Toward sensitive and specific electrodiagnostic techniques in early carpal tunnel syndrome

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Context
There remains no gold standard or even true agreement among clinicians as to which electrophysiological tests are most important and most relevant particularly in the mild and early carpal tunnel syndrome (CTS).
Aim
The aim of this study was to determine the sensitivity and specificity of electrodiagnostic (EDX) techniques to confirm the clinically diagnosed patients with mild CTS.
Patients and methods
This is a descriptive study. A total of 109 hands (68 right hands and 41 left hands) with symptoms consistent with mild idiopathic CTS, as well as 100 hands from controls, were clinically examined and underwent EDX evaluation.
Results
The ring-difference and thumb-difference had the highest sensitivity, with the distal sensory latency (DSL) of the median nerve coming next. Combined sensory index (CSI) test at a cutoff point more than 1.1 had 100% specificity and positive predictive value. Abnormal DSL of the median nerve had the best negative predictive value. In patients with early and mild CTS and with normal distal motor latency and DSL, the CSI at cutoff point more than 1.1 is the best EDX test that is able to detect most of these patients.
Conclusion
CSI and its individual components appear as the best EDX tests that help in the diagnosis of patients with early and mild idiopathic CTS.

Keywords:
diagnosis of idiopathic carpal tunnel syndrome, electrodiagnosis of median nerve, idiopathic carpal tunnel syndrome

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Introduction

Carpal tunnel syndrome (CTS) is the most common peripheral compression neuropathy [1]. CTS results from compression of the median nerve (MN) as it passes within the carpal tunnel (CT) at the wrist, which has relatively tight boundaries. The prevalence of CTS ranges from 2 to 3% in the general population [2,3].

CTS remains a primarily clinical diagnosis. Making a diagnosis for CTS depends on the presence of classic symptoms in addition to positive signs and reproduction of symptoms with provocative tests. However, the studies that had been conducted to evaluate the validity of symptoms and the clinical tests had resulted in large inconsistencies as regards the usefulness of certain symptoms and signs in detection of patients with CTS. Besides, lesions of the C6–C7 nerve roots, the brachial plexus, or the proximal MN can be confused clinically with MN neuropathy at the wrist, especially in early or mild cases [4,5]. In an attempt to take a step further, a diagnostic criteria was developed in 2006 [3]. They investigated cases with CTS and determined the clinical criteria that significantly contributed to the diagnosis of definite CTS. The model was purely clinical as they did not include any electrodiagnostic (EDX) test in the criteria. Unfortunately, the model has also not been tested for validity.

In practice, clinical findings are usually combined with EDX testing to confirm the diagnosis. In spite of this apparently simple scenario, still there is no gold standard or even strong agreement among physicians as to which findings are most significant and most relevant, and it is up to the individual physician to decide which test to use [6–8].

The use of EDX findings in the diagnosis of CTS is further complicated by the fact that a sector of patients

had classic symptoms of CTS but show no parallel changes on EDX tests. For example, in a recent study in 2016, Srikanteswara *et al.* [9] reported that despite the fact that the subjective sensory symptoms are common in patients with CTS, sometimes these symptoms are not supported by objective findings in the neurological examination and with negative EDX findings. Moreover, although symptoms most commonly occur in an MN distribution, in some patients symptoms may present in other distribution patterns, whereas EDX findings clearly indicate MN involvement [10,11]. This probably may lead to misdiagnosis and poor treatment outcome [12]. In addition, EDX testing can help in recognizing cases with peripheral neuropathies that can be confused with CTS [8].

Many different EDX methods have been developed over the years for diagnosis of CTS, and the EDX practitioner is faced with many uncertainties in the proper use of these tests in clinical practice. For example, the problem of misdiagnosis of the mild cases is partially improved by EDX identification of sensory nerve changes [13]; this is because changes in sensory nerves develop more early than the changes in larger motor fibers. On the other hand, it was detected that the motor fibers may be involved earlier through an observation of a difference in motor axon recruitment pattern of the abductor pollicis brevis muscle (APBm) among patients with mild CTS [14].

Besides the standard EDX techniques, the comparison of wrist–palm motor conduction velocity (MCV) or the comparison of sensory latency between the MN and either the radial nerve or ulnar nerve (UN) can improve diagnostic efficiency EDX testing [15]. Despite this, the false negative rate of EDX results in recognition of cases with CTS ranges from 10 to 15% [16]. There is additional difficulty in defining the limits of normality for patients [17]. Again there remains no gold standard as to which EDX test is most beneficial to detect cases with mild CTS, and clinicians are often unclear about the selection of the most appropriate test from a long list of available choices.

