Original Article

Comparison of high-resolution sonography and electrophysiology in the diagnosis of carpal tunnel syndrome

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Abstract

Background: The diagnostic accuracy of high-resolution ultrasonography (HRUS) in comparison to electro-diagnostic testing (EDX) in carpal tunnel syndrome (CTS) is debatable. **Objective:** The aim of this study was to compare the diagnostic accuracy of HRUS with EDX in patients with various grades of CTS and CTS associated with peripheral neuropathy (CTS + PNP). **Materials and Methods:** A prospective cohort of 57 patients with possible CTS was studied along with matched controls. The cross-sectional area (CSA) of the median nerve at the inlet of carpal tunnel was assessed by a sonologist blinded to the clinical and EDX data. Palm wrist distal sensory latency difference (PWDSLD), second lumbrical-interosseus distal motor latency difference (2LIDMLD) and CSA were compared in patients with different grades of severity of CTS and CTS+PNP. **Results:** Total 92 hands of 57 patients met the clinical criteria for CTS. Mean CSA at the inlet of carpal tunnel was 0.11 ± 0.0275 cm^2. It had the sensitivity, specificity, positive predictive value and negative predictive values of 76.43%, 72.72%, 89.47% and 68%, respectively ($P < 0.0001$). Overall, HRUS had good correlation with PWDSLD and 2LIDMLD electro-diagnostic studies in all grades of CTS and CTS + PNP. **Conclusion:** HRUS can be used as a complementary screening tool to EDX. However, EDX has been found to be more sensitive and specific in mild CTS.

Key Words

Carpal tunnel syndrome, electro-diagnostic test, high-resolution sonography

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Ann Indian Acad Neurol 2015;18:219-225

Introduction

Carpal tunnel syndrome (CTS) is the most common entrapment neuropathy.[1,2] It is the commonest occupational disease affecting the peripheral nerves.[3] The prevalence of CTS has been estimated to be 2.7 to 5.8% in general adult population.[4,5] It accounts for 7% of all the peripheral nerve disorders and 90% of all entrapment neuropathies.[6]

The diagnosis of CTS is usually based on clinical and electrophysiological findings. It has been concluded that median sensory conduction studies are more sensitive than median motor conduction studies for diagnosis of CTS. Electro-diagnostic studies (EDX) have a false negative rate with sensitivities ranging from 49% to 86%.[7] Moreover, these methods provide no morphologic information regarding the median nerve and possible etiologic factors.[7] The diagnosis of CTS using standard EDX remains difficult in patients with very mild or severe CTS and CTS associated with polyneuropathy (CTS+PNP) when median nerve sensory and motor potentials are indeterminate.[8] Second lumbrical (2L) is relatively spared in severe CTS, as the motor fibers innervating the lumbrical are centrally located in the median nerve.[9,10] Difference between distal median motor latency recording from the second lumbrical and distal ulnar motor latency recording from the underlying interossei is a sensitive and specific nerve conduction technique in the diagnosis of CTS.[7,9-12]

The role of conventional radiology in imaging the nerves has been limited. There are many studies emphasizing the role of imaging in the diagnosis of CTS.[13-17] It has been shown that high-resolution ultrasonography (HRUS) is very useful where EDX has been equivocal and in assessment of recurrent

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DOI: 10.4103/0972-2327.150590

or unrelieved symptoms after surgical carpal tunnel release. A reliable diagnosis of CTS could be made sonographically, mainly based on an increase in cross-sectional area (CSA) of the median nerve at the level of the Pisiform or Hamate bone.[18] However, there are few studies that compare the diagnostic capabilities of sonography to those of EDX, because the latter was applied as the gold standard. Several other reports on the possible extra value like anatomical details of sonography in CTS are considered.[18] Magnetic resonance image is superior to HRUS[14] but it is an expensive, time-consuming procedure with limited availability. However, low cost and less time requirement favor the use of HRUS as the initial imaging study in evaluating the CTS. In a previous study from the same center, it was found that there was no correlation between median nerve sensory conductions and HRUS findings (AP diameter of median nerve) in the diagnosis of CTS (unpublished data). Data on the diagnostic value of HRUS in subcategories of CTS and CTS with peripheral neuropathy (CTS + PNP), in which EDX is equivocal; is limited. Therefore, the authors prospectively studied the diagnostic value of HRUS and EDX in patients, who were referred to the neurology outpatient clinic with the symptoms of CTS and CTS + PNP.

