



Published in final edited form as:

*J Clin Neurosci.* 2017 May ; 39: 111–113. doi:10.1016/j.jocn.2017.01.006.

## Is carpal tunnel syndrome present in acute stroke patients? An investigative study using clinical and imaging screening tools

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### Abstract

Carpal tunnel syndrome (CTS) is known to develop post-stroke. Median nerve ultrasound (US) is an inexpensive, effective means of screening. In this prospective feasibility study, we compared the ability of the physical exam, the Boston Carpal Tunnel Questionnaire (BCTQ) and median nerve US to screen for carpal tunnel syndrome (CTS) within 72 hours of stroke onset. We enrolled 24 consecutive patients. Using US, 19 (79%,  $p = 0.0386$ ) of the 24 patients screened positive for CTS on the paretic side and 20 (83%,  $p = 0.0042$ ) on the nonparetic side. With clinical examination, only 11 out of 24 (46%) screened positive for CTS on the paretic side and 8 (33%) on the nonparetic side. The BCTQ did not predict CTS. US can be an effective screening tool post-stroke. Further research is needed to determine specificity and efficacy compared to electrodiagnostic testing in this population.

### Keywords

Ultrasound; Stroke; Carpal tunnel syndrome; Median nerve; Entrapment neuropathy; Stroke rehabilitation; Stroke complications

## 1. Introduction

Previous literature has suggested that carpal tunnel syndrome (CTS) can be seen post-stroke, but its incidence is uncertain [1–4]. This warrants further exploration, as untreated CTS may impair stroke recovery through peripheral nerve mediated loss of hand strength and sensation. Given the prevalence of CTS in the general population, it is suspected that many patients will have CTS prior to their stroke. It is also unclear if our current methods of physical exam and symptom questions are sufficient to diagnose CTS in the setting of co-existent central nervous system deficits.

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Median nerve ultrasound (US) is a painless, inexpensive and useful adjunctive tool for investigating carpal tunnel syndrome (CTS) [5–7] that allows for visualization of anatomical structures. Buchberger et al. [8,9] were the first to use the concept of median nerve cross-sectional area (CSA) at the distal wrist crease in comparing landmarks at the wrist and forearm to diagnose carpal tunnel using ultrasonography. Increased median nerve CSA is present in patients with CTS. Mhoon et al. [10] demonstrated that median nerve ultrasound is highly sensitive in screening for CTS, 99% for a CSA of 9 mm<sup>2</sup> and 97% for a wrist-forearm ratio (WFR) of 1.4. Some centers consider a median nerve at the wrist CSA 14 mm<sup>2</sup> to provide a definitive diagnosis of CTS with a specificity of 100% [10]. While most agree that it should not be used as a stand-alone diagnostic tool, it has excellent potential for screening patients for CTS [7].

No previous study has used nerve US to screen for CTS acutely post-stroke. In this observational, prospective feasibility study, our primary aims is to determine if acute stroke patients have a high rate of abnormality on CTS screening tools, and which screening tools are most sensitive. This data will be informative for planning future prospective trials.

## 2. Methods

### 2.1. Study group

This feasibility study was approved by the institutional review board of Duke University. All patients or their legal representative provided written informed consent prior to their participation. 24 participants were enrolled on continuous selection who met the inclusion criteria. Patients > 18 years of age, admitted to the stroke inpatient service or neurological intensive care unit at Duke University Medical Center with a radiographically confirmed diagnosis of stroke, symptom onset within 72-h of presentation and unilateral hemiplegia/paresis or monoparesis of either the upper or lower extremity were recruited for this study. Written consent was then obtained. Patients were excluded if they had a previous diagnosis of stroke, previous diagnosis of CTS, clinical evidence of CTS mimic syndromes (cervical radiculopathy, polyneuropathy, orthopedic abnormalities in affected limbs), inability to consent within 72 h including cognitive deficits and aphasia, and inability to return to Duke University for follow-up visits. A previous diagnosis of polyneuropathy was not an exclusion criteria. (These patients are part of a longitudinal study and follow-up data will be reported in a separate study.)