Some promise has emerged in using noninvasive imaging modalities to diagnose CTS, for example, ultrasound (US) or MRI. Diagnosis with imaging modalities relies on detection of nerve swelling or nerve compression by measuring cross-sectional area, signal change, or dimensions of the CT [8,18]. On the other hand, US is operator dependent and there is no standardized neuromuscular US scanning protocol for cases with CTS [19]. Moreover, US is not able to identify patients with mild CTS [20]. MRI may not be widely available and may require up to 45 min to be completed. US and MRI modalities currently serve as confirmatory techniques in the diagnosis of puzzling cases and those with recurrence after surgery, and have not yet been proven useful as initial or routine screening tools in CTS [8]. Both techniques are more useful in identifying the underlying cause of CTS but had limited value in detection of idiopathic carpal tunnel syndrome (ICTS) [21].

These data indicate that the current standard test for the diagnosis of CTS is under debate [22] and that this debate is even greater in mild and early cases of the CTS and in idiopathic cases. Therefore, there is a great need to go a step further, and to determine a validated diagnostic test for the hope to improve consistency in evaluating cases with early and mild ICTS.

Aim

Aims of this study were as follows:

(1) To determine the sensitivity and specificity of EDX techniques to confirm the clinically diagnosed patients with mild CTS.
(2) To determine which technique to choose to confirm the diagnosis in mild CTS patients with normal sensory and motor latency.

Patients and methods

In the present study, we recruited 109 patients with mild ICTS from the Rheumatology and Rehabilitation Outpatient Clinic of Mansoura University Hospital, from January 2015 to July 2016. All patients provided a written consent.

Diagnosis of CTS was based on the criteria for the diagnosis of CTS [23].

(1) Nocturnal or activity-related pain or dysthesia limited to the hand.
(2) Sensory deficit or reduced two-point discrimination in MN distribution.
(3) Isolated atrophy of the APBm.
(4) Positive Phalen's or Tinel's signs.

The diagnosis was made when the patient had painful dysthesia in the sensory area of the MN and one of the criteria 2–4 was fulfilled. However, in the current study, we did not depend on the third criterion (one of the exclusion criteria).

In this study, 100 normal control participants apparently healthy without any evidence of CTS were included.

Exclusion criteria

Patients with any of the following were excluded from the study:

(1) Patients with severe CTS: patients with a fixed or continuous sensory complaint or with marked reduction of sensation over the MN distribution and those with APBm wasting or weakness.
(2) Secondary CTS.
(3) Patients with cervical radiculopathy.
(4) Patients with history of steroid injection, splint, or operation of the CTS.

Methods

The following methods were used:

(1) Detailed history taking:
This includes the current symptoms, the duration and distribution of pain and paraesthesia, and symptoms suggestive of severe CTS such as grip weakness and dropping things.
(2) Physical examination:
   (a) Examination of the cervical spine and upper extremity.
   Musculoskeletal and neurological examination of the cervical spine and upper extremity to exclude occurrence of cervical radiculopathy.
   (b) Wrist examination:
      (i) Inspection: for presence of local condition of the hand that is associated with CTS (e.g. deformity, local scar of previous operation or trauma, tenosynovitis).
      (ii) Sensory examination for MN (diminished pin-prick sensation, a two-PD test, in which the inability to discriminate points less than 6 mm apart is assessed) [24].
      (iii) Weakness of the APBm: by instructing the patient to raise the thumb perpendicular to the palm as downward pressure was applied on the distal phalanx, resisting thumb abduction [25].
   (c) Provocative tests:
      (i) Phalen maneuver: the patient is asked to hold his/her wrist in complete and forced flexion (pushing the dorsal surfaces of both hands together) for 30 s. If the hand symptoms are reproduced, then the test is positive.
      (ii) Tinel sign: the test is positive if there is reproduction of the patient's hand symptoms when the wrist is percussed on the volar surface.
(3) Electrophysiologic studies.

