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Original Research Article

Ultrasound evaluation of carpal tunnel syndrome in patients with bifid median nerve

Smiti Sripathi, Anurag Ayachit*, Rebin Bos

Department of Radiodiagnosis & Imaging, Kasturba Medical College, Manipal, Karnataka, India

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***Correspondence:**
Dr. Anurag Ayachit,
E-mail: ayachit@gmail.com

ABSTRACT

Background: Patients with high division of the median nerve proximal to carpal tunnel, or bifid median nerve, may present with carpal tunnel syndrome (CTS). Ultrasound (US) measurements indicative of CTS in this subset of patients differ from those in patients with non-bifid median nerve. The objectives were to evaluate the parameter ΔCSA [difference between the maximum cross-sectional area of bifid median nerve within carpal tunnel (CSAc) and outside tunnel (CSAp)] in the diagnosis of CTS, to compare sensitivity and specificity of ΔCSA with nerve conduction velocity studies (NCS), and to compare the cross-sectional area (CSAc, CSAp & ΔCSA) of bifid median nerve in CTS patients with that in asymptomatic controls.
Methods: 20 wrists with bifid median nerves and symptoms suggestive of CTS were included in the study group. Nerve conduction velocity studies (NCS) were performed in all cases. 4 wrists of asymptomatic age-matched subjects had bifid median nerves and normal NCS and were included in the control group. High resolution ultrasonography was performed for all wrists and findings documented. Statistical Analysis: Receiver Operating Characteristics curves were used to obtain the level of significance (p-value) and assessment of correlation between ΔCSA and NCS findings.
Results: There was significant correlation between ΔCSA and NCS. A cut-off value of 2.3mm^2 gave the best calculated sensitivity (76.9 %) and specificity (100%).
Conclusions: CSA criteria for diagnosing CTS in patients with bifid median nerves are different from those in patients with non-bifid median nerve. ΔCSA is a sensitive and specific parameter for confirming the diagnosis of CTS in patients with bifid median nerve with sensitivity approaching that of NCS.

Keywords: Bifid median nerve, Carpal tunnel syndrome, Ultrasound

INTRODUCTION

The sensory and motor innervation of the upper limb is via three nerves originating from the brachial plexus - the ulnar, radial and median nerves. Ultrasound (US) of the forearm can effectively reveal structural abnormalities and variants of the median nerve. Bifid median nerve, defined as high division of the median nerve proximal to the carpal tunnel, is a variation of nerve anatomy first described by Lanz in 1977 and has an incidence of 2.8%.[1,2]

The forearm and hand are supplied by radial and ulnar arteries, however the median artery (accompanying the median nerve) normally regresses in the early embryonic period.[3] Persistence of the median artery, demonstrated effectively by colour doppler, is commonly associated with bifid median nerve.[4]

The median nerve is supplied by epineural, interfascicular, and intrafascicular vascular plexuses that link to one another and form a free vascular network. Vascular compromise involving the median nerve in

carpal tunnel syndrome (CTS) is the most common peripheral entrapment neuropathy accounting for 90% of all cases. It is clinically diagnosed based on a combination of characteristic symptoms and electrophysiological abnormalities. It is still not completely understood whether the neuropathy is a result of vascular compromise due to a rise in intracanal pressure or secondary to intermittent mechanical compression.[5]

Carpal Tunnel Syndrome occurs in 3 stages:

- Venous congestion
- Nerve edema
- Impairment of venous and arterial blood supply

Although ultrasonographic parameters for diagnosing CTS have been studied and defined by many researchers (6), very few studies have focused on the diagnosis of CTS in patients with bifid median nerves.[7] Due to bifid nature, the combined cross-sectional area of the nerve is expected to be greater compared to non-bifid median nerves, regardless of CTS being present. The well-established parameters defining CTS in patients with non-bifid nerves differ significantly from those with bifid median nerves and, if applied to the latter subset of patients, will tend to misdiagnose and overestimate the severity of the condition. Symptoms in patients that are NCV negative or indeterminate but have higher-than-normal CSA due to bifid median nerves may be incorrectly attributed to CTS without considering parameters like ΔCSA, leading to unnecessary medical or surgical (flexor retinaculum release) treatment. Therefore, it is imperative that ultrasound parameters for diagnosing CTS be defined specifically for patients with bifid median nerves.