Materials and Methods

Study site and ethics

This was a prospective case control study. The study was performed between January 2011 and December 2011 at Nizam's Institute of Medical Sciences, Hyderabad, South India. It was initiated as per good clinical practice guidelines after obtaining permission from the institutional ethics committee and informed consent from the participants.

Inclusion and exclusion criteria

The study included 57 consecutive patients (92 hands) with the clinical diagnosis of CTS and 50 (100 hands) age- and sex-matched healthy controls. All the study subjects and controls underwent clinical, electrophysiologic and ultrasonographic examinations. The CTS cases were diagnosed by experienced neurologists based on clinical features. Subjects fulfilling the consensus criteria for diagnosis of CTS were included for further electro-diagnostic evaluation. Criteria for clinical diagnosis of CTS[19] were 1) history of nocturnal or activity-related pain or dysesthesia limited to the hand 2) sensory deficit in the median nerve distribution 3) isolated weakness or atrophy of abductor pollicis brevis (APB) and 4) positive Phalen's or Tinel's sign. CTS were diagnosed when criteria 1 and one or more of criteria 2 to 4 were fulfilled. Patients with clinical evidence of CTS in addition to polyneuropathy (PNP) were also included. The diagnosis of PNP was based on attenuation or loss of tendon reflexes, distal symmetrical paresthesia and sensory decrease in the lower and upper limbs, reduced motor conduction velocity of <45 m/s in the median nerve and of <47 m/s in the ulnar nerve, and reduced sensory nerve conduction velocity of <42 m/s in both nerves and reduced sural amplitude.[8]

Patients with history or clinical examination or investigations suggestive of cervical radiculopathy (C_6, C_7, C_8), brachial plexopathy, proximal median neuropathy, motor neuron disease, spondylotic myelopathy, syringomyelia, stroke, multiple sclerosis and polyneuropathy without fulfilling CTS criteria were excluded. Acute and chronic demyelinating polyneuropathy (AIDP and CIDP) were also excluded in view of the possibility of focal conduction blocks in the distal part of the nerves. A screening history and examination were performed on control subjects to rule out CTS. All the standard EDX studies for CTS, including 2LIDMLD were performed on them.

EDX studies

EDX studies were performed using Nicolet Viking IV system EMG machine. All studies were performed in a warm room. The skin temperature was maintained at >33°C. The median and ulnar nerve conduction studies of both upper limbs and tibial, peroneal and sural nerve conduction studies of one or both lower limbs were performed in all participants. Radial and superficial peroneal nerves were studied whenever indicated. MDML, PWDSLD and 2LIDMLD of both upper limbs were studied in all patients. 2LIDMLD was studied as it is the only test, which can possibly detect severe CTS with absent SNAP and preserved median motor response. Based on previous study of the authors,[12] it was decided to fix PWDSLD cut-off value >0.4ms and 2LIDMLD cut-off value >0.6ms to diagnose CTS.

CTS grading

Using Bland's electrophysiological grading scale[20] [Table 1] patients with CTS were classified into mild [Grades1 and 2], moderate [Grades 3 and 4], and severe [Grades 5 and 6] grades. The sensitivities of 2LIDMLD, PWDSLD and HRUS were compared in these different grade sub-groups.

HRUS

HRUS was done using Philips Envisor 500 ultrasonogram scanner with a 7.5 MHz linear-array transducer by a sonologist who was blinded to the clinical and EMG data. The study subjects were seated facing the examiner. The arms were extended, wrists were rested on a hard flat surface, and forearms were supinated and the fingers were semi-extended. The transverse images of the median nerve CSA were then obtained at carpal tunnel inlet at the level of pisiform bone near wrist crease. After this, CSA of the median nerve was determined by outlining the nerve contour by the internal rim using area measurement software (continuous boundary trace) of the ultrasound system [Figure 1]. For each wrist, measurements were repeated five times, and the average of the eve was taken as final CSA.

