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ORIGINAL ARTICLE

# The efficiency of acoustic radiation force impulse (ARFI) elastography in the diagnosis and staging of carpal tunnel syndrome

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## Abstract

**Objectives** The aim of the present study was to quantify the stiffness of the median nerve (MN) at the carpal tunnel inlet by acoustic radiation force impulse (ARFI) elastography and to evaluate whether ARFI can be used in diagnosis and staging of carpal tunnel syndrome (CTS).

**Methods** Sonographic examinations of 96 wrists in 50 patients were included in the study. The cross-sectional area and stiffness of the MN were quantitatively measured by B-mode ultrasonography (USG) and ARFI. The findings of CTS were assigned to four groups: (I) normal ($n = 21$), (II) mild ($n = 39$), (III) moderate ($n = 38$), and (IV) severe ($n = 19$). The differences between CTS patients and controls and the differences in electrodiagnostic tests among subgroups were statistically compared. ROC analysis was performed to determine the cut-off values between subgroups.

**Results** Bilateral CTS was present in 46 patients (92 wrists) and unilateral CTS in four patients. Of the 96 nerves in the 50 symptomatic "idiopathic CTS" patients (48 women, 2 men; mean age 45.9 years, range 23–73 years), 39 (40.4%) were mild, 38 (39.8%) were moderate, and 19 (19.8%) were severely affected. When compared to controls, MN stiffness was significantly higher in the CTS group ($P < 0.001$); furthermore, it was higher in the severe or extreme severity group than the mild or moderate severity group ($P < 0.001$). A 3.250 m/s cut-off value on ARFI revealed sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 81, 82, 95.1, 50, and 82%, respectively.

**Conclusion** The MN stiffness measured by ARFI elastography is significantly higher in patients with CTS then in controls. ARFI elastography appears to be a highly efficient imaging modality for the diagnosis and staging of these patients.

**Keywords** Carpal tunnel syndrome · Shear wave elastography · Median nerve

## Introduction

Carpal tunnel syndrome (CTS) is the most common compression neuropathy in the upper extremities with a reported incidence of 5.8% in women and 0.6% in men [1]. Increased pressure in the carpal tunnel results in median nerve (MN) compression. The diagnosis of CTS is based on clinical symptoms and confirmed by a nerve conduction study; however, there is still no gold standard for CTS diagnosis. Nerve conduction study provides valuable information about the function of the MN, but it provides no morphological information regarding the MN and the causes of local compression.

Ultrasound (USG) and magnetic resonance imaging (MRI) have been successfully used in the evaluation of CTS. These techniques, via direct visualization of the affected MN, can also identify the reasons for secondary CTS and define structural variations, such as persistent median artery, bifid MN, or space-occupying lesions such as tenosynovitis and ganglion cysts. Moreover, the imaging modality is extremely critical for postoperative patients with persistent symptoms [2]. Although MRI may show the morphological variations in CTS patients, the sensitivity of MRI findings is very low [3]. On the other hand, diffusion tensor imaging and tractography have been recently shown to have better

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sensitivity and specificity compared to the conventional MRI [4, 5]. The potential role of USG is limited because of the wide range of sensitivity and specificity, which probably results from the absence of a standard procedure and also a wide range of cut-off values used for the measurement of cross-sectional area (CSA) [6].

Elasticity is defined as the ability of a substance to resist a deforming force or stress and to return to its original size and shape after that force or stress is removed [7]. In numerous studies reporting on musculoskeletal system practices, USG elastography has been shown to be a valuable tool in the detection of muscle and tendon abnormalities [8]. Moreover, USG elastography has also been used in the assessment of the elasticity of peripheral nerves [9, 10]. On the other hand, recent studies reporting on strain elastography have revealed that the MN is markedly stiff in patients with CTS [9–11].

To our knowledge, there has been no study in the literature reporting on the use of acoustic radiation force impulse (ARFI) elastography in the evaluation of peripheral nerve tissue. The aim of the present study was to measure the stiffness of the MN at the carpal inlet by ARFI elastography and to determine whether ARFI can be used in carpal tunnel syndrome diagnosis and staging.

## Materials and methods

### Study design

The study has been conducted in accordance with the principles of the Helsinki Declaration and approved by the local Institutional Review Board. Written informed consent was obtained from each participant.