Management of CTS includes one or more of the following: therapeutic ultrasound (short-wave diathermy), yoga and carpal bone mobilization techniques, wrist splinting in neutral or slight extension, non-steroidal anti-inflammatory drugs and/or diuretics, steroid injection into the carpal tunnel, and if all conservative treatments fail, surgical release of the flexor retinaculum provides high initial success rates.[8]

METHODS

This prospective study was conducted in a tertiary care hospital in South India over a period of 20 months, from February 2012 to September 2013, after obtaining clearance from the Institutional Ethical Committee.

Out of 139 wrists (in 89 patients) referred for ultrasound evaluation to the department of radiology with symptoms suggestive of CTS, 20 wrists with bifid median nerves were included in the study group. NCS was performed in all cases. Out of 72 wrists (in 49 asymptomatic age matched controls), 4 wrists with bifid median nerves were included in the control group. These age-matched controls were patients referred to the department of radiology for musculoskeletal ultrasound for indications other than peripheral neuropathy, and whom NCS was negative for median nerve neuropathy. NCS of median nerve was considered the gold-standard investigation for diagnosis of CTS.

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Both groups were evaluated by ultrasound using Philips IU22 ultrasound machine with broadband linear array transducer of 5-17 MHz frequency.

Each wrist was evaluated independently by two radiologists, having 5 years and 12 years' experience in musculoskeletal ultrasound respectively. In case of discordance of the findings between the two radiologists, the pertinent case was evaluated together and a consensus was reached.

Selection criteria

Inclusion criteria for study group

All patients with clinical symptoms of carpal tunnel syndrome referred for ultrasound who underwent nerve conduction velocity (NCV) study.

Exclusion criteria for study group

Patients who underwent prior surgery for carpal tunnel syndrome.

Inclusion criteria for control group

Asymptomatic age matched individuals with NCS negative for neuropathy.

The median nerve was defined as bifid when it branched proximal to the level of the distal radioulnar joint, as determined at the ultrasound evaluation. The characteristic clinical symptoms of CTS included: paresthesia, pain, weakness, or clumsiness of the hand worsened by sleep or sustained hand or arm position; sensory deficits in the region innervated by median nerve or motor deficit or atrophy of thenar muscles.

Ultrasound technique

The subjects were seated facing the examiner with arm extended, wrist resting on a flat surface, forearm supine, and fingers semi-extended. Ultrasonic gel was used as a coupling agent. The CSA of median nerve was measured using electronic calipers by free-tracing the nerve margins. Individual areas of the medial and lateral divisions of the bifid median nerve were added to give a combined CSA at the following levels:

- In the distal forearm (at proximal third of pronator quadratus muscle): CSAp
- In the carpal tunnel at the level of maximum swelling of the nerve: CSAc
- Difference between the CSA at the level of maximum swelling and CSA proximal to tunnel was recorded as ΔCSA (CSAc – CSAp).

Qualitative analysis was also performed

- Nerve edema: Homogeneous hypoechoic appearance of the nerve with or without loss of fascicular discrimination.
- Hypervascularity: Presence of perineural and/or intraneural blood flow on Color Doppler.
- Persistent Median Artery: Color Doppler was used to confirm the presence of a persistent median artery.

Statistical analysis

Statistical analysis was performed using SPSS Version 20.0.0.

The various ultrasonographic parameters were correlated with NCV findings using Receiver Operating Characteristics curves (ROC) to obtain p-values. Cross tabulation statistics were used and sensitivity, specificity and accuracy were calculated on the basis of the 2x2 tables. Chi-square test was used to obtain the level of significance (p-value). Independent sample t-tests were used to assess statistical significance between various parameters of median nerve in cases and controls.

RESULTS

The patients ranged in age from 25 to 68 years with a majority of cases between 40 and 50 years. The mean age of the patients with bifid median nerve was 45.5 years. 75.5% of the cases were females and 24.5% were males.