All EDX tests performed in the present study were done using a NEUROWERK EMG machine (manufactured by Medizin-Technik GmbH, Germany). The skin temperature of the hand was maintained at or above 32°C. The following parameters were maintained for all EDX tests: distal sensory latencies were measured to the negative peakof the sensory nerve action potential (SNAP), whereas distal motor latencies (DML) were measured to the onset of the negative deflection of the CMAP. Amplitude was measured from the baseline to the peak of negative deflection of the SNAP and the CMAP in the sensory and motor MN testing, respectively. All tests rely on percutaneous supramaximal stimulation of the tested nerve. Pulse duration was 0.05/0.1 ms for sensory and mixed nerve stimulation and 0.2/0.5 ms for motor nerve stimulation. The filters were set at 20 Hz and 2 kHz. The sweep time was set at 1 ms per division. The sensitivity was set at 5 mV per division for the motor tests and at 10 μV per division for the sensory and mixed tests. The surface disc recordings were used for recording from muscles in motor studies, whereas ring electrodes were used for sensory studies. The ground electrode is placed between the recording and the stimulation electrodes.

The EDX tests are shown in Table 1.

From these EDX tests, the following parameters were obtained:

(1) DML of the MN.
(2) Sensory latency of the MN.
(3) Motor-difference: calculated by subtraction of the ulnar latency from the median latency.
(4) Median terminal latency index (TLI) (median sensory distoproximal conduction time ratio): it is obtained by dividing the median sensory palmar latency (obtained in test 4) by the median sensory wrist latency (obtained in test 2).

Calculation of the combined sensory index (CSI) was obtained by adding the three latency differences of tests 5, 6, and 7. The latency was measured to the peak for all tests. When any test is negative, that is, the median is faster, a negative number is used:

Table 1 Conduction techniques performed in this study

Test	Recording site	Stimulation site
Test 1–Median nerve motor distal latency	From APBm	Wrist: middle of the wrist between the tendons to the FCRm and PLm at a fixed distance from recording electrodes (7 cm)
	The active recording electrode (GI) placed over the muscle belly and reference electrode (G2) over the first MCPj	
Test 2 – Median nerve sensory wrist latency (DSL)	Middle finger – ring electrodes with G1 placed over the MCPj and G2 placed 3–4 cm distally over the DIPj	Wrist: middle of the wrist between the tendons to the FCRm and PLm at a fixed distance from the recording electrodes (13 cm)
Test 3 – Median vs. ulnar – lumbrical – interossei study (motor-difference)	Second lumbrical muscle (innervated by MN) and first palmar interosseous muscle (innervated by UN); same recording electrodes for both: G1 placed slightly lateral to the midpoint of the third metacarpal and G2 placed distally over the MCPj of digit 2	MN at the wrist: middle of the wrist between the tendons to the FCRm and PLm
		Ulnar nerve at the wrist: medial wrist, adjacent to the tendon of flexor carpi ulnaris muscle (FCUm)
		Distal distance between stimulation site and G1: 8–10 cm (the same distance is used for both the median and ulnar studies)
Test 4 – Median sensory palmar study	Middle finger – ring electrodes were used with G1 placed over the PIPj and G2 placed over the DIPj	Stimulation in the palm, on a line drawn from the site of MN
		Stimulation at the wrist (in test 2) to the middle finger at a fixed distance of 7 m from G1
Test 5 – Median vs. ulnar – palmar mixed nerve study (palm-difference)	Median nerve – median nerve at the wrist with G1 placed over the middle of the wrist between the tendons to the FCRm and PLM and G2 placed 3–4 cm proximally	Median nerve – median nerve in the palm: 8 cm from the G1 on a line drawn from the median wrist to the web space between the index and middle finger
	Ulnar nerve – ulnar nerve at the wrist with G1 placed over the medial wrist, adjacent to the FCUm tendon, and G2 placed 3–4 cm proximally	Ulnar nerve – ulnar nerve in the palm: 8 cm from the active recording electrode on a line drawn from the ulnar wrists space between the ring and little fingers
Test 6 – median vs. ulnar – digit 4 sensory study (ring-difference)	Ring finger (digit 4): ring electrodes with G1 placed over the MCPj and G2 placed distally over the DIPj	MN at the wrist: 14 cm from G1, middle of the wrist between the tendons to the FCRm and PLm
		Ulnar at the wrist: 14 cm from G1. Medial wrist, adjacent to the FCUm tendon
Test 7 – median vs. radial – digit 1 sensory study (thumb-difference)	Thumb (digit 1): ring electrodes with G1 placed over the MCPj and G2 placed distally over the DIPj	MN at the wrist: 10 cm from G1, middle of the wrist between the tendons to the FCRm and PLm
		RN at the wrist: 10 cm from G1, lateral forearm, over the radial bone

APBm, abductor pollicis brevis muscle; MN, median nerve; RN, radial nerve; UN, ulnar nerve.