This prospective diagnosis-based study was conducted between August 2015 and December 2015.

This study was designed prospectively, and included 50 consecutive patients with a definitive clinical diagnosis of CTS who underwent electrodiagnostic testing (EDT). Examinations of the patients were performed consecutively on the same day, with EMG followed by US followed by US elastography. Electrodiagnostic tests were not performed in the healthy volunteers.

Patients were excluded from the study if they had CTS surgery, diabetes mellitus, hypothyroidism, hyperthyroidism, renal disease, hepatic disease, pregnancy, alcohol abuse, rheumatologic diseases, traumatic nerve damage, polyneuropathy, myelopathy, radiculopathy, ulnar neuropathy, or stroke. Patients with CTS variants such as accessory muscles, bifid MN, and persistent median artery or any mass lesion identified on the US examination of the wrist were excluded from the study. In both groups, the elasticity of the MN was measured on a high-resolution USG device and recorded prospectively.

### ARFI imaging

All ARFI images were evaluated by the same experienced radiologist blinded to the assessment results. Radiological examinations were performed using a Siemens ACUSON S2000 (Medical Solutions USA Inc., Mountain View, CA, USA) with a 9L4 linear array transducer (4–9 MHz). Prototype ARFI imaging technology is incorporated in the USG system by Virtual Touch IQTM software, which provides quantitative assessment of tissue stiffness through shear wave velocity (SWV) measurements. The SWV color map is generated by a pulse sequence consisting of up to 256 acquisition beam lines. For each beam line, sequencing of push pulses and tracking vectors is used to estimate the shear wave propagation time for each depth along the beam direction. The image field depth was set to 3 cm, and the imaging frequency was set to 9 MHz.

The images were taken with the patient sitting in the neutral position. During the examination, the participants were sitting face-to-face with the examiner with the wrists resting upon a flat surface, the palms facing upward, the fingers being kept relaxed in a semi-flexed position, and the affected wrist placed on a rolled-up towel. The 9-MHZ transducer was placed on the volar aspect of the wrist (Fig. 1). Measurements of median nerve CSA and median nerve perimeter and US elastography were performed at the point of maximum nerve swelling at the carpal tunnel inlet at the level deep to the proximal edge of the flexor retinaculum.

CSA measurements were performed by tracing a continuous line within the hyperechoic boundary of the nerve. The MN at the carpal tunnel inlet was identified on the transverse

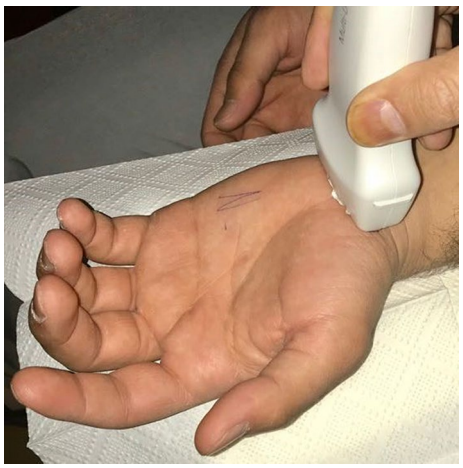

**Fig. 1** Positioning of the hand and ultrasound transducer for ARFI imaging. The left hand and forearm were put on the knee, the wrist in supination, and the fingers relatively relaxed, half-extended during the examination. The ultrasound transducer was placed on the volar aspect of the wrist

plane, and the transducer was rotated 90° to obtain a sagittal imaging plane. For SWE measurements, light compression was applied with the US probe on the median nerve in the transverse axis perpendicular to the wrist at the carpal tunnel inlet at the level deep to the proximal edge of the flexor retinaculum.

A rectangular electronic box provided by the system software was used to display the tissue stiffness in a chromatic scale with progression from blue to red, indicating low-to-high shear modulus. The display scale of the color map was set to 0.5–10 m/s. Different colors show diverse stiffness. Red, green, and blue areas represent high, medium, and low stiffness regions, respectively. Three region-of-interest (ROI) boxes were manually placed within the MN to quantitatively measure the SWV. We measured the average of the three. Each ROI box had a pre-set size of 2 mm × 2 mm. The SWV measurements corresponding to these ROI boxes were shown to the right of the ultrasound image (Figs. 2, 3). The maximum SWV value that the current Virtual Touch IQTM software with the 9L4 linear transducer can measure is 10 m/s. When the SWV is greater than 10 m/s, "HIGH" is displayed instead of a numerical value. When the SWV cannot be determined due to poor shear wave signal-to-noise ratio, "NA" is displayed.