Subjects were then asked a series of questions including: handedness, height, weight, use of assistive devices, use of wrist splint, smoking status, and history of diabetes mellitus, hypertension, thyroid disease or hyperlipidemia. A neurologist then completed a BCTQ as well as medical research council (MRC) strength testing of the affected and unaffected limbs. Tinel's testing at the wrist was performed bilaterally, as was Phalen's maneuver. Assessment of thenar muscle mass and median nerve distribution sensory testing using pinprick stimulation was also recorded. The National Institute of Health Stroke Scale (NIHSS), hemoglobin A1C (HgA1C), low density lipoprotein (LDL) level, thyroid stimulating hormone level (TSH) and modified rankin scores (MRS) were recorded during hospitalization. Stroke anatomical location, the use of IV-Alteplase, and if interventional therapy was performed were recorded where applicable.

## 2.2. Ultrasound testing

Patients had median nerve US performed of the bilateral upper extremities, both paretic (P) and nonparetic (NP), by trained personnel from the Duke Electromyography Laboratory. Based upon pre-existing guideline established normative values, the abnormal measurements of the median nerve cross-sectional area (CSA) considered to be diagnostic of CTS are:  $>12 \text{ mm}^2$  at the distal wrist crease and wrist to forearm ratio (WFR) $>1.8$  [7,10,11]. The chances of having abnormal nerve conduction studies consistent with CTS has a 99% sensitivity when median CSA at the wrist is  $9 \text{ mm}^2$  and 97% sensitivity if the WFR is  $1.4$  [10].

The median nerve was imaged in cross-sectional and longitudinal planes with an Esaote MyLabSix US machine with an 18–6 MHz linear-array transducer using standard Esaote MyLab software (Esaote). The median nerve was imaged in cross section at the distal wrist crease and approximately 12 cm from this point in the forearm. The CSA of median nerves was calculated using continuous trace measuring around the perimeter of the median nerve just under the hyperechoic epineurial rim. The WFR was calculated as  $\text{WFR} = \text{median nerve CSA at wrist} / \text{median nerve CSA at forearm}$ .

## 2.3. Statistical analysis

Data were analyzed using SAS 9.3 software (SAS Institute Inc., Cary, NC). Descriptive analyses (mean, standard deviation and frequency) were conducted to characterize the sample. The McNemar test was used to assess whether the proportions of CTS diagnosed by clinical examination and US testing are significantly different from each other. Because BCTQ and NIHSS are ordinal variables and not normally distributed, with a small sample size, Wilcoxon rank-sum test was carried out to compare subjects diagnosed as CTS positive and negative by ultrasound testing and physical exam with respect to BCTQ and NIHSS. For the same reason, the Spearman rank correlation was used to measure the strength of association between BCTQ and median nerve size on paretic side and nonparetic side.

## 3. Results

Descriptive data (mean, standard deviation and frequency) on the demographic and clinical variables of the patient sample are presented in Table 1. There were 24 subjects, 13 women (54.17%) and 11 men, aged  $68.50 \pm 17.14$  years (mean  $\pm$  SD).

Table 2 illustrates that nerve US testing tends to have a higher positive CTS screening rate in stroke patients than clinical examination for both paretic and nonparetic limbs. 19 out of 24 (79%) and 20 out of 24 (83%) patients screened positive for CTS by ultra-sound guidelines on paretic side and nonparetic side respectively, whereas only 11 out of 24 (46%) and 8 out of 24 (33%) patients were positive for possible CTS by clinical examination on the paretic and nonparetic side, respectively. The proportion of CTS cases screened by clinical examination and nerve US was significantly different ( $p = 0.0386$  for the paretic side and  $p = 0.0042$  for the nonparetic side). Table 2 also lists the mean median nerve CSA at the wrist and their standard deviations on subjects' paretic and nonparetic sides based on if they were exam positive or negative for CTS.