There were a total of 20 wrists with CTS and bifid median nerve out of a total of 139 wrists. 60% of the cases with bifid median nerve were females and 40% were males. Out of these 20 wrists, 8 (40%) had a persistent median artery (PMA). Amongst the controls, bifid median nerve was seen in 4 wrists and persistent median artery in two wrists.

Cases and controls

Independent t-test was used to compare the dimension of bifid median nerve at various levels in both cases and controls (Table 1). The p values calculated at all levels were <0.01 implying that median nerve cross sectional areas are significantly higher in cases as compared to controls both outside and inside the tunnel.

Using Receiver Operator Characteristic Curve (Figure 1), a cut-off value of 2.3mm^2 for ΔCSA gave the best sensitivity (76.9 %) and specificity (100%) for diagnosis of CTS in bifid median nerve.

Table 1: Dimensions of bifid median nerve at various levels in cases and controls.

CSA (mm^2)	Outside tunnel (CSAp) (mm^2)	CSA at level of maximum swelling (CSAc) (mm^2)	ΔCSA (mm^2)
Cases	7.7±1.9	10.3±2.9	2.6±2.1
Controls	5.5±1.8	6.1±2.1	0.56±0.4

We found nerve hypervascularity (Table 2) in 6 out of 13 NCS positive wrists. Hypervascularity was absent in all NCS negative wrists. Hypervascularity was absent in all NCS negative wrists. On the other hand, nerve edema (Table 2) was present in 11 out of 13 NCS positive wrists and 2 out pf 7 NCS negative wrists, giving a sensitivity of 84.6% and a specificity of 71.4% for CTS.

Table 2: Correlation of nerve vascularity and nerve edema with NCS in bifid median nerve.

Nerve vascularity			
Vascularity	**NCS positive**	**NCS negative**	**Total**
Present	6	0	6
Absent	7	7	14
Total	13	7	20
Nerve edema			
Edema	**NCS positive**	**NCS Negative**	**Total**
Present	11	2	13
Absent	2	5	7
Total	13	7	20

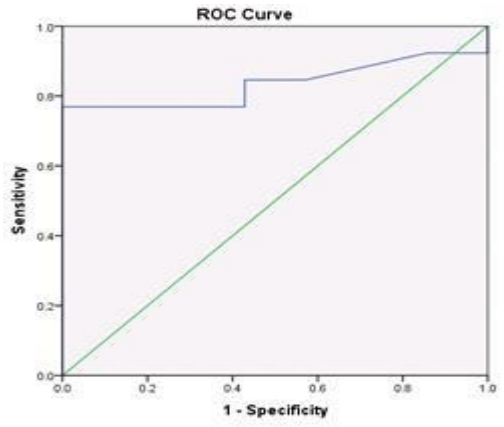

Figure 1: ROC curve to obtain the level of significance (p-value) of correlation between ΔCSA and NCV findings. A value of 2.3mm^2 for ΔCSA gave the best sensitivity (76.9 %) and specificity (100%).

