PDFS: Proton density fat suppressed, CTS: Carpal tunnel syndrome, FA: Fractional anisotropy, DTI: Diffusion tensor imaging.

FA, ADC, and RD were obtained from DTI raw data using dedicated vendor-specific software. Manual region of interest (ROI) of size 2–4 mm<sup>2</sup> was drawn at the center of the median nerve on the FA image at two different anatomic locations, that is, proximal to the carpal tunnel (at the levels of the distal radioulnar joint) and within the tunnel (at the level of hook of hamate). The ROI was then cloned to all the series that included FA, ADC, and Eigenvector maps. Standard axial PDFS images served as the anatomic reference. Position of ROI over the nerve was also confirmed in corresponding coronal and sagittal images [Figure 1].

Data were analyzed using Statistical Package for the Social Sciences 20.0 version software. Categorical data were represented in the form of frequencies and proportions, and continuous data as mean and standard deviation. The Independent “*t*” test was used as a test of significance to identify the mean difference between two groups. “*p*” < 0.05 was considered as statistically significant.

## RESULTS

The study was conducted on 56 wrists of 43 CTS patients and 52 asymptomatic wrists as control. Thirty-three (76.7%) were female. Out of 43 controls 28 were female. Mean age of patients was 41.7 ± 9.2 years and control 41.4 ± 11.3 years (*P* = 0.95). Mean BMI in CTS patients was 27.8 ± 2.4 kg/m<sup>2</sup> and control (27.46 ± 2.4) kg/m<sup>2</sup>, *P* = 0.33. There was no significant difference in age, gender and BMI between CTS patients and control group.

Out of 43 CTS patients, 30 had unilateral involvement (26 right and 4 left side). Rest 13 patients had bilateral CTS. 12 (28%) patients had associated co-morbidities like diabetes, hypertension, or a thyroid disorder which were controlled/stable on medications. The mean duration of the pain was 7.4 ± 2.6 months (range 4–12 months).

The mean cross-sectional areas of the median nerve; CSA1 (13.2 ± 4.2 mm<sup>2</sup>), CSA2 (12.5 ± 3.5 mm<sup>2</sup>), and CSA3 (9.2 ± 1.5 mm<sup>2</sup>) in CTS patients were significantly higher compared to control group CSA1 (10.15 ± 1.64 mm<sup>2</sup>),

CSA2 (9.38 ± 1.37 mm<sup>2</sup>), and CSA3 (8.4 ± 0.9 mm<sup>2</sup>), (*P* = 0.001, *P* = 0.001, and *P* = 0.001, respectively) [Table 1].

The mean of CSA1 to CSA3 ratio in CTS patients (1.46 ± 0.48) was significantly higher than those of control (1.2 ± 0.15), *P* = 0.001. CTS can be diagnosed if the ratio of CSA of median nerve at the level of distal radio ulnar joint to that of distal tunnel is ≥1.25 with 80% sensitivity and 74% specificity.

The FR at tunnel outlet, at the level of hamate bone, was also found to be significant between the two groups. The mean FR of CTS patient was 2.7 ± 0.7 compared to that of control 2.4 ± 0.5, *P* = 0.01. The mean thickness of flexor retinaculum in CTS patients (1.2 ± 0.4 mm) was higher compared to the controls (1.0 ± 0.1 mm), (*P* = 0.001).

In MRI, we found the increased signal intensity of median nerve in 12 out of 56 wrists. 47 out of 56 (83.9%) showed normally located median nerve within the tunnel. Rest 9 showed variations in location of the median nerve either between flexor pollicis longus and flexor digitorum superficialis or between tendons of flexor digitorum superficialis and flexor digitorum profundus. Increased signal intensity of thenar muscles was seen in 21 out of 56 wrists in CTS patients. Thenar muscles signal intensity was assessed by visual inspection, in comparison with hypothenar muscles.