As shown in Table 3, there were no significant differences in the BCTQ scores of patients who screened CTS positive and CTS negative on the paretic side ( $p = 0.9715$  for nerve US and  $p = 0.9073$  for Exam) and nonparetic side ( $p = 0.9071$  for nerve US and  $p = 0.1097$  for exam). Comparison of NIHSS scores gave similar results on both the paretic side ( $p = 0.8306$  for nerve US and  $p = 0.4326$  for physical examination) and the nonparetic side ( $p = 0.5600$  for nerve US and  $p = 0.6231$  for physical examination). BCTQ scores were examined for an association with nerve size on both paretic and nonparetic sides. However, the relationship between BCTQ and nerve size was not significant for either the paretic (Spearman's rho = 0.1858,  $p = 0.3847$ ) or nonparetic sides (Spearman's rho = 0.2659,  $p = 0.2091$ ).

#### 4. Conclusion

The proportion of subjects that screen positive for CTS with US was significantly greater than using clinical examination alone, consistent with previous studies of high sensitivity using US [7,10]. Our study demonstrated eight cases that would qualify for CTS even when using this rigorous standard. Thirteen cases would qualify for CTS based on the WFR of 1.4. Many patients that screened positive for CTS on US did not have clinical or symptomatic complaints, another label to consider for these patients instead of CTS is median mononeuropathy of the wrists. The prevalence of asymptomatic median mononeuropathy at the wrists is unknown, along with its potential to impact stroke rehabilitation. It is unclear how prevalent asymptomatic CTS is within the general population. Previous studies have considered why CTS has been reported in the weak hand after acute stroke including a possible inflammatory process or due to subclinical CTS, which can make them prone to develop symptomatic CTS [1,12]. However, the current study and prior publications provide evidence that median neuropathy of the wrists may be prevalent enough in the post-stroke setting to warrant further investigation.

Our secondary outcomes were to evaluate if any symptom scales would be useful in diagnosing CTS in the post-stroke population. When we compared the screening positive for CTS using ultrasound with those who did not, there was no significant difference in the BCTQ outcome scores on the paretic ( $p = 0.4858$ ) nor nonparetic ( $p = 0.4535$ ) sides. This suggests that stroke patients' symptoms and findings are complicated, and symptoms may be obscured by symptoms and findings due to stroke.

There were several limitations in our study. This was an observational, feasibility pilot study. No randomization or blinding occurred, so observer and selection bias are possible. Another limitation is the small size, although this was intended to provide pilot data for larger, longitudinal trials. Frequently, CTS is diagnosed using electrodiagnostic testing. Unfortunately, this can prove painful, costly, and difficult during the acute stroke setting. Performing confirmatory electrodiagnostic testing was not possible due to funding constraints. In our study, if US demonstrated a concern for CTS, the primary neurology provider was notified and the diagnosis and management of symptoms were determined by the subject's primary team. Future trials are needed where US and electrodiagnostic testing are compared to determine if US is as sensitive and specific as electrodiagnostic testing.

Additionally, further studies are needed to determine if patients with CTS will have improved post-stroke outcomes through treatment intervention.

In conclusion, the current study demonstrates that median nerve US abnormalities are common in the post-stroke setting, and may prove a more feasible screening tool than the clinical exam or questionnaire alone. US is non-invasive, more accessible and less expensive than electrodiagnostic testing for post-stroke patients at risk for CTS and could be used as a rapid screening tool. Hand weakness and numbness can be present in either side of stroke patients. Providers need to consider possibilities other than stroke including CTS as a potential etiology and the exam and symptom questionnaire can be unreliable during the acute period. Further studies are needed to determine if US can change outcomes after stroke.