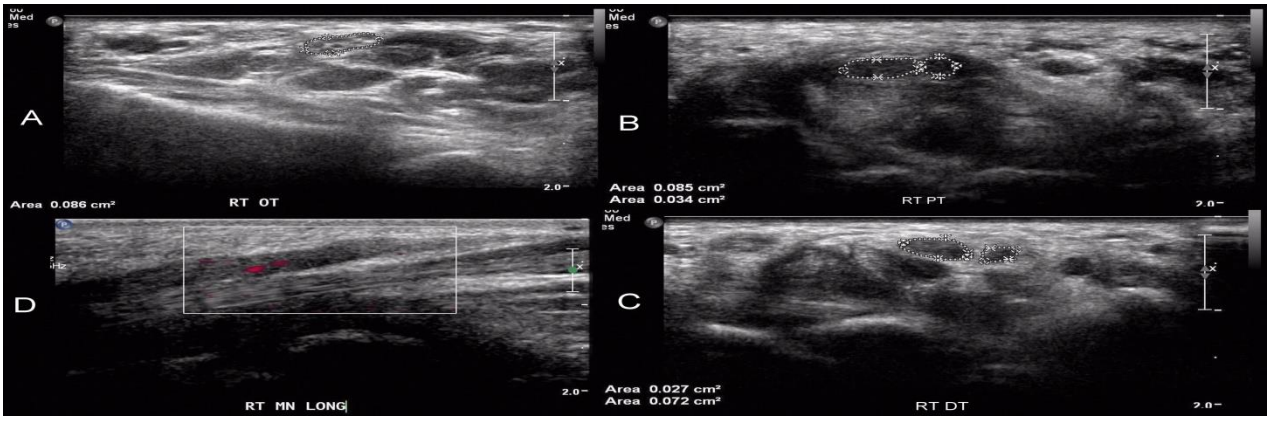

Figure 2: A 35 year old hypothyroid female came complaints of paresthesia and tingling in the right hand. Tinel's and phalen's tests and NCV test was positive. On ultrasound, bifid median nerve was seen in the proximal and distal tunnel with ΔCSA 3.3mm^2. (A) Transverse sonogram at level of proximal third of pronator quadratus muscle showing CSAp (8.6mm2) of the median nerve outside the tunnel; (B) Transverse sonogram at scaphoid-pisiform level showing CSAprox (2.7+7.2= 9.9mm^2) and edematous nerve; (C) Transverse sonogram at trapezium-hamate level showing CSAdist (8.5+3.4=11.9mm^2) and hypoechoic edematous nerve; (D) Longitudinal section of the bifid median nerve showing hypervascularity on power Doppler.

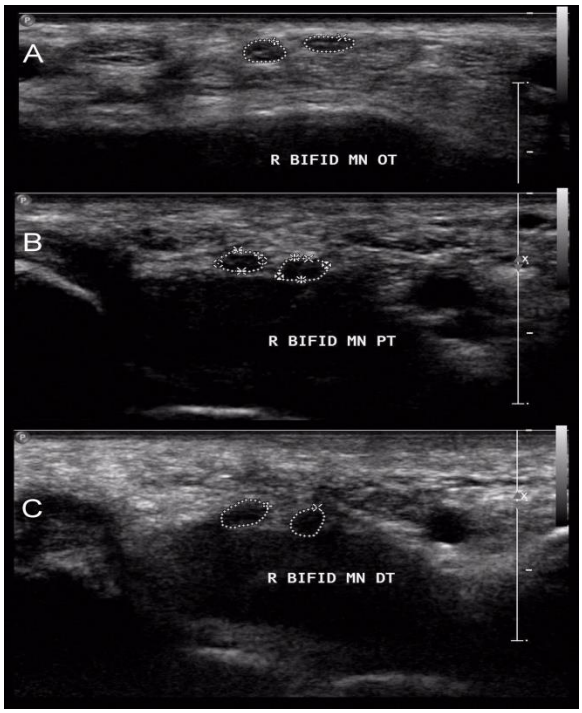

Figure 3. A 59 year old male came with symptoms of tingling and numbness in right hand. Both Phalen's and Tinel's tests were negative but NCV test was positive. On ultrasound, bilateral bifid median nerve with persistent median artery was noted with ΔCSA 2.9mm^2. (A) Transverse sonogram at level of proximal third of pronator quadratus muscle showing bifid median nerve. CSAp outside the tunnel (5.3+4.1=9.4mm^2); (B) Transverse sonogram at scaphoid-pisiform level showing CSAprox (6.4+4.9=11.3mm^2) and mildly edematous nerves; (C) Transverse sonogram at trapezium-hamate level showing CSAdist (7.1+5.2=12.3mm^2) and hypoechoic mildly edematous nerve.