## Electrodiagnostic studies

The American Association of Electrodiagnostic Medicine has recommended a protocol for electrodiagnostic studies [12, 13]. All tests were performed with skin temperature kept at > 33 °C. The severity of the disease was classified into three stages by a neurophysiologist: (I) mild involvement

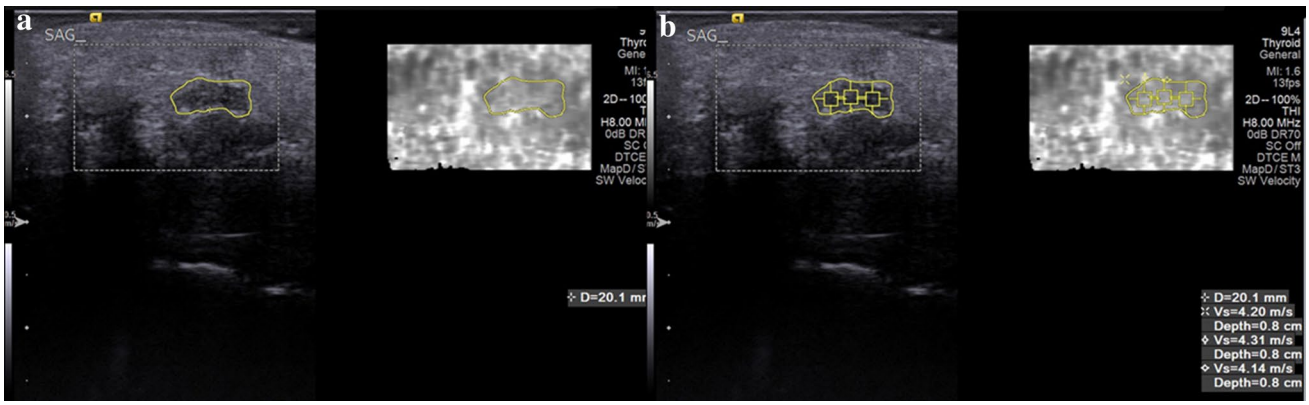


**Fig. 2** ARFI quantification method was summarized. **a** Borders of the median nerve were encircled manually. **b** Region-of-interest boxes were placed within this frame to quantify the stiffness of the median nerve

