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Radiology Section

Ultrasound Assessment of Carpal Tunnel Syndrome in Comparison with Nerve Conduction Study: A Case-control Study

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ABSTRACT

Introduction: Carpal Tunnel Syndrome (CTS) is the entrapment neuropathy which is diagnosed based on the clinical history, examinations and the electrophysiological findings. The Cross-sectional Area (CSA) measurement of the median nerve has emerged as an alternative to Nerve Conduction Studies (NCS) for diagnosis of CTS. This study was done to correlate NCS and Ultrasonography (USG) in clinically diagnosed CTS patients.

Aim: To evaluate the diagnostic value of Cross-sectional Area (CSA) of median nerve at carpal tunnel inlet in patients with clinically and NCS confirmed Carpal Tunnel Syndrome (CTS) and to assess severity of the syndrome by NCS and its correlation with USG results.

Materials and Methods: This was a hospital based, case-control study done on a total of 109 patients of CTS and analysed during the period from June 2017 to June 2019. Total 203 hands of the patients with abnormal NCS formed case group while 101 hands from healthy volunteers constituted the control group. All the patients underwent neurological evaluation by Boston Carpal Tunnel Questionnaire (BCTQ) and were divided into mild, moderate and severe according to the score. An electromyography machine was used to perform electrophysiological studies of both the limbs in all subjects. CTS was diagnosed electro-diagnostically based on the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) guidelines and were classified as mild (Grades 1 and 2), moderate (Grades 3 and 4), and severe (Grades 5 and 6) grades using Bland's electrophysiological grading scale. USG was performed for all the subjects and all the data of various investigations was analysed using Statistical Package for Social Sciences (SPSS) version 22.0 software. Chi-square test and Mann Whitney U-test were used as test of significance for qualitative data.

Results: The mean age of subjects was 44.38±9.561 years. Strongly significant association was observed in BCTQ symptom, functional and total scores with NCS severity grading (p-value <0.001). Moderately significant association was found between BCTQ symptom and total scores with USG severity grading (p-value<0.02). Tunnel grade and NCS grade were found significantly correlated (p-value <0.001). The mean CSA cut-off value of 8.5 mm^2 at the inlet of carpal tunnel had a good sensitivity 86.21%, specificity 83.17%, Positive Predictive Value (PPV) 91.1% and Negative Predictive Value (NPV) 75%.

Conclusion: The diagnostic accuracy of USG assessment and NCS was found to be correlated comparably and complement each other in all grades of CTS. USG, can be considered a preferable screening tool by the patients of CTS due to its painless nature and easy accessibility. It requires minimal time and many a times detects those structural abnormalities which have great therapeutic implications. In mild CTS cases, USG should always be combined with NCS for proper diagnosis as USG might give negative result.

Keywords: American association of neuromuscular and electrodiagnostic medicine, Boston carpal tunnel questionnaire, Cross-sectional area, Electrodiagnosis, Ultrasonogram

INTRODUCTION

Carpal Tunnel Syndrome (CTS) is the most common neuropathy leading to entrapment [1,2] and the most common occupation related ailment which affects the peripheral nerves [3]. CTS has been associated with many causes including chronic diseases like obesity, diabetes, arthritis, gout, hypothyroidism or occupational conditions like clerical, office or data entry or industrial construction or mining, kitchen or supermarket dealing etc. which are associated with rigid, forceful, and repetitive hand movements, uncomfortable postures, mechanical stress at the base of the palm and vibration [4,5].

Currently, the diagnosis of CTS is typically based on history, physical examination and electrophysiological findings [6-8]. The diagnosis of this condition are largely based on clinical history, examination and Electro-diagnostics (EDx), which is a combination of NCS and electromyography studies. Although NCS is useful for locating the pathology site and also to determine the severity of the condition, but still technique has limitations: it is painful, it does not allow for the visualisation of intrinsic nerve abnormalities and no information is provided about structures surrounding the nerve [9]. NCS is a technique with false negative rate with sensitivity ranging from 49-86% [10]. Previous studies [6,11-13] have shown that musculoskeletal USG, might offer diagnostic accuracy in a similar manner [14]. If the median nerve within the carpal tunnel gets compressed, it leads to nerve swelling proximally and distally to the site of compression. For a long time, USG has been considered a good diagnostic modality for proper evaluation and assessment in CTS patients.