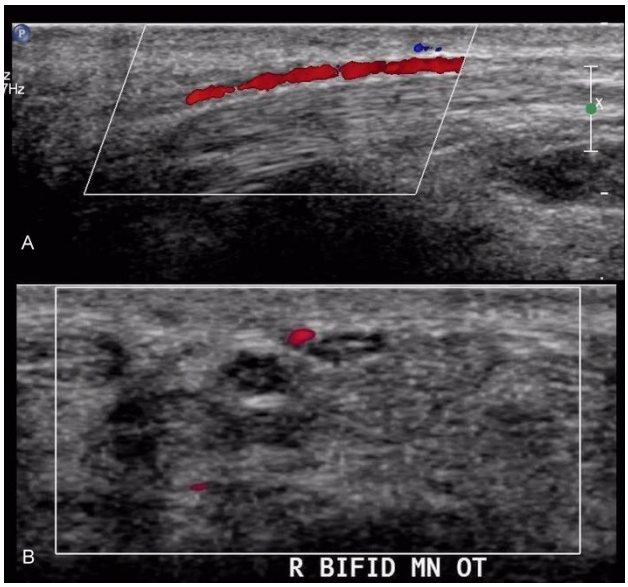

Figure 4: Longitudinal (A) and transverse (B) sonograms of right wrist in same patient as Figure 2. Power Doppler shows bifid median nerve with persistent median artery showing colour flow.

Table 3: Bifid median nerve sizes: cases versus controls, present study versus Klauser et al.

Measurement	Our study	Klauser et al[7]
CSAp – cases	7.7±1.9	8.4±2.3
CSAp – controls	5.5±1.8	9.3±2.3
CSAc – cases	10.3±2.9	16.4±4.8
CSAc – controls	6.1±2.1	11.4±2.0
ΔCSA – cases	2.2±2.1	2.8±1.9
ΔCSA – controls	0.56±0.4	2.1±1.8

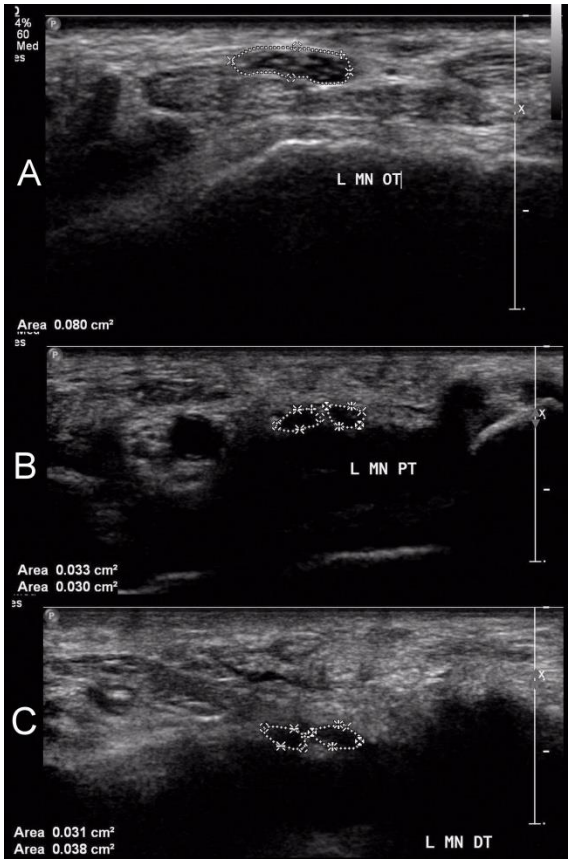

Figure 5: Asymptomatic control with bifid median nerve and no signs or symptoms of CTS. The CSA of bifid median nerve was actually less in the tunnel compared to outside tunnel; (A) Transverse sonogram at level of proximal third of pronator quadratus showing single median nerve. CSAp (8.0mm^2) outside the tunnel; (B) Transverse sonogram at scaphoid-pisiform level showing CSAprox (3.3+3.0=6.6mm^2); (C) Transverse sonogram at trapezium-hamate level showing CSAdist (3.1+3.8=6.9mm^2).

DISCUSSION

Carpal tunnel syndrome is a peripheral compression neuropathy which presents with characteristic clinical features of progressive weakness and clumsiness in hands associated with hypoaesthesia and tingling in median nerve distribution. The clinical diagnosis of CTS is based on a combination of these characteristic symptoms with electrophysiological abnormalities on NCV testing.