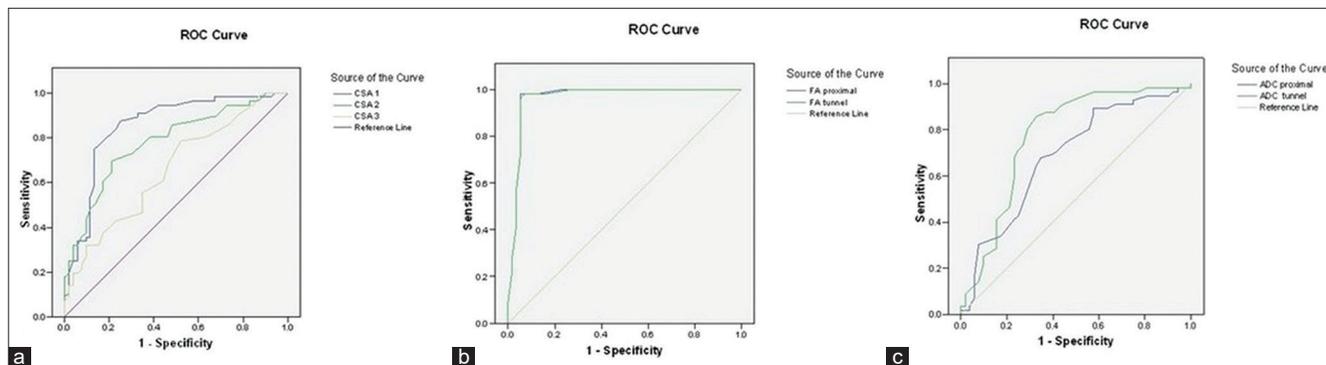
Mean FA value was lower in CTS patients as compared to the control group both proximal to the tunnel and within the carpal tunnel. The mean FA proximal to the tunnel was 0.47 ± 0.04 in CTS patients versus 0.58 ± 0.04 in control, *P* = 0.001, and within the tunnel was 0.45 ± 0.05 in CTS patients versus 0.59 ± 0.04 in control, *P* = 0.001 [Table 1].

Receiver operating characteristic (ROC) plot for FA of median nerve in proximal carpal tunnel against NCS shows area under the curve (AUC) 0.97, with 95% confidence interval *P* = 0.001. The cutoff value at which CTS was best predicted measured 0.52 (sensitivity = 96.2% and specificity = 94.6%). AUC for FA median nerve within tunnel was 0.964 with 95 % confidence interval (*P* = 0.023). With a FA cutoff of 0.54 in the median nerve within carpal tunnel CTS can be diagnosed with 96.4% sensitivity and 86.5% specificity.

**Table 1:** Comparison of CSA, flattening ratio, and flexor retinaculum thickness in MRI at various levels between CTS patients and control group.

MRI parameters	Wrist of CTS patients (n=56) Mean±SD	Wrists of control (n=52) Mean±SD	'P' Value
CSA1 (mm <sup>2</sup> )	13.2±4.2	10.1±1.6	0.001
CSA2 (mm <sup>2</sup> )	12.5±3.5	9.38±1.37	0.001
CSA3 (mm <sup>2</sup> )	9.2±1.5	8.4±0.9	0.001
Flattening ratio	2.7±0.7	2.4±0.5	0.01
Ratio of CSA1 to CSA3	1.46±0.48	1.2±0.15	0.001
Flexor retinaculum thickness (mm)	1.2±0.4	1.0±0.1	0.001

CSA: Cross-sectional area of the median nerve, CSA1: CSA at distal radio-ulnar joint level, CSA2: CSA at the level of proximal row of carpal bone, CSA3: CSA at tunnel outlet at the level of hook of hamate bone. MRI: Magnetic resonance imaging, CTS: Carpal tunnel syndrome



**Figure 2:** ROC curve for cross sectional area of median nerve (a) at the level of distal radioulnar joint (CSA1), at the level of proximal row of carpal bone (CSA2) and at tunnel outlet (CSA3). ROC curve for FA (b), and ADC (c), proximal to the tunnel and within the carpal tunnel. CSA: Cross-sectional areas, FA: Fractional anisotropy, ADC: Average diffusion coefficient.

**Table 2:** Comparison of DTI parameters between CTS patients and controls.

DTI parameter	CTS patient (n=56) Mean±SD	Control (n=52) Mean±SD	"P"-value
FA (Proximal)	0.47±0.04	0.58±0.036	0.001
FA (Tunnel)	0.45±0.05	0.58±0.040	0.001
ADC (Proximal) (mm <sup>2</sup> /s)	1.51±0.1	1.47±0.09	0.02
ADC (Tunnel) (mm <sup>2</sup> /s)	1.54±0.11	1.489±0.082	0.004
RD (Proximal)	0.833±0.143	0.810±0.098	0.002
RD (Tunnel)	0.889±0.147	0.852±0.102	0.136

DTI: Diffusion tensor imaging, CTS: Carpal tunnel syndrome, FA: Fractional anisotropy, ADC: Average diffusion coefficient, RD: Radial diffusivity

ROC plot for ADC in proximal carpal tunnel against NCS showed AUC 0.69. The cut-off value for ADC proximal to carpal tunnel at which CTS was best predicted measured 1.5 mm<sup>2</sup>/s (sensitivity = 71.4% and specificity = 57.7%). AUC for ADC of median nerve within tunnel was 0.78 with 95% confidence interval ( $P = 0.047$ ). With an ADC cutoff of 1.52 mm<sup>2</sup>/s within the tunnel, CTS can be diagnosed with 80.4% sensitivity and 71.2% specificity [Figure 2].