Table 1: Neurophysiologic grading scale for CTS s

Grade	EDX Abnormality
1-Very mild	CTS detected by only PWDSLD*
2-Mild	Median DML <4.5 and sensory NCV <40
3-Moderately severe	Median DML• >4.5 and <6.5 with preserved SNAP
4-Severe	Median DML >4.5 and <6.5 with absent SNAP
5-Very severe	Median DML >6.5 with CMAP >0.2 mv
6-Extremely severe	Median CMAP from APB <0.2 mv

*PWDSLD = Palm wrist distal sensory latency difference, •DML = Distal motor latency

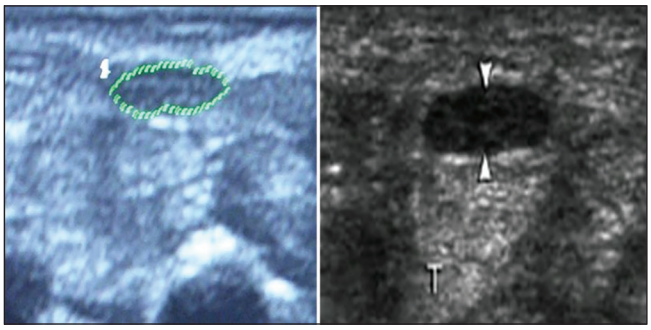

Figure 1: HRUS of normal and abnormal median nerve at the inlet of carpal tunnel

Statistics

Data were entered in a spreadsheet and statistical evaluation was done using SPSS 14 software. Descriptive statistics, including mean and standard deviation [SD] were applied to each nerve conduction value and differences in median and ulnar latencies. Statistical evaluation was obtained using paired Student's '*t*' test within a single group and an unpaired Student's '*t*' test within different groups. Receiver operating characteristics (ROC) curves and linear regression curves were then plotted to determine the accuracy and correlation of the tests, respectively. For comparison of proportions, the chi-square (χ^2) test was used. The level of significance in all analyses was set at 0.05. Spearman rank correlations and corresponding p-values were used to evaluate the relationships between ordinal and other quantitative variables.

Results

Demography

In the control group, a total of 50 subjects (100 hands) were examined by PWDSLD, 2LIDMLD in addition to the routine EDX studies. The age, gender and side of the disease had no statistically significant effect on the test results (P = 0.78, 0.09 and 0.12, respectively). The mean values for PWDSLD and MDML were 0.14 ± 0.08 ms and 3.38 ± 0.35 ms, respectively. Abnormal values for 2LIDMLD, PWDSLD and MDML were ≥0.6 ms, >0.4 ms and > 4.08 ms, respectively. In the patient group, a total of 57 consecutive patients (92 wrists) with clinical symptoms and signs of CTS were included in the study. There were 38 women and 19 men. Their mean age was 48.7 ± 11.7 years (range, 24 to 80 years) with a mean duration of symptoms of 54.69 ± 102.82 weeks. Out of 57 patients, 35 had bilateral CTS and 22 had unilateral CTS (right 15, left 7). CTS were associated with diabetes mellitus in 14 patients (26 hands) and hypothyroidism in 7 (12 hands). CTS associated with peripheral neuropathy (CTS + PNP) was observed in 9 hands with diabetes mellitus and 2 hands with uremic neuropathy. CTS was idiopathic in 21 patients (41 hands) [Table 2]. The mean 2LIDMLD in patient group was 1.35 ± 1.07 ms and mean PWDSLD was 1.72 ± 1.10 ms [Table 3]. The means of 2LIDMLD and PWDSLD showed statistically significant difference between patient and control groups on Student's '*t*' test (P < 0.0001). 2LIDMLD had the sensitivity and specificity of 88.23% and 94.36%, respectively and PWDSLD had the sensitivity and specificity of 90.53% and 96.12%, respectively. The positive predictive value, negative predictive value of 2LIDMLD was 96% and 86.6%, respectively. The positive predictive value and negative predictive value of PWDSLD was 96.2% and 80%, respectively.