The bifid median nerve anomaly has an incidence of 0.8% to 2.8% in patients with CTS, and in most cases it has been reported with a concomitant persistent median artery.[9-11]

Propeck et al reported three cases of bifid median nerve, one of which was in a patient with CTS, whereas the remaining two were found in cadaveric specimens.[12] He suggested that ultrasound size criteria used for diagnosing CTS in non-bifid median nerves may not be accurate for evaluating bifid median nerves. Sonographic and magnetic resonance imaging findings in six patients with bifid median nerve selected from a population of 294 patients with CTS were compared by Iannicelli et al.[13] Both studies concluded that sonography can provide effective diagnosis and delineation of bifid median nerve. Doppler sonographic findings in two patients with CTS associated with a persistent median artery were described by Gassner et al who also reported 16 hands with a persistent median artery among 50 asymptomatic volunteers.[4]

We found a total of 20 wrists (14.8%) with bifid median nerve, out of which 8 (40%) had a persistent median artery. Our findings are similar to Bayrak et al, who also found a relatively high percentage of bifid median nerve (19%) with a concomitant persistent median artery (45%).[14]

Various ultrasound studies on carpal tunnel syndrome have given a wide range of dimensions of non-bifid median nerve area in the proximal tunnel (at the scaphoid-pisiform level), varying from 8.5 to 15.0 mm^2 with sensitivities and specificities ranging from 67%-94% and 57%-97% respectively.[15-17] It is evident that several investigators have attempted to determine the most appropriate median nerve CSA cut-off value, however there still remains a lack of consensus.

In an attempt to improve accuracy in the diagnosis of CTS, Klauser et al described a new parameter ΔCSA by including an additional cross-sectional measurement of the median nerve located more proximally at the level of the pronator quadratus muscle.[6] This was described as the difference between the CSA at the level of maximum swelling (CSc) and CSA proximal to tunnel at the level of pronator quadratus muscle (CSAp) and recorded as ΔCSA (CSAc-CSAp). He evaluated both bifid and non-bifid median nerves using the above parameter, (7) and found a sensitivity of 94.3% and specificity of 50.0% for a cut-off of 3.0mm^2 for ΔCSA in patients of CTS with bifid median nerve. The cut-off ΔCSA of 2.3mm^2 in our patients of CTS with bifid median nerve gave the best sensitivity of 76.9% and specificity of 100% and showed a statistically significant positive correlation with nerve conduction studies.

As compared to a study by Klauser A et al both cases and controls in present study showed smaller cross sectional area of bifid median nerve.[7] This can be attributed to the demographic differences in the study populations, and is important to emphasize, since the cut-off values standardized on a Caucasian population may not apply to the Indian population. By using an additional parameter like ΔCSA instead of CSA alone for diagnosing CTS, we can partially compensate for individual variation in size of the bifid median nerve, thus improving the diagnostic accuracy of ultrasound.

Apart from the quantitative assessment of the median nerve, qualitative parameters like nerve edema and

hypervascularity also provide additional diagnosing information and can be used for evaluation of median nerve.

Nerve edema: Nerve hypoechogenicity (with or without loss of normal fascicular discrimination) as a criterion for nerve edema gave a sensitivity of 84.6% and specificity of 71.4% in the present study. As observed by Chan K et al, qualitative assessment of the nerve is subjective and as such cannot be used as a stand-alone criterion for diagnosis of CTS but as complementary to other quantitative measurements.[18]

Nerve hypervascularity: Increase in nerve vascularity detected by power Doppler ultrasound showed 100% specificity in detecting CTS. Histopathological evaluation of median nerve in CTS patients have demonstrated an increase in expression of vascular endothelial growth factor (VEGF) in synovial tissue, which might explain the hypervascularity of median nerve in CTS.[19] Power Doppler ultrasound is considered superior to colour Doppler in demonstration of vascular flow due to high sensitivity to slow flow, no angle dependency, and no aliasing.[20] Malhoui et al used colour Doppler for evaluation of hypervascularity of non-bifid median nerve and found that it has a good sensitivity and specificity for diagnosing CTS.[21]

CONCLUSION

Ultrasound is a widely available, cost effective, fast and non-invasive tool for evaluation of median nerve calibre, anatomical variation, edema and hypervascularity. Therefore it is immensely valuable in confirming the clinical diagnosis of CTS, with sensitivity approaching that of NCV testing, which has important implications when surgical management is contemplated.

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