Mean ADC and RD values were higher in CTS patients as compared to control for both levels. The mean ADC of median nerve in CTS patients proximal to the tunnel (1.51 ± 0.1 mm<sup>2</sup>/s) and within the tunnel (1.54 ± 0.11 mm<sup>2</sup>/s) were higher compared to the control group at proximal to the tunnel (1.47 ± 0.09 mm<sup>2</sup>/s) and within the tunnel (1.489 ± 0.082 mm<sup>2</sup>/s),  $P = 0.023$  and  $P = 0.004$ , respectively. The mean RD in CTS patients proximal to the tunnel (0.833 ± 0.143) and within the tunnel (0.889 ± 0.147) were significantly higher than the control group proximal to the tunnel (0.810 ± 0.098) and within the tunnel (0.852 ± 0.102),  $P = 0.002$  and 0.136, respectively. Details of FA and ADC values in CTS patients and controls are given in [Table 2].

## DISCUSSION

Our study describes MRI changes in the median nerve, carpal tunnel and adjacent thenar muscles in CTS patients. MRI is

a non-invasive diagnostic modality to access the structural changes in the median nerve in patients with CTS. Similar to other studies,<sup>[7,8]</sup> we also found female predominance in CTS patients. This is supposed to be due to anatomical differences like narrower carpal tunnel in women compared to men, other risk factors like thyroid disorder has female predominance and certain risk factors unique to women are pregnancy and menopause, which can affect fluid retention and subsequent increased pressure within tunnel.<sup>[9]</sup>

Increased FR of the nerve is supposed to be due to compression of median nerve within the tunnel, resulting in flattened contour of the nerve. This ratio is maximum at the level of the hook of hamate, as tunnel outlet is the narrowest part of tunnel.<sup>[10,11]</sup> The previous literatures based on MRI changes in CTS patients have shown FR of more than 3 at tunnel outlet.<sup>[12]</sup> In our study, FR at the level of hamate was 2.7 ± 0.6 in CTS patients that was significantly higher than controls.

The mean cross-sectional area of the median nerve in CTS patients was higher than control proximal to carpal tunnel, within the tunnel and in the distal tunnel. The proposed pathophysiology of proximal median nerve enlargement is intermittent mechanical compression and vascular compromise leading to venous congestion, followed by nerve edema. Thickening of flexor retinaculum in CTS patients

could be another factor causing compression of the median nerve within the carpal tunnel.

Increased signal intensity of the nerve is most prominent at the level of compression and proximal to it and manifested as hyperintense signal on T2 or PDFS images. Subsequently, venous congestion in the compressed nerve causes ischemia and interruption of axoplasm flow. Persistent ischemia may lead to loss of axons and Wallerian degeneration when chronic.<sup>[13]</sup>

Increased signal intensity of thenar muscles in PDFS sequences is seen in early cases of nerve entrapment.<sup>[13]</sup> In chronic CTS patients, thenar muscle atrophy with intramuscular fatty infiltration can be seen. Signal abnormality of the median nerve and the thenar muscles is better appreciated on MRI.<sup>[14]</sup>

Recent studies have shown that DTI is a promising technique to visualize the peripheral nerves up to its microstructure level. DTI can assess structural integrity of nerve including demyelination, axonal damage, and nerve integrity. Brienza *et al.*<sup>[15]</sup> used a 3T MRI system to study the median, ulnar, and radial nerves and the tibial and peroneal nerves in healthy subjects. Several parameters such as FA, ADC, and RD are derived from raw DTI data that can be used for quantitative analysis of nerve fibers. ADC detects molecular diffusivity, which is an intrinsic tissue property. FA value ranges from 0 to 1, measures range of anisotropy. High FA indicates good nerve integrity, while high ADC reflects presence of axonal damage and nerve demyelination. Axonal diffusivity measures diffusivity along long axis indicating axonal integrity while RD measures perpendicular diffusivity and indicates integrity of the myelin.<sup>[16]</sup>