Table 2: Demographic data of patients with CTS

Parameter	*N* = 57 (%)
Age in years mean±SD (range)	48.7±11.9 (24-80)
Gender (M:F)	19:38
Mean duration of CTS (weeks)	54.691± 102.8
Side of the CTS	
Right	15 (26.3)
Left	7 (12.3)
Bilateral	35 (61.4)
Diabetes	14 (24.5)
Arthritis	15 (26.3)
Hypothyroidism	7 (12.3)
Idiopathic	21 (36.8)
Polyneuropathy	6 (8.7)
Diabetes	5
Uremia	1

Table 3: Mean median nerve parameters by various techniques

Test	Controls-100 hands Mean + SD	Cases-92 hands Mean + SD	*P*-value	95% CI
2LIDMLD	0.15+0.25 ms	2.29±1.72 ms	<0.0001	1.80-2.46
PWDSLD	0.14+0.08 ms	0.94±0.63 ms	<0.0001	1.62-2.50
HRUS	0.084±0 .01 cm^2	0.11±0.02 cm^2	<0.0001	0.10-0.116

HRUS

A total of 100 hands in the control group were scanned. There was no difference between right and left hands of males and females for median nerve CSA at the inlet of carpal tunnel. The mean CSA in control group was 0.084 ± 0 .01 cm^2. In patient group, CSA was measured in 92 hands with the mean CSA of 0.11 ± 0.02 cm^2 with the range 0.05-0.19 cm^2 [Table 3]. Mean CSA in patient group was significantly higher compared to control group (P < 0.0001). Using the ROC analysis, cut-off CSA was found to be 0.11 cm^2 (area under the curve was 0.777, P < 0.0001) [Figure 2]. This cut-off CSA showed the sensitivity of 76.43%, specificity of 72.72%, positive predictive value of 89.47% and negative predictive value of 68% in patient group [Table 4]. There was a strong relationship between HRUS and SPW (PWDSLD) (Spearman r =0.71, P < 0.0001) [Table 5 and Figure 3].

Electrophysiologically, 19 patients out of 57 (33.3%) were classified into mild CTS (electrophysiological grade 1 + 2). Mean CSA in this group was 0.10 ± 0.017 cm^2. Moderate CTS (grade 3 + 4) with the mean CSA of 0.11 ± 0.02 cm^2 was observed in 26 patients out of 92 (45.6%). Remaining 12 patients (21%) had severe CTS (grade 5 + 6) with the mean CSA of 0.127 ± 0.03 cm^2 [Table 6]. The sensitivity of 2LIDMLD, PWDSLD and HRUS was 82%, 79% 54.8%, respectively in mild cases; 92%, 90% and 88.7%, respectively in moderate cases and 97%, 96% and 95%, respectively in severe CTS [Table 7 and Figure 4].

CTS associated with PNP was diagnosed in 6 patients (11 hands). Severe CTS was present in 70% of the symptomatic