CSI=palm-difference+ring-difference+thumb-difference, where,
Palm-difference=MN peak latency–UN peak latency (obtained from test 5),
Ring-difference=MN peak latency–UN peak latency (obtained from test 6),
Thumb-difference=MN peak latency–radial nerve peak latency (obtained from test 7),
(abnormal if the difference is more than 0.4ms).

To exclude MN involvement proximal to the wrist, the MN MCV along the wrist–elbow segment was evaluated as a routine in all participants. Similarly, the ulnar motor distal latency (wrist to ADMm at 7 cm), the ulnar MCV between wrist and elbow, and the ulnar sensory NCS between the wrist and little finger (at 14 cm) were performed in each participant to ensure the absence of UN involvement, polyneuropathy, or both.

Statistical analysis

All statistical analyses were performed using SPSS for Windows, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous data were expressed as mean±SD, whereas categorical data were expressed in number and percentage. The differences between the groups were determined using independent sample Student's *t*-test for continuous data or χ^2-test for categorical data. Sensitivity, specificity, positive, and negative predictive values of the EDX tests were calculated and were expressed as percentages for ease of interpretation. Receiver operating characteristic (ROC) curves were generated to assess the diagnostic accuracy of the different EDX tests in

the detection of patients with mild early ICTS, and the area under the ROC curve (AUC) was used to assess the sensitivity and specificity. Statistical significance was set at a *P* value less than 0.05.

Results

A total number of 100 (72 female and 28 male) patients with mild early ICTS and 100 (72 female and 28 male) matched healthy controls were invited to participate in the present study. The average age of the CTS patients was 49.6±9.6 years (ranged from 36 to 65 years), and the average age of the controls was 49.5±8.9 years (ranged from 35 to 56 years). The two groups were matched for age and sex. A total of 62 patients had unilateral CTS (44 had right-sided CTS and 18 had left-sided CTS) and 38 patients had bilateral CTS in whom only the hands with mild CTS were examined in the current study. In patients with bilateral CTS, the mild clinical symptoms were in 27 and 23 right and left hands, respectively. Therefore, a total of 109 hands (68 right hands and 41 left hands) with symptoms consistent with mild ICTS, as well as 100 hands from controls, were clinically examined and underwent EDX evaluation.

The duration of CTS in the examined hands in the patient group ranged from 3 to 8 months with an average of 5.6±1.8 months. Of the 109 hands that were subjected to EDX examination, we found that 77 (70.6%) hands had nocturnal painful dysthesia in MN distribution, whereas 41 (37.6%) hands had activity-related painful dysthesia. Forty-seven hands (accounting for 43.1%) had sensory deficit in MN distribution, and 59 (54.1%) hands had impaired two-PD in MN distribution. Phalen's test and Tinel's test were positive in 88.1% (*n*=96) and 20.2% (*n*=22), respectively, in the hands that were subjected to EDX examination.

The DML of the MN was significantly longer in the hands with mild CTS compared with the controls (3.94±0.46 vs. 3.79±0.43 ms respectively, *P*=0.016). The amplitude of the CMAP of the MN in the hands with mild CTS was significantly lower than in the hands of controls (10.3±3.9 vs. 11.4±3.8 mV, respectively, *P*=0.041), whereas the MN conduction velocity did not differ significantly between the two groups. The distal sensory latency (DSL) of the MN was also significantly longer in the hands with mild CTS compared with the controls (3.27±0.25 vs. 3.16 ±0.37 ms, respectively, *P*=0.012). Moreover, the SNAP amplitude of the MN in the hands with mild CTS was significantly lower than the control hands (39.91±21.54 vs. 51.11±32.71 μV, respectively, *P*=0.004). On the other hand, the DML and the DSL of the UN did not differ significantly between the hands of the two groups.