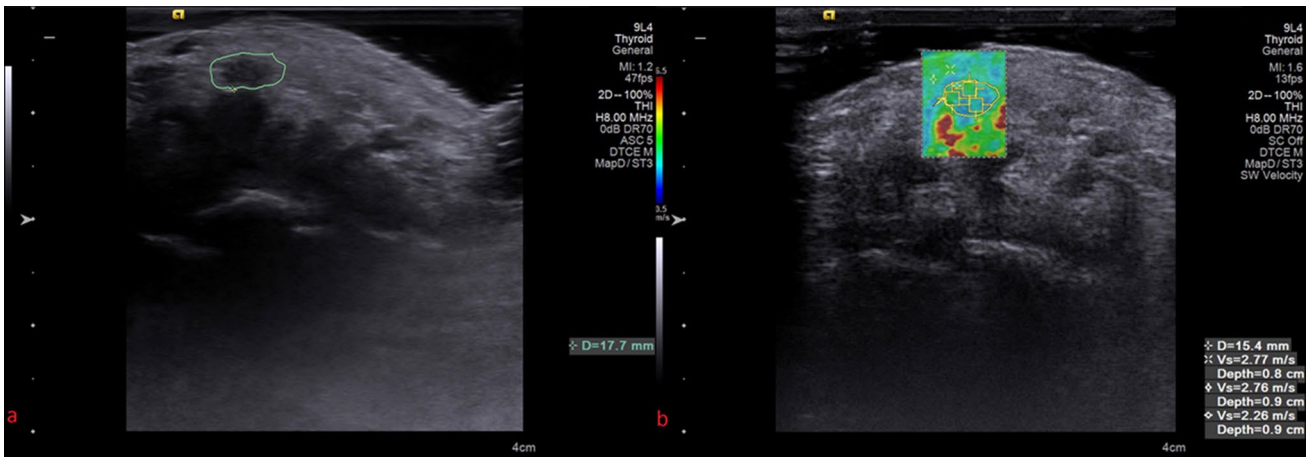


**Fig. 3** For the session without compression, a thick ultrasound gel layer is visible in both the B-mode (**a**) and the ARFI (**b**) ultrasound images. The display scale of the color map is 0.5–10 m/s. The color correlates with tissue stiffness. In general, red, green, and blue areas correspond to high, medium, and low stiffness regions, respectively. Three ROIs were placed on each of the SWV color maps to obtain the shear wave velocity measurements

(myelinic damage), (II) moderate involvement (mild axonal damage), and (III) severe involvement (severe axonal damage). A grading scheme for the severity of CTS by electromyography criteria was used:

1. Mild CTS: prolonged (relative or absolute) sensory or mixed NAP distal latency ± SNAP amplitude below the lower limit of normal.
2. Moderate CTS: abnormal median sensory latencies as above and (relative or absolute) prolongation of median motor distal latency.
3. Severe CTS: prolonged median motor and sensory distal latencies, with either an absent SNAP or mixed NAP, or low amplitude or absent thenar CMAP. Needle examination often reveals fibrillations, reduced recruitment, and motor unit potential changes [14].

### Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v20 (SPSS Inc., Chicago, IL, USA). A normal distribution of the quantitative data was checked using Kolmogorov–Smirnov test. Intra-observer reliability coefficient was computed to assess observations made by the same observer during the first and second evaluations. Mean values of the groups with regard to continuous variables were compared using one-way ANOVA, followed by Duncan's post hoc test. Receiver-operating characteristics (ROC) analysis was performed to determine the best cut-off value for the separation of patient and healthy groups. Continuous data were presented as mean ± standard deviation or median [minimum–maximum], as appropriate. All differences associated with a chance probability of 0.05 or less were considered statistically significant.

## Results

The study group included two (4%) men and 48 (96%) women with a mean age of 45.9 years (range 23–73 years, interquartile range 24–73 years). Eleven healthy volunteers formed the control group (21 wrists). No significant difference was found between the two groups with regards to age, gender, and distribution of right vs. left wrists. Of the 50 patients, 49 patients were right-handed and one patient was left-handed. All the patients were examined bilaterally. Bilateral symptoms were seen in all of the patients, and bilateral electrophysiological findings were found in 46 patients (96 wrists).

The EMG results of four patients were within normal ranges. Of the 96 hands in 50 patients, 39 had mild CTS (40.6%), 38 had moderate CTS (39.6%), and 19 had severe CTS (19.8%).

Table 1 presents mean CSA values in both groups. The control group included 11 healthy volunteers, 77 hands with mild-moderate symptoms, and 19 hands with severe symptoms. Overall, the CSA of the median nerve at the carpal tunnel was significantly larger for the patient group (mean 11.27 $mm^2$) when compared to the control group (8.04 $mm^2$) ($P < 0.001$). In patients with severe CTS, the median nerve CSA (14.31 $mm^2$) was significantly higher than that in patients with mild or moderate CTS (10.51 $mm^2$) ($P < 0.001$).

Table 2 presents mean ARFI scores measured in the control and patient groups. As seen in the table, the mean

**Table 1** Mean CSA values in the control and patient groups were summarized

| CSA | *N* | Mean[a] | Std. deviation | Minimum | Maximum | *P* |
|---|---|---|---|---|---|---|
| Control | 21 | 8.05 c | 1.322 | 6 | 11 | 0.01 |
| Mild–mod. | 77 | 10.52 b | 1.924 | 6 | 14 | |
| Severe | 19 | 14.32 a | 1.974 | 11 | 19 | |
| Total | 117 | 10.69 | 2.601 | 6 | 19 | |

*CSA* cross-sectional area

[a]Statistical comparison between CTS patients (total, $n = 96$) and control group