Buchberger W et al., first showed USG comparable accuracy to Magnetic Resonance Imaging (MRI) for the diagnosis of CTS [11]. Their work was further confirmed by Altinok T et al., [15], using NCS as the reference standard. Duncan I et al., [16] showed that CSA as a diagnostic parameter is a real good criteria as compared to other USG parameters for CTS detection. Supporting this, many other previous studies established that the measurement of carpal tunnel inlet at the level of pisiform to be considered as standard [7,17-20]. Baiee RH et al., performed study on patients who had signs and symptoms of CTS as well as a positive NCS [21]. There was a significant correlation between age and severity of disease determined by NCS. Their study also observed positive correlations between the USG findings and all the other measures in NCS technique for severity of disease in Carpal Tunnel patients.

Kwon HK et al., amongst the analysed mild, moderate, and severe CTS subjects observed that the CSA of the median nerve varied significantly between the severe and moderate CTS groups and this factor was also found to correlate with EDx parameters in both severe and mild CTS wrists [22]. Kasundra GM et al., used to evaluate and compare patients with clinical and electro-diagnostic proof of CTS and healthy volunteers in the case-control design [23].

The median nerve's CSA was determined at the inlet and outlet of the carpal tunnel, and the Inlet Outlet Ratio (IOR) was estimated for each wrist. Using the IOR rather than the inlet CSA had a diagnostic benefit (p-value <0.01), according to Receiver Operating Characteristic (ROC) analysis. Optimum sensitivity and specificity in the diagnosis of CTS were obtained at IOR>1.3. They also conducted a comparative research for CTS, diagnostic modalities in cases and controls. The sensitivity of the USG was low, but the specificity was high, and the sensitivity of the MRI was moderate. BCTQ-S and NCS, as well as BCTQ-S and USG, showed a significant correlation. Kanikannan MA et al., [12] carried the study with average CSA at the carpal tunnel inlet was 0.11± 0.0275 cm^2, 76.43%, 72.72%, 89.47%, and 68%, respectively, for sensitivity, accuracy, positive predictive value, and negative predictive value (p-value-0.0001). Billakota S and Hobson-Webb LD performed the study with median nerve CSA greater than 9 mm^2 and/or a wrist-to-forearm ratio of greater than 1.4 were used to make a USG diagnosis of CTS [24]. For diagnosis, EDx studies were the gold standard. In 97.6% of EDx-confirmed CTS, USG was positive. Roghani RS et al., evaluated that 203 of the clinically diseased patients, EDx supported the best diagnostic accuracy for CTS at the CSA of tunnel inlet as 8.5 mm^2 and an inlet-to-antecubital CSA ratio of 0.65. The objective of the present study was to evaluate the diagnostic value of the CSA of median nerve at carpal tunnel inlet in patients with clinically and NCS confirmed CTS and to assess the correlation of its severity with NCS and USG assessment.

MATERIALS AND METHODS

This prospective case-control study was conducted in the Department of Neurology and Radiology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India, with clinically diagnosed cases of CTS included in the study, over a period of two years from June 2017 to June 2019. The study was approved by the Institutional Ethics Committee (Approval no.ECR/747/Inst/KA/2015).

Inclusion criteria: All patients who came to the Department of the Institute during the time period of the study and were diagnosed with CTS based on clinical and NCS according to American Association of Neuromuscular and Electro-diagnostic Medicine (AANEM) diagnostic criteria [25-27,29] were included in the study.

