Original Article
Value of high-frequency ultrasound in diagnosing carpal tunnel syndrome

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Abstract: This study aimed to evaluate the diagnostic value of high-frequency ultrasound examination for carpal tunnel syndrome (CTS). A total of 63 wrists from 45 patients diagnosed with CTS were selected as the study group, and 43 asymptomatic wrists of 40 cases were included as the normal control group. Parameters such as the transverse diameter, vertical diameter, cross-sectional area (CSA), and flattening rate (FR) of the carpal tunnel radioulnar joint, postular bone, and median nerve in the hamate bone hook plane were measured, and the differences between the two groups were compared. The median nerve CSA in the postular bone plate was significantly greater in the study group than in the normal control group (0.17±0.05 vs. 0.09±0.02, *P*<0.01), and the FR at the hook of the hamate was significantly higher in the study group (3.52±0.86 vs. 3.21±0.26, *P*<0.01). Our results suggest that ultrasonography can effectively provide dynamic real-time images of the wrist in addition to being painless, non-invasive, and associated with relatively low costs. Based on our findings, we believe that ultrasonography is an effective examination method for CTS. When the threshold of the median nerve CSA in the postular bone plate was set as 10 mm^2, the diagnostic sensitivity and specificity were 92% and 86%, respectively. Therefore, the median nerve CSA may represent a good clinical indicator of CTS.

Keywords: Carpal tunnel syndrome, high-frequency ultrasound, diagnosis

Introduction

Carpal tunnel syndrome (CTS) can result from various factors, and develops as a result of increased carpal tunnel pressure and compression of the median nerve, which in turn induce a series of sensory and motor dysfunction syndromes in the median nerve distribution area below the wrist [1, 2]. CTS is a common peripheral neuropathy that occurs at any age, especially in individuals in their 40 s to 60 s, and the male: female ratio is reported to be 3:7 [3]. Worldwide, approximately 8% of the population has experienced CTS [4]; in 2006, CTS patients accounted for 0.2% of all American outpatients [5].

CTS is conventionally diagnosed based on disease history along with physical and neurophysiological examination findings. Electrophysiological testing is considered the gold standard for the diagnosis of CTS [6-8]; however, electrophysiological testing can only evaluate the functional status of the median nerve, and cannot reflect the adjacent anatomical relationships around the median nerve. Carpal tunnel magnetic resonance imaging (MRI) has been demonstrated to be able to make up for the deficiencies of electrophysiological testing [9, 10]; Nuclear MRI can be used to visualize the carpal tunnel at a higher resolution, identify even very mild median nerve compression, and view the positions of adjacent bony structures [11-14]. However, because of the high cost associated with the machine itself and its inspection fees, its clinical application has been limited.

A simple, effective, and inexpensive screening method that allows effective and widespread evaluation of soft tissue lesions is needed. Ultrasonography is simple to operate and master, and the price advantages associated with this technology have already resulted in its

widespread use in clinical practice. With advances in ultrasound technology, high-frequency ultrasound (HFU) has recently been introduced an ultrasound technique that can be used for the evaluation and diagnosis of peripheral nerve entrapment syndrome. The frequency of the ultrasound probe reaches 18 MHz, with a resolution of 400 Lm. The evidence-based medicine guidelines of the American Association of Neuromuscular & Electrodiagnostic Medicine state that ultrasound can be used to accurately diagnosis CTS as well as directly observe any abnormal anatomic structures of the wrist. Similar to MRI, HFU can provide real-time dynamic images, thus representing a novel, simple, and much more inexpensive imaging method for peripheral neuropathy compared to MRI. Furthermore, HFU has several advantages for morphological diagnosis compared to neurophysiological evaluations [15, 16].

However, there is currently no uniform standard for the use of clinical ultrasound for the diagnosis of CTS, and the advantages and maneuverability of HFU for the diagnosis of CTS are not well known. Therefore, this study investigated the clinical usefulness of HFU to help determine its clinical application and provide a theoretical basis for developing a unified standard in diagnosing CTS.

Methods

Subjects

Patients at the Department of Neurology and Orthopedics of First People's Hospital of Yunnan province between March 2011 and May 2013 were included in this study. The study group comprised 45 patients with CTS (63 CTS wrists) confirmed by the disease history, physical examination, and nerve electrophysiological testing, including 19 men (20 wrists) and 26 women (43 wrists) aged 20-68 years (mean age, 45 years). The control group included 40 sex-matched patients (43 wrists) without CTS symptoms who visited the hospital for other conditions during the same period (age, 27-56 years; mean, 42 years). All observed subjects provided informed consent to participate in the study. The demographic characteristics of the two groups did not significantly differ (*Ptin*>0.05) and could thus be compared. This study was conducted in accordance with the

declaration of Helsinki. This study was conducted with approval from the Ethics Committee of The First People's Hospital. Written informed consent was obtained from all participants.

Examination instrument and position of examinees

The Siemens S2000 color Doppler ultrasonic diagnostic apparatus was used, with the probe frequency set at 7-14 MHz and the checking condition set as "small organ". The examinations by non-operators were performed within 3 weeks of the electromyography (EMG) study. All patients were asked to position themselves in the sitting or lying position, with the upper extremity placed on the examination table. A wrist pillow was used to maintain the wrist in a neutral position with the palm facing upward and the hand in a natural resting position. Scanning was first performed towards the median nerve along the longitudinal axis, after which all-level transection diameters of the median nerve on the cross-section plate of the carpal tunnel were measured.

Ultrasound identification of the median nerve

The median nerve was identified based on the following characteristics on ultrasound images: 1) nerve-inherent hypoechoic imaging characteristics, 2) uniform consistent echo on each section (isotropy), 3) superficial location in the carpal tunnel, and 4) intact median nerve or slight passively moved median nerve along with the tendon.

Determination of anatomical position in the measurement planes

The median nerve was measured in three planes on the carpal tunnel transverse section, namely the radioulnar joint, pisiform bone, and hamate bone hook planes. The horizontal level of the radioulnar joint plane was defined as the space between the proximal end of the transverse striation of the wrist palm side and the middle wrist transverse striation. The horizontal level of the pisiform bone plane was defined as the area located approximately 1 cm from the distal middle wrist transverse striation of the wrist palm side when the pisiform bone was on the vertical site of the lateral finger-straight pointing directions, which could be directly touched by the fingers. The horizontal level of