**Table 2** Mean ARFI scores measured in the control and patient groups were summarized

| | *N* | Mean[a] | Std. deviation | Minimum | Maximum | *P* |
|---|---|---|---|---|---|---|
| Control | 21 | 2.9719 d | 0.40936 | 2.21 | 3.80 | 0.001 |
| Mild | 39 | 3.6351 c | 0.53342 | 2.69 | 4.78 | |
| Moderate | 38 | 4.0134 b | 0.69465 | 2.91 | 5.70 | |
| Severe | 19 | 5.0589 a | 0.57330 | 3.50 | 6.10 | |
| Total | 117 | 3.8702 | 0.85432 | 2.21 | 6.10 | |

[a]Statistical comparison between CTS patients (total, $n = 96$) and control group

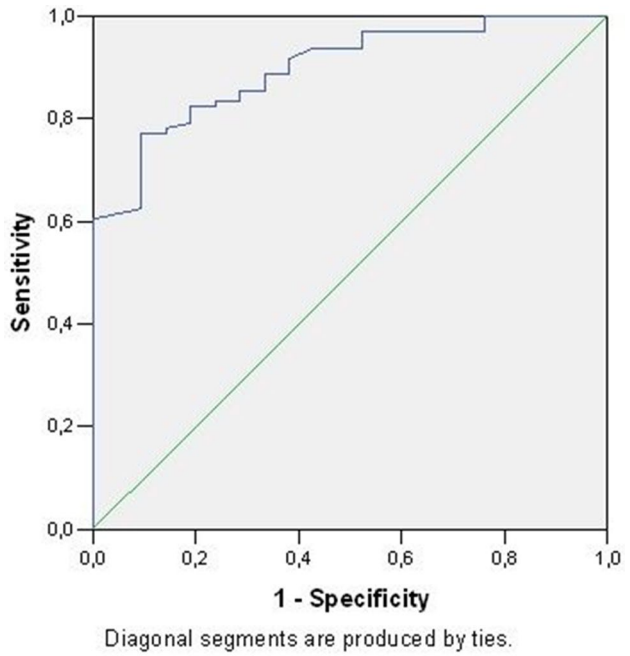


**Fig. 4** ROC curve for the diagnosis of CTS based on ARFI measurements

**Table 3** Value of "area under the curve" provided by ROC analysis was indicated

| Area | Std. error(a) | Asymptotic sig. (b) | Asymptotic 95% confidence interval | |
|---|---|---|---|---|
| | | | Lower bound | Upper bound |
| Test result variable(s): elasto | | | | |
| 0.897 | 0.032 | 0.000 | 0.834 | 0.959 |

ARFI score was 2.97 ± 0.41 m/s in the 21 patients in the control group, 3.64 ± 0.53 m/s in the 39 patients with mild CTS, 4.01 ± 0.69 m/s in the 38 patients in the moderate group, and 5.06 ± 0.57 m/s in the 19 patients with severe CTS. A statistically significant difference was found among the groups with regard to mean ARFI score ($P < 0.01$).

The ROC analysis (Fig. 4) results for the accuracy of elasticity scores in the separation of healthy and patient groups were achieved. According to the ROC analysis results, the median nerve stiffness cut-off value for determining the diagnosis of CTS that maximizes the accuracy was 3.250 m/s (AUC 0.897, 90% CI 0.834, 0.959) (Table 3), and its sensitivity, specificity, PPV, NPV, and accuracy were 81, 82, 95.1, 50, and 82%, respectively.

Intra-observer agreement was excellent for both the CSA and SWE measurements for both the patient and the control groups. Intra-observer reliability coefficient was found to be more than 80%.

## Discussion

The study results showed that quantitative evaluation of the MN by means of ARFI elastography could be helpful in differentiating CTS cases from controls and predicting the disease severity. These findings indicate that quantitative measurements of MN elasticity at the carpal tunnel inlet by means of ARFI elastography are compatible with EDT findings.

Our data confirm a significant positive correlation between MN, CSA, and severity of CTS. The gold standard for the diagnosis of CTS is electrodiagnostic testing [3]. In the present study, DML, MNCV, DSL, and amplitude differed significantly among patients with mild, moderate, and severe CTS. The reliability of nerve conduction velocity to evaluate the MN has been supported by many reports in the literature [12]. However, EMG is disturbing, uncomfortable, and operator-dependent, and may produce false-negative results [10]. As a result, investigators have concentrated on USG examination of CTS. In the present study, we aimed to present a method that can be standardized, reproducible, and quick to respond to clinical variations.