Age and sex matched healthy hospital staff and volunteers who had been screened for history and examination were included as control group subjects. All cases and control subjects were included after obtaining proper written informed consent.

Exclusion criteria: Patients with history of wrist surgery or fracture, any accompanying condition other than CTS, like proximal median neuropathy, cervical radiculopathy or polyneuropathy and underlying disorders associated with CTS such as, pregnancy and acromegaly were excluded from the study.

Universal sampling was followed in the study, making the total sample to 109 patients. Total 203 abnormal NCS hands formed the case group while 101 normal NCS hands formed the control group.

Neurological Evaluation

Detailed clinical history and examination with CTS provocative tests like tinels and phalens test were done. BCTQ [23] was applied to all patients, hence the assessment was done on basis of symptoms and functional status. Scores were assigned from 1 (normal) to 5 (most severe). No response to a certain question was given 0 points. Each score was calculated as the mean of the responses of the individual items. Patients were divided into three groups according to their mean score:

I. Mild (0.1-2 points),

II. Moderate (2.1-3 points),

III. Severe (3.1-5 points).

No patients showed negative results on the self-administered questionnaire. The patients who had bilateral symptoms were asked to answer two questionnaires, one for each hand separately.

Nerve Conduction Studies

The electro-physiological studies were performed on both upper limbs in all patients and control subjects utilising an electromyography machine (Neuropack X1-MEB-2300) in a shielded room. NCS were performed according to the American Association of Electro-diagnostic Medicine criteria [25-27,29]. The abnormal values of various NCS parameters [28] used in this study are depicted in [Table/Fig-1].

NCS	Abnormal value
Median SNAP peak latency	>3.7 milliseconds
SNAP amplitude	<20 microvolts
Conduction block with a SNAP amplitude decrease	>50% with wrist stimulation compared to palm stimulation
SNAP peak latency	Longer in the proximal 7 cm segment than in the distal 7 cm segment
5-cm transcarpal conduction time	>1.3 ms
Median CMAP distal latency	>4.2 ms
CMAP amplitude	<4.5 microvolts

[Table/Fig-1]: Abnormal values of various Nerve Conduction Studies (NCS) parameters used in this study.
SNAP: Sensory nerve action potentials; CMAP: Compound muscle action potential

CTS was diagnosed electro-diagnostically based on the American Association of Neuromuscular and Electro-diagnostic Medicine (AANEM) guidelines [25-27,29] and were classified into mild (Grades 1 and 2), moderate (Grades 3 and 4), and severe (Grades 5 and 6) [Table/Fig-2] using Bland's electrophysiological grading scale [30].

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

[Table/Fig-2]: Bland's Neurophysiologic grading scale for Carpal Tunnel Syndrome (CTS).
PWDSLD: Palm wrist distal sensory latency difference; DML: Distal motor latency; NCV: Nerve conduction velocity; APB: Abductor pollicis brevis

USG

High resolution USG was performed by the single radiologist, within one-week period of EDx study after blinding the operator to other tests results. A real-time scanner (Philips affinity 50) with a 8-14 MHz linear array transducer was used and transverse USG of the median nerve was performed from the distal forearm to the outlet of the carpal tunnel. The CSA measurements were performed at the inner border of the thin hyperechoic rim of the nerve (perineurium) using the manual tracing technique. The authors in the present study considered CSA values, by logistic regression model of the control group (101 hands) CSA greater than 8.5 mm^2 to be abnormal. These abnormal values of CSA measurements of the nerve were classified as: Mild- 8.5 mm^2-10.5 mm^2, Moderate- 10.5 mm^2, 13 mm^2 and Severe >13 mm^2.

STATISTICAL ANALYSIS

Data was entered into Microsoft Excel data sheet and was analysed using Statistical Package for Social Sciences (SPSS) version 22.0 (IBM SPSS Statistics, Somers NY, USA) software. Categorical data was represented in the form of frequencies (n) and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean±Standard Deviation (SD). Independent t-test or Mann Whitney U-test was used as test of significance for quantitative variables.