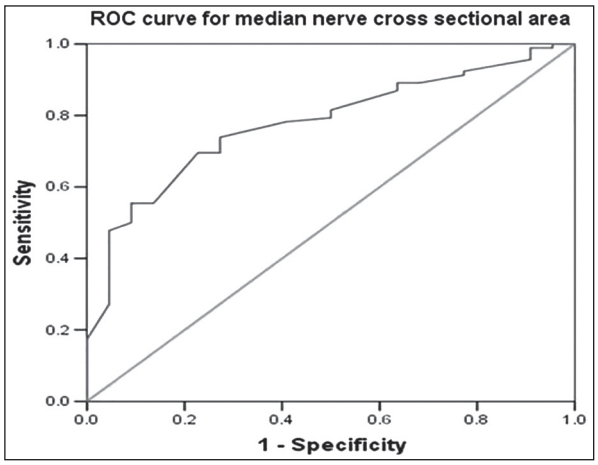

Figure 2: ROC for HRUS CSA of median nerve at inlet of carpal tunnel >0.11 cm²

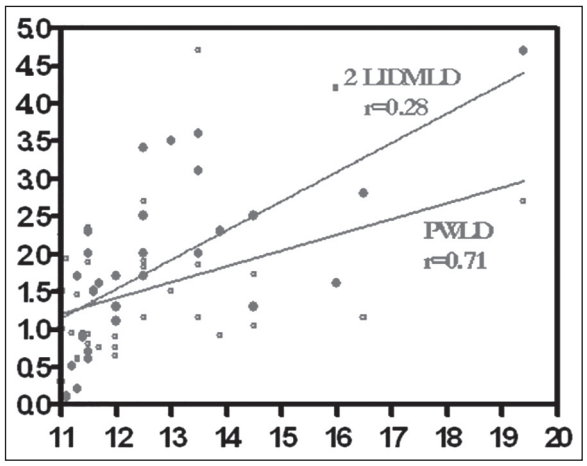

Figure 3: Linear regression analysis for HRUS, PWDSLD and 2LIDMLD

Table 4: Sensitivity and specificity of EDX and HRUS

Test	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
2LIDMLD	88.23	94.36	96	86.6
PWSDLD	90.53	96.12	96.2	80
HRUS	76.43	72.72	89.47	68

Table 5: Correlation of EDX and HRUS in patients

Correlation of HRUS	PWSDLD	2LIDMLD
Number of XY Pairs	57	57
Spearman 'r'	0.71	0.28
95% confidence interval	0.47 to 0.85	0.08 to 0.58
P value (two-tailed)	< 0.0001	0.0175

hands in this group. This was considerably higher than the proportion of severe disease (26%) in the total number of symptomatic hands. PWDSLD alone was diagnostic in only 5 hands (50%), whereas 2LIDMLD and MDML were diagnostic in 10 hands (90%) ($P = 0.05$). HRUS was positive in 10 hands