Kwon *et al.* proposed that FA is the best among the DTI parameter to be used as a diagnostic cut-off.<sup>[17]</sup> In a study by Tasdelen *et al.*,<sup>[18]</sup> they found cut off value of FA is 0.66 with AUC of 0.884, sensitivity of 82.5% and specificity of 80%. In another study by Guggenberger *et al.*<sup>[19]</sup> FA value of 0.47 was proposed (AUC: 0.773, sensitivity 83% and specificity 67%). In our study, with a cutoff value of 0.52 in FA of median nerve at distal radio-ulnar joint and 0.54 within the carpal tunnel at the level of hamate bone, we found maximum sensitivity of 96.2% and 96.4% and specificity of 94.6% and 86.6%, respectively.

Lower FA indicates that the median nerve becomes relatively more isotropic in CTS patient. In CTS, the maximum compression occurs at the level of carpal tunnel causing disruption of intraneural microcirculation, nerve edema, and increase in extracellular fluid. This increased extracellular fluid shows isotropic water diffusivity. Thus, lower FA value indicates increasing disease severity.<sup>[17]</sup>

The increased extracellular fluid due to compressive neuropathy also causes an increase in ADC values as shown

in the study by Brienza *et al.*<sup>[15]</sup> with the lower FA and increase in ADC in CTS patients. Barcelo *et al.*<sup>[20]</sup> obtained lower FA, but non-significant difference in ADC values. This suggests in CTS patients, first the FA value decreases before the changes in ADC, therefore making FA a more sensitive parameter while evaluating CTS. We found significantly reduced FA and increased ADC in the median nerve within the tunnel and proximal to the tunnel in CTS patients compared to control. It could be due to relatively late presentation of patient to us.

Our study also shows higher RD values in CTS patients proximal to the tunnel and within the tunnel. High RD may be caused by loss of myelin sheath integrity in early nerve entrapment. This supports the pathology in CTS where nerve compression is believed to cause demyelination of nerve in the initial phases before axonal damage. This is noted in studies by Stein *et al.*<sup>[21]</sup> and Kwon *et al.*<sup>[17]</sup>

At present, CTS is diagnosed by clinical assessment and NCS.<sup>[22]</sup> NCS has a false-negative rate of about 10% and a false-positive rate of about 15%.<sup>[23,24]</sup> It cannot distinguish primary from secondary CTS. MRI is a non-invasive diagnostic modality that may be useful in equivocal cases and to exclude secondary causes of CTS. It may be useful in detecting other secondary causes of CTS like accessory hand muscles over transverse carpal ligament and median nerve schwannoma.<sup>[25]</sup> It is not operator dependent. MRI has advantage of imaging the nerve directly can detect subtle changes in the median nerve at carpal tunnel. Hyperintensity in the thenar muscles can be easily detected by MRI which also provides evidence of median nerve pathology in proper clinical settings.

Strength of our study is a good sample size with age and gender matched control. It has been performed in eastern Indian patients who were clinically diagnosed as CTS with positive electrophysiological tests, and thus representative sample of this patient population. Also, all the measurements were taken at specified levels which make the study systematic and reproducible.

We could not perform post-treatment follow-up of the cases due to the corona pandemic. This is the limitation of our study. Comparison with follow-up imaging may give more insight into the pathophysiology.

## CONCLUSION

MRI is an excellent imaging modality that provides structural changes of the median nerve. CSA of median nerve, FR of the median nerve at the tunnel outlet are highly sensitive parameters in CTS. MRI can also rule out secondary causes. Median nerve hyperintensity can be seen on MRI. MRI is also useful in detection of abnormality of thenar muscles in the form of long TR hyperintensity or fatty atrophy of the muscles. Because of high soft tissue resolution, MRI

can better evaluate abnormality in adjacent structures. DTI shows reduced FA and increased ADC and RD in CTS patients compared to controls.

### Declaration of patient consent

The authors certify that they have obtained all appropriate consent.

### Financial support and sponsorship

Nil.

### Conflict of interest

There is no conflict of interest.

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**How to cite this article:** Naik S, Mahanty S, Bhoi SK, Lahre Y, Bag ND, Mohakud S. MRI of wrist and diffusion tensor imaging of the median nerve in patients with carpal tunnel syndrome. *J Neurosci Rural Pract* 2023;14:302-7.