RESULTS

Total of 109 patients attended to Department of Neurology during the study time period fulfilling the inclusion criteria were considered for the study. Mean age was 44.38±9.561 years and age range was 16-68 years with maximum (48%) patients in 41-50 years age group. Females were 78 (71.6%) and males were 31 (28.4%). Among the 109 subjects of abnormal NCS, 94 subjects had bilateral involvement, 4.4% had right side involvement and 3% had left side involvement. Hence, a total of 203 hands were considered in analysis of abnormal group while 101 hands of normal NCS were included as controls making a total of 304 hands in this study [Table/Fig-3].

Hands		Frequency	Percent
Bilateral (94 subjects×2 hands)		188	92.6%
Unilateral (15 subjects one hand)	Right	9	4.4%
	Left	6	3%
Total (Abnormal hands)		203	100%

[Table/Fig-3]: Hand distribution in the study population.

In the present study, all NCS positive were considered cases 203 (66.8%) and controls were 101 (33.2%). Amongst the case group sample, the categorisation was observed as mild grade in 41 (20.2%), moderate grade in 110 (54.2%) and severe grade in 52 (25.6%). In this study, there was a significant association between BCTQ symptoms, functional and total grades with NCS grade (p-value <0.001) as is well evident in [Table/Fig-4].

In this study, 162 (79.8%) had abnormal tunnel findings and 41 (20.2%) had normal tunnel findings. The grading according to tunnel USG findings was observed as mild in 85 (41.9%), moderate in 42 (20.7%) and severe in 35 (17.2%). In the present study, there was significant positive correlation between BCTQ total with tunnel values i.e., with increase in BCTQ score, there was increase in tunnel values and vice versa [Table/Fig-5,6].

On clinically analysing the data, most common symptom amongst the subjects of present study was tingling and numbness in 97% subjects and the most common sign was Phalen's test in 85.20%. Tingling and numbness did not correlate with NCS and USG severity grading. Pain was noted in 31.5% population, correlated with NCS grading (p<0.001) and USG grading (p-value=0.039). Weakness was noted in 19.2% population correlated with NCS grading (p<0.001) and USG grading (p-value=0.04). Sensory disturbances were noted in 33.5% population correlated with NCS grading (p<0.001) but not with USG grading (p-value=0.076). Wasting was noted in 6.9% population correlated with NCS grading (p<0.001) but not with USG grading (p-value=0.678). Tinels sign was noted in 59.6% population which did not correlate significantly with NCS and USG grading. Phalens sign was noted in 85.2% population which correlated with NCS grading (p<0.001) and USG grading (p-value=0.557).

The severity of CTS by NCS comparing with severity by USG, that most of mild cases by NCS are mostly mild (48.8%), moderate (12.2%) and even negative (36.6%) by USG. In moderate cases by NCS most of cases are between mild (49.1%) and moderate (19.1%) by USG and in severe cases by NCS most of cases are between mild (21.2%) and moderate (30.8%) by USG. In the present study, there was strongly significant association between NCS grade and tunnel grade (p-value <0.001) [Table/Fig-7].

Grading in all study subjects		NCS grade (n=203)						p-value
		Mild (n=41)		Moderate (n=110)		Severe (n=52)		
		Count	%	Count	%	Count	%	
BCTQ symptoms grade (n=203)	Mild (n=73)	27	65.9	42	38.2	4	7.7	**<0.001**
	Moderate (n=113)	14	34.1	65	59.1	34	65.4	
	Severe (n=17)	0	0	3	2.7	14	26.9	
BCTQ functional grade (n=203)	Mild (n=140)	39	95.1	85	77.3	16	30.8	**<0.001**
	Moderate (n=1)	0	0	0	0	1	1.9	
	Severe (n=62)	2	4.9	25	22.7	35	67.3	
BCTQ total grade (n=203)	Mild (n=98)	33	80.5	59	53.6	6	11.5	**<0.001**
	Moderate (n=104)	8	19.5	51	46.4	45	86.5	
	Severe (n=1)	0	0	0	0	1	1.9	