Ultrasonography is an ideal imaging method to evaluate the standard anatomy and peripheral nerve pathologies. Advantages include the ability to evaluate the long parts of nerves and to accomplish dynamic studies. USG is also economical, easily tolerated, and according to several authors, is thought to be the principal technique for peripheral nerve pathologies; however, USG cannot evaluate nerve stiffness [9]. Sonoelastography, a relatively recent technology, has led to the better evaluation of the musculoskeletal system. Gray-scale USG-based diagnostic tests have aimed to identify the morphological variations of the MN in CTS. MN compression is presented on USG as nerve swelling within the proximal tunnel and nerve flattening in the distal tunnel [11, 15]. In the present study, the stiffness of the MN was determined using ARFI imaging. The MN was stiffer on SWE even in patients with mild and moderate CTS compared to controls.

The increased MN stiffness can be elucidated by subsequent pathophysiological means. First, although the etiology of CTS is thus far unidentified in most cases, it has been frequently documented that the pressure in the carpal tunnel is elevated [16]. Wang et al. [17] showed a relationship regarding shear wave propagation speed and carpal tunnel pressure. Wang et al. worked on the Achilles tendon to demonstrate their testing and demonstrated that both the absolute wave speed and the speed difference between the inside and outside tunnel improved linearly with pressure measured in the tunnel. The association between the tunnel pressure and increased tendon shear wave speed might similarly be valid for the MN.

Second, increased pressure in CTS affects the MN circulation, and long-term edema triggers fibroblast penetration. The outcome is the deposit of scar tissue in the MN [18] with possibly improved MN shear wave speed. Both mentioned mechanisms might have a causative role in increased shear wave speed. Using strain elastography, Kantarci et al. [11] found a 40.4-kPa cut-off strain value on SWE that revealed a sensitivity, specificity, PPV, NPV, and accuracy of 93.3, 88.9, 93.3, 88.9, and 91.7%, respectively. The present study is similar to that of Kantarci et al., but our sample size was larger [11]. Using strain elastography, Orman et al. [10] found a cut-off value of 0.0635 as the most sensitive value and a cut-off value of 0.19 as the most specific value. In the present study, high sensitivity and specificity rates were achieved at a single cut-off value.

Conversely, CSA measurements in the study of Kantarci et al. [11] yielded a low sensitivity (60%) at a cut-off value of 9.5 $mm^2$. In CTS, the relationship between electrophysiological and USG findings was significant in some studies [19]; and in some cases, the results were uncertain [20]. Although the population of our study was mostly composed of mild and moderate CTS patients, the relationship between electrophysiological study and sonoelastography was statistically significant. In our study, it was also found in a few patients that nerve stiffness increased before apparent nerve CSA increased.

Acoustic radiation force impulse elastography has definite benefits over strain elastography, since it is reproducible, quantitative, and operator-independent. ARFI elastography offers more quantitative estimations of Young's modulus (stiffness). Strain elastography only produces semiquantitative data indirectly related to stiffness. ARFI elastography does not depend on operator compression of the probe, and thus, it is more reproducible.

Our study had several limitations. First, our study groups had more females than males. However, this reflects the true prevalence of CTS, which has a predilection towards females [10]. We could not investigate correlations with hand preference or profession, which may influence MN thickness or stiffness. Second, our hypothesis was dependent on improved carpal tunnel pressure and its outcome on the MN; however, we did not find a correlation between SWE findings and carpal tunnel pressure. Even though this point is principal, the emphasis of the present study was the evaluation of a recently developed USG technique to measure MN stiffness. Third, we performed MN measurements only at the carpal tunnel inlet, and therefore, we had no data on the variations in nerve stiffness at the distal tunnel or the forearm level on SWE.

## Conclusion

In conclusion, the present study revealed that ARFI elastography assessment of the MN may be helpful to differentiate CTS cases from controls and to predict CTS severity. ARFI elastography is a useful instrument that can be used for non-invasive evaluation of MN stiffness and has the potential of recognizing tissue changes associated with CTS.

### Compliance with ethical standards

**Ethical statements** This study was approved by the Yuzuncu Yil University ethics committee. Written informed consent was obtained from all individuals included in the study. This manuscript has not been published and is not under consideration for publication elsewhere. There is no overlap of our present work with any previously published studies.

**Conflict of interest** The authors declare that they have no conflicts of interest or industry support to disclose.

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