## Funding source

Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Number UL1TR001117. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

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**Table 1**Clinical characteristics of the study participants ( $n = 24$ ).

	<b>N (%) or Mean <math>\pm</math> SD</b>
Sex	
Male/Female	11 (45.83)/13 (54.17)
Age (years)	68.50 $\pm$ 17.14
Height (cm)	169.44 $\pm$ 12.88
Weight (kg)	85.74 $\pm$ 21.17
Hand	
Right/Left	22 (91.67)/2(8.33)
Assistive Device	
Yes/No	9 (37.50)/15 (62.50)
mRS at DC (range: 0–6)	2 $\pm$ 1.48
Disposition	
Home	12 (50.00)
Rehab	6 (25.00)
SNF	6 (25.00)
Smoker	
Yes/No	7 (29.17)/17 (70.83)
DM	
Yes/No	6 (25.00)/18 (75.00)
A1C (%)	6.24 $\pm$ 1.06
LDL (mg/dL)	105.96 $\pm$ 35.09
Thyroid disease	
Yes/No	5 (20.83)/19 (79.17)
IV-alteplase	
Yes/No	9 (37.50)/15 (62.50)
Intervention	
Yes/No	5 (20.83)/19 (79.17)
NIHSS on admission	7.63 $\pm$ 4.80
BCTQ score	6.46 $\pm$ 6.47
NP wrist (mm <sup>2</sup> )	10.50 $\pm$ 2.96
P wrist (mm <sup>2</sup> )	10.63 $\pm$ 3.37
NP WFR	2.02 $\pm$ 0.68
P WFR	1.81 $\pm$ 0.63

mRS = modified Rankin Score SNF = skilled nursing facility; DM = diabetes mellitus A1C = glycated hemoglobin A1C; LDL = low-density lipoprotein NIHSS = National Institute of Health Stroke Scale; BCTQ = Boston Carpal Tunnel Questionnaire P = paretic NP = nonparetic; WFR = wrist-forearm ratio.

Comparison of neurologic exam and ultrasound testing screening for carpal tunnel syndrome on the paretic and nonparetic side in stroke patients.

**Table 2**

Carpal Tunnel Syndrome						
	Exam (%)	Ultrasound (%)	p-value*	Mean CSA mm <sup>2</sup> at wrist for Exam (+) CTS	Mean CSA mm <sup>2</sup> at wrist for Exam (-) CTS	
Paretic side	11 (45.83)	19 (79.17)	0.0386	10 ± 1.95	11.15 ± 4.03	
Nonparetic side	8 (33.33)	20 (83.33)	0.0042	10.38 ± 2.06	10.56 ± 3.24	

N = 24. CTS = Carpal Tunnel Syndrome CSA = cross-sectional area.

\* McNemar's test p-value.

Comparison of BCTQ and NIHSS scores of stroke patients screened with CTS (+) and CTS (-) in the paretic and nonparetic sides using nerve ultrasound and the clinical exam, respectively.

**Table 3**

	US diagnosis		Exam diagnosis		<i>p</i> -value*
	CTS (+) (mean ±SD)	CTS (-) (mean ± SD)	CTS (+) (mean ±SD)	CTS (-) (mean ±SD)	
Paretic side	N= 19	N= 5	N= 11	N= 13	
BCTQ	6.47 ± 6.46	6.40 ± 7.27	6.09 ± 6.82	6.77 ± 6.42	0.9073
NIHSS	7.47 ± 5.05	8.20 ± 4.15	8.45 ± 5.41	6.92 ± 4.31	0.4326
Nonparetic side	N= 20	N= 4	N= 8	N= 16	
BCTQ	6.60 ± 6.87	5.75 ± 4.57	9.75 ± 7.36	4.81 ± 5.49	0.1097
NIHSS	7.25 ± 4.79	9.50 ± 5.07	8.63 ± 5.60	7.13 ± 4.46	0.6231

\* Wilcoxon two-sample test two-sided *p*-value.