[Table/Fig-4]: Comparison of BCTQ Symptoms, functional and total grade with NCS grade among abnormal hands.
Chi-square test used to calculate p-value; p-value <0.05 considered significant

Analysis of the data		USG tunnel grade (n=203)								p-value
		Mild (n=85)		Moderate (n=42)		Severe (n=35)		Normal (n=41)		
		Count	%	Count	%	Count	%	Count	%	
BCTQ symptoms grade	Mild	32	37.6	12	28.6	7	20	22	53.7	**0.012**
	Moderate	50	58.8	23	54.8	24	68.6	16	39	
	Severe	3	3.5	7	16.7	4	11.4	3	7.3	
BCTQ functional grade	Mild	61	71.8	24	57.1	23	65.7	32	78	0.239
	Moderate	24	28.2	17	40.5	12	34.3	9	22	
	Severe	0	0	1	2.4	0	0	0	0	
BCTQ total grade	Mild	46	54.1	15	35.7	11	31.4	26	63.4	**0.02**
	Moderate	39	45.9	26	61.9	24	68.6	15	36.6	
	Severe	0	0	1	2.4	0	0	0	0.0	

[Table/Fig-5]: Comparison of BCTQ Symptoms, functional and total grade with USG Tunnel grade among abnormal hands.
Chi-square test used to calculate p-values; p-value <0.05 considered significant

	BCTQ total	Tunnel
Pearson correlation®	1	r=0.301
p-value		**<0.001**

[Table/Fig-6]: Correlation between BCTQ Total with USG values among hands with abnormal NCS (N=203).
p-value <0.05 considered significant

in 85.2% population which correlated with NCS grading (p<0.001) and USG grading (p=0.557). Phalens and tinels sign correlated with NCS grading in Kasundra GM et al., study [23].

In the present study, strong association was found between BCTQ total grading and NCS grading (p-value <0.001). Similarly, strong association was established between BCTQ symptom, functional

		NCS grade									
		Mild		Moderate		Severe		Normal		Total	
Grades		Count	%	Count	%	Count	%	Count	%	Count	%
Tunnel grade	Mild	20	48.8	54	49.1	11	21.2	10	9.9	95	31.2
	Moderate	5	12.2	21	19.1	16	30.8	1	1	43	14.1
	Severe	1	2.4	17	15.5	17	32.7	0	0	35	11.5
	Normal	15	36.6	18	16.4	8	15.4	90	89.1	131	43.1
	Total	41	100	110	100	52	100	101	100	304	100

[Table/Fig-7]: Tunnel USG severity compared to NCS severity.
Chi-square value=170.02; df=9, p-value <0.001

Sensitivity, Specificity, PPV and NPV of USG for the diagnosis of CTS. From the statistical point of view the sensitivity and specificity were calculated for mean values of CSA at the carpal tunnel inlet and at 8.5 mm^2 as cut-off value. The sensitivity of 86.21%, a specificity of 83.17%, a PPV of 91.1%, a NPV of 75.0% and an accuracy of 87.32%. Cut-off CSA at inlet >8.5 mm^2 had highest sensitivity and specificity.

DISCUSSION

In the present study, 109 total subjects had abnormal NCS. There are numerous studies in the literature on comparison of NCS with tunnel USG in CTS. However, very few studies [12,23] were available with data on Indian population. Hence, the present study was conducted to evaluate NCS and USG and compared them. The authors compared BCTQ scores with both diagnostic modalities, NCS and USG since many previous studies had led to conflicting results in their association [12,31,32].

USG has emerged as a viable, convenient, low-cost, fast and reliable method for evaluating CTS patients. Based on CTS grading, it was possible to compare USG and NCS findings in the current research. USG had comparable accuracy to NCS in all grades of CTS in patients with a clinical diagnosis of CTS.