Table 2 demonstrates the diagnostic value of the EDX motor and sensory findings of the MN in diagnosis of CTS. The abnormal DSL of the MN had the highest sensitivity among these tests (90.83%), whereas the abnormal DML comes second with a sensitivity that is greatly lower than that of DSL (43.12%). The abnormal DSL had also the highest positive predictive value (PPV) (=97.06%) and negative predictive value (NPV) (63.9%). The abnormal SNAP had a sensitivity of 40.37%, whereas the abnormal amplitude of the

Table 2 Diagnostic value of the electrodiagnostic motor and sensory findings of the median nerve in diagnosis of carpal tunnel syndrome

	Abnormality					
	Criteria	Sensitivity	Specificity	PPV	NPV	AUC
DML	>4.2	43.12	96.00	92.16	60.76	69.6
Amplitude of CMAP	<4	25.69	97.00	90.32	54.49	61.3
DSL	>3.5	90.83	97.00	97.06	90.65	93.9
SNAP	<20	40.37	96.00	91.67	59.63	68.2

AUC, area under the curve; DML, distal motor latency; DSL, distal sensory latency; NPV, negative predictive value; PPV, positive predictive value; SNAP, sensory nerve action potential.

Table 3 Comparison of the electrodiagnostic internal latency difference between hands with mild carpal tunnel syndrome and hands of controls

	Hands with mild carpal tunnel syndrome (mean±SD)	Hands of controls (mean±SD)	*t*	*P*
Motor-difference (ms)	0.47±0.03	0.43±0.04	4.141	<0.001
Palm-difference (ms)	0.63±0.2	0.16±0.1	14.100	<0.001
Ring-difference (ms)	0.96±0.6	0.14±0.1	9.043	<0.001
Thumb-difference (ms)	0.95±0.3	0.25±0.07	6.166	<0.001

CMAP of the MN had the lowest sensitivity among the parameters of the MN (25.69%).

Table 3 compares the internal latency difference between hands with mild CTS and hands of controls. The motor-difference was significantly higher in the hands with mild CTS than in the hands of controls (0.47±0.03 vs. 0.43±0.04, respectively, $P<0.001$), the palm-difference was significantly higher in the hands with mild CTS than in the hands of controls (0.63±0.2 vs. 0.16±0.1, respectively, $P<0.001$), the ring-difference was significantly higher in the hands with mild CTS than in the hands of controls (0.96±0.6 vs. 0.14±0.1, respectively, $P<0.001$), and the thumb-difference was significantly higher in the hands with mild CTS than in the hands of controls (0.95±0.3vs. 0.25±0.07, respectively, $P<0.001$).

Table 4 demonstrates the diagnostic value of the EDX internal latency differences in the diagnosis of CTS.

The TLI was significantly lower in the hands with mild CTS than in the hands of controls (0.38±0.03 vs. 0.42±0.04, respectively, $P<0.001$). The CSI was significantly higher in the hands with mild CTS than in the hands of controls (1.17±0.09 vs. 1.07± 0.10, respectively, $P<0.001$).

Table 5 demonstrates the TLI and CSI in the diagnosis of CTS. The sensitivity was 89.91% for the recognition of cases with CTS; however, it has low specificity (=58%). The CSI at the cutoff point of 0.9 had a lower sensitivity than TLI (=93.49%), but had a high specificity (=96%). The CSI at the cutoff point of 1.1 had a sensitivity of 81.65% but with a specficity of 100%, indicating that none of the control hands in this study had a CSI of 1.1 or more. The CSI at the cutoff point of 1.1 had the highest PPV (=100%), whereas the CSI at the cutoff point of 1.1 had the highest NPV (=84.21%).

As regards the diagnostic ability of the TLI and CSI in the diagnosis of cases with mild CTS, the CSI test at the cutoff point of 1.1 had the highest AUC (=90.8%), with the CSI test at the cutoff point of 0.9 coming next (AUC=89.7%), whereas the TLI had an AUC of 66%.

Table 4 Diagnostic value of the electrodiagnostic internal latency differences in diagnosis of carpal tunnel syndrome

	Abnormality					
	Criteria	Sensitivity	Specificity	PPV	NPV	AUC
Motor-difference	>0.4	83.49	97.00	96.81	84.35	90.2
Palm-difference	>0.3	81.65	98.00	97.80	83.05	89.8
Ring-difference	>0.4	93.49	98.00	97.85	84.48	95.8
Thumb-difference	>0.5	93.49	98.00	97.85	84.48	95.8

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value.