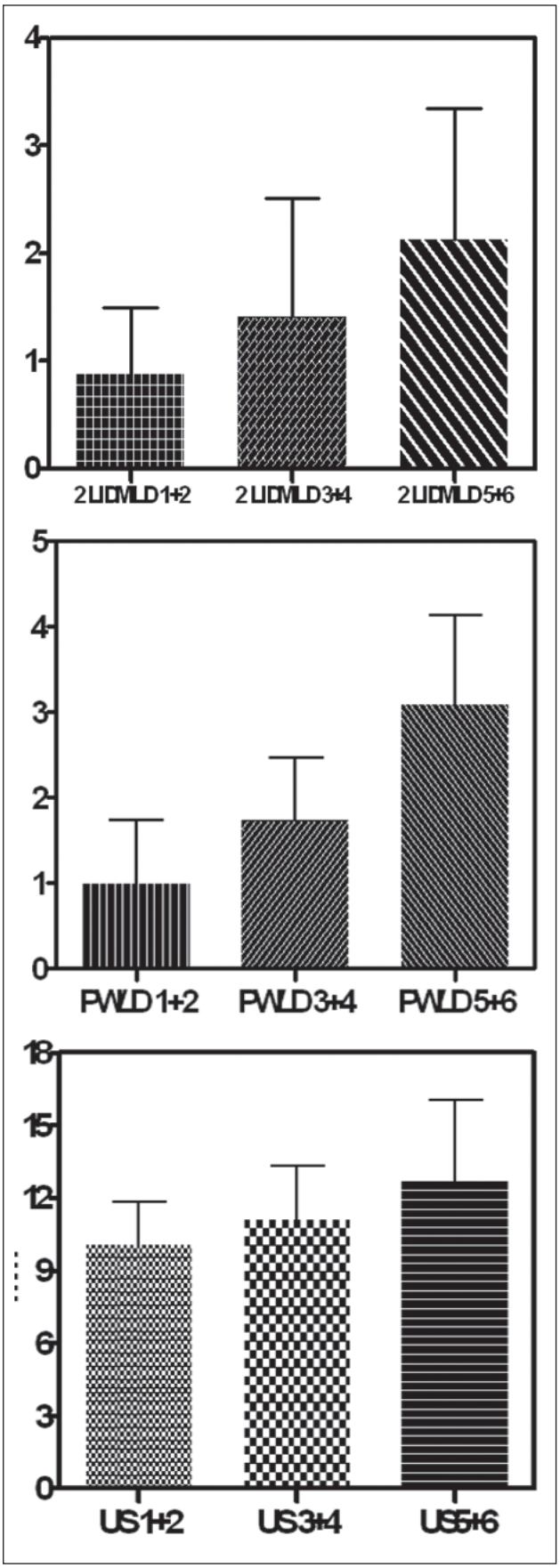

Figure 4: HRUS, SPW and 2LIDMLD in different grades of CTS

Table 6: HRUS, PWSDLD and 2LIDMLD in different grades of CTSs

statistical parameters	CTS grade 1 + 2			CTS grade 3 + 4			CTS grade 5 + 6		
	PWSDLD	2LIDMLD	HRUS	PWSDLD	2LIDMLD	HRUS	PWSDLD	2LIDMLD	HRUS
Number of values	19	19	19	26	26	26	12	12	12
Minimum	0.1	0.06	5.7	0.6	0.16	6.6	1.6	0.02	7.6
25% Percentile	0.5	0.355	9.05	1.3	0.75	9.6	2.4	1.3	10
Median	0.9	0.91	10	1.7	1.15	11.5	2.8	1.85	12.5
75% Percentile	1.25	1.345	11.25	2	1.695	12.5	3.6	2.7	14.5
Maximum	3.40	2.25	13.9	3.7	4.2	16	5.1	4.7	19.4
Mean	0.98	0.88	10.08	1.74	1.41	11.11	3.09	2.13	12.68
Std. Deviation	0.75	0.62	1.75	0.73	1.11	2.21	1.05	1.22	3.34
Std. Error	0.16	0.14	0.38	0.14	0.22	0.44	0.32	0.37	1.01
Lower 95% CI of mean	0.63	0.59	9.27	1.44	0.95	10.2	2.38	1.31	10.44
Upper 95% CI of mean	1.31	1.16	10.87	2.04	1.87	12.02	3.80	2.95	14.92

out of 11 with CTS + PNP. Pearson's correlation showed that HRUS had good correlation with MPW (r = 0.671) [Table 8].

Discussion

HRUS has emerged as a feasible, simple, relatively low-cost, rapid, accurate and noninvasive imaging method for evaluating the median nerve in CTS. Despite that, there are controversies about the usefulness of this diagnostic test. Few authors have proposed an algorithm using initial HRUS in suspected CTS and secondary EDX performed only when US results were negative.[21] US could be used to grade the severity of CTS and to detect space-occupying lesions or anatomical variation of median nerve.[17] In the present study, it was possible to correlate HRUS findings and EDX findings based on CTS grading. It showed that the accuracy of HRUS was similar to that for EDX in all grades of CTS and CTS + PNP in patients with a clinical diagnosis of CTS.

In this study, the mean CSA cut-off value of 0.11 cm^2 at the inlet of carpal tunnel had a good sensitivity and specificity which is comparable to previous studies.[22-24] In the literature, four criteria are used to diagnose CTS by sonography:

1. Increase in cross-sectional area at the level of the pisiform bone;
2. Increase in the cross-sectional area at the level of the pisiform bone compared with the cross-sectional area at the level of the distal radius (swelling ratio);
3. Increase in the flattening ratio at the level of the hook of the Hamate; and
4. Palmar bowing of the flexor retinaculum by sonography.[13-17,21,22,25,26]

After reviewing the literature on sonography in CTS, it was found that the most reliable test was an increase in the CSA at the level of the pisiform bone [18]. Hence this parameter was used in the present study. It was observed that there exists a good diagnostic accuracy with median nerve CSA at the level of pisiform bone, in patients with CTS and a good correlation between HRUS and EDX. This correlation was consistent in all grades of CTS and CTS + PNP. Other studies have shown that ultrasound measurements have a good inter and intra-observer reliability. Few authors directly compared the measurements of the median nerve obtained sonographically with the measurements found in anatomical cross-sections in cadaver limbs. They concluded that ultrasound is a precise method for determining these measurements. This was later confirmed by other studies.[26,27] The cut-off values used for EDX in this study are comparable to those cited in previously published literature. Overall, sensitivity and specificity of 2LIDMLD and PWDSLD were similar to those described by other authors.[7,11,28-31]