After reviewing the literature [12] authors found that the most reliable sonography parameter for CTS was an increase in the CSA at the inlet. Hence, this parameter was used in the present study. Authors observed a good diagnostic accuracy with median nerve CSA at the tunnel inlet, in patients with CTS and a good correlation between USG and NCS. This correlation was consistent in all grades of CTS. Other sonographic parameters include, bowing of the flexor retinaculum, change in CSA of median nerve and flattening ratio. Various ranges for abnormal cut-off USG parameters have been reported with CSA ranging from 9 mm^2 to 15 mm^2. However, a lack of a consensus leads to difficulties in using USG as a diagnostic modality. Also the ideal site of CSA measurement is of debate. Based on the cut-off values considered in the study, sensitivity of CSA in diagnosing CTS ranges from 48% to 89% and specificity from 47% to 100% [19-21,33]. The sensitivity and specificity of the mean CSA cut-off value of 8.5 mm^2 at the inlet of the carpal tunnel in present study was comparable to previous studies [7,16,20,21,34].

The mean age and sex ratio in the present study were comparable to the subjects of previous studies [12,23,24,33]. Out of 109 patients, 94 had bilateral hand involvement, and 15 had unilateral involvement. In unilateral hands, right hand was involved in 9 and left hand in 6 cases. Right hand was involved more than left, which was similar with other studies[12,23, 24.33].

Tinels sign was noted in 59.6% population which did not correlate significantly with NCS and USG grading and Phalens sign was noted

and total scores and NCS severity grading (p-value <0.001) and significant positive correlation with USG grading (p-value <0.001). BCTQ symptom scores showed significant association with USG severity grading (p-value <0.02) while BCTQ function grading did not show significant association with USG grading. Few studies showed correlation between BCTQ and NCS or USG [12,32] whereas few showed no correlation between these scores and diagnostic modalities [31]. Kasundra GM et al., [23] also showed correlation between BCTQ symptom, function and total score to NCS grading. In the present study there was significant positive correlation between BCTQ total with tunnel values i.e., with increase in BCTQ score there was increase in tunnel values and vice versa.

In present study, the mean CSA cut-off value of 8.5 mm^2 at the inlet of carpal tunnel, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy were found comparable to other previous studies [7,16,19-21,34]. In the severe CTS group, USG had high sensitivity and specificity. In mild CTS, USG was found to be less sensitive. Thus, it can be inferred that in mild CTS patients, USG despite being negative should mandatorily accompany electrophysiological assessments for confirmatory diagnosis. There was a small group (n=11) of patients with normal NCS and abnormal USG that had clinical symptoms and signs of CTS. Billakota S and Hobson-Webb LD described that despite having some inflammation in the median nerve, the NCS was not affected, yielding an abnormal USG with a normal NCS results [24]. Roghani RS et al., [13] highlighted that USG complements NCS in diagnosis, as it was shown to be 73% sensitive in patients with CTS but giving negative NCS, hence the diagnostic sensitivity for clinically suspected CTS is commendably increased. Hence, the study supported the idea of using USG, especially for patients with clinical findings suggestive of CTS but representing normal NCS.

Limitation(s)

In the present study, inclusion of symptomatic hand as a control, led to a subgroup of patients, NCS negative USG positive CTS patients. This subgroup patients could not be statistically analysed due to the inclusion and exclusion criteria of the study. There is a need to study this subgroup of patients, as false negative rates of NCS can be as high as 10-46%. Secondly, in this study, population of mild cases were very less, contributing to better USG sensitivity.

CONCLUSION(S)

The diagnostic accuracy of USG assessment and NCS was found to be correlated comparably and complement each other in all grades of CTS. USG being a painless and easily accessible technique also requires minimal time and detects structural abnormalities that may have therapeutic implications. Hence, it can be used as a good

screening technique preferred by the patients. However, electrodiagnosis should be the preferred diagnostic modality for mild CTS.

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