Table 5 Diagnostic value of the terminal latency index and combined sensory index in diagnosis of carpal tunnel syndrome

	Abnormality					
	Criteria	Sensitivity	Specificity	PPV	NPV	AUC
TLI	<0.3	89.91	58.00	70.00	84.06	66.0
CSI	>0.9	83.49	96.00	95.79	84.21	89.7
CSI	>1.1	81.65	100	100	83.33	90.8

AUC, area under the curve; CSI, combined sensory index; NPV, negative predictive value; PPV, positive predictive value; TLI, terminal latency index.

Table 6 Diagnostic value of the electrodiagnostic tests in patients with clinical evidence for carpal tunnel syndrome but with normal distal motor latency and distal sensory latency

	Abnormality (%)					
	Criteria	Sensitivity	Specificity	PPV	NPV	AUC
Motor-difference	>0.4	60	97	66.7	96.04	79.9
Palm-difference	>0.3	80	98	80	98	89
Ring-difference	>0.4	80	98	80	98	89
Thumb-difference	>0.5	80	98	80	98	89
TLI	<0.3	70	58	14.3	95.1	59.3
CSI	>0.9	8	96	66.7	97.9	85.2
CSI	>1.1	90	100	100	99	97.3

AUC, area under the curve; CSI, combined sensory index; NPV, negative predictive value; PPV, positive predictive value; TLI, terminal latency index.

The best sensitivity, specificity, PPV, and NPV were obtained by the CSI test (at cutoff point >1.1). The CSI had also the best AUC, indicating the high ability of this test in the diagnosis of cases with early CTS who also had normal DML and DSL, as shown in Table 6.

Discussion

This study was designed to identify the most appropriate approach with regard to patients with mild early ICTS among the large number of EDX tests.

The first main finding of this study is that the ring-difference and thumb-difference had the highest sensitivity followed by the DSL of the MN. These results agreed with those of Kodama *et al.* [26].

In another study, the ring-difference test was more sensitive than the motor-difference test in the early CTS (77 and 10%, respectively) [27]. Our results agreed for this higher sensitivity of ring-difference in comparison with the DML of the MN despite the discrepancy for the values of sensitivity obtained by them. This discrepancy was attributed to the difference of type of enrolled patients, as 50% of the hands investigated in their study had normal median DML and normal or borderline DSL from index finger stimulation.

In 2006, Sheu and his colleagues [28] assessed four EDX tests in 131 hands with mild CTS and 136 control hands and they reported that the TLI had the highest sensitivity among the EDX tests in the diagnosis of early CTS. Moreover, the values for sensitivity of all these tests were lower than ours. These results disagreed with those of ours. This discrepancy comes from the in abnormality criteria for the EDX tests. The cutoff point or the abnormal TLI used in our study was less than 0.3 versus less than 0.34 used in the other study. The authors derived the normal cutoff point for all EDX tests in their study by calculation of mean +2 SD for the latency difference tests and by mean −2 SD for the TLI.In the present study, the motor-difference sensitivity was 83.49% compared with 43.12% for the DML. The higher sensitivity of the motor-difference test in comparison with the DML in cases who had mild CTS was also reported by several previous studies [26,29–32]. In agreement with our results, there were two studies [33,34] that confirmed our findings; they reported that the sensitivity of the motor-difference test in hands with early CTS was 92.8 and 86.1%, respectively.

Conflicting results have been obtained as regards the sensitivity of the TLI in the diagnosis of early mild CTS. Simovic and Weinberg [35] reported a high degree of sensitivity of the TLI in the diagnosis of mild CTS. The sensitivity of the TLI in this study was 81.5%, which was similar to ours but the DSL was more sensitive than TLI. Another study concluded that TLI is a sensitive test in the diagnosis of CTS and the sensitivity was 79.3% in hands of CTS patients less than 40 years of age and 93% in hands of CTS patients more than 40 years of age [36].

Our study had also shown that the best sensitivity, specificity, PPV, and NPV was obtained by the CSI test (at cutoff point >1.1). The CSI had also the best AUC, indicating the high ability of this test in the diagnosis of cases with early CTS who also had normal DML and DSL. The high specificity of CSI test was in accordance with that of Robinson *et al.* [37].

This is an area of future research. We recommend that future research should explore whether the CSI technique identifies patients with CTS patients when the standard tests reveal normal values in a larger number of patients.

Conclusion

CSI and its individual components appears as the best EDX test that helps in the diagnosis of patients with early and mild ICTS. CSI is also particularly helpful in patients with early mild CTS when the standard EDX tests (DML and DSL of the MN are normal).

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Conflicts of interest

There are no conflicts of interest.

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