Table 7: Sensitivity of diagnostic tests in various CTS sub-groups

CTS grade	Sensitivity		
	PWDSLD (%)	2LIDMLD (%)	HRUS (%)
Mild	79	82	54.8
Moderate	90	92	88.7
Severe	96	97	95

Table 8: Correlation of HRUS, PWDSLD and 2LIDMLD in CTS + PNP

Parameter	Correlation	HRUS	PWDSLD	2LIDMLD
HRUS	Pearson Correlation	1	−.043	.671 (*)
	Sig. (2-tailed)		.900	.024
	N	11	11	11
PWDSLD	Pearson Correlation	−.043	1	−.346
	Sig. (2-tailed)	.900		.297
	N	11	11	11
2LIDMLD	Pearson Correlation	.671 (*)	−.346	1
	Sig. (2-tailed)	.024	.297	
	N	11	11	11

*Correlation is significant at the 0.05 level (2-tailed)

In mild CTS, PWDSLD and 2LIDMLD were equally sensitive but HRUS was less sensitive. Thus, it can be inferred that HRUS may be negative in mild CTS and such patients require mandatory electrophysiological studies. Previous studies also mentioned that HRUS may not be ideal for diagnosing mild CTS and those patients with neuropathy might benefit more from this test. HRUS can give an idea about the underlying pathology, or the extent of involvement of the tendon sheath.[32,33] In moderate grade CTS, comparable high sensitivity and specificity were observed for these three tests.

In the severe CTS group, all these tests had high sensitivity. HRUS had a good correlation with the severity of CTS. A strong relationship between HRUS and PWDSLD was found in all grades of CTS. Though 2LIDMLD and HRUS were comparable but statistically significant correlation was noted in severe CTS only. The incidence of severe CTS was more common in patient hands associated with polyneuropathy, when compared to subjects with CTS without polyneuropathy (70% vs. 26%). Hence, this study documented good correlation between HRUS and 2LIDMLD in CTS + PNP. This suggests that CTS tends to be more severe on neurophysiological grading when associated with polyneuropathy. Other authors also showed similar association.[8] Median nerve CSA offers high diagnostic accuracy as indicated by high correlation with the present standard EDX. However, patients with a negative sonogram can have a positive EDX and vise versa. Sonography can be negative in patients with a short duration of symptoms. Therefore, this study coincides with the recommendations of previous authors that HRUS may be the first diagnostic procedure considered in patients with typical CTS.[16] EDX should remain the first diagnostic method in patients with atypical symptoms, in which the differential diagnosis involves a C6/C7 radiculopathy, an underlying polyneuropathy, a sensory neuropathy or a proximal lesion of the median nerve. Limitations of the present study were small sample size of CTS + PNP group. Also, the anatomical abnormalities were not studied.

Conclusion

The diagnostic accuracy of HRUS correlates well with the present standard EDX in all grades of CTS and CTS+PNP and they complement each other. However, EDX should be the preferred diagnostic modality for mild CTS. HRUS may be a screening tool in CTS because it is painless, easily accessible, requires minimal time and preferred by the patients, and it also detects structural abnormalities that may have therapeutic implications. Further studies with large sample size of CTS+PNP are required to confirm these findings.

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How to cite this article: Kanikannan MA, Boddu DB, Umamahesh, Sarva S, Durga P, Borgohain R. Comparison of high-resolution sonography and electrophysiology in the diagnosis of carpal tunnel syndrome. Ann Indian Acad Neurol 2015;18:219-25.
Received: 11-07-14, **Revised:** 07-10-2014, **Accepted:** 07-10-14
Source of Support: Nil, **Conflict of Interest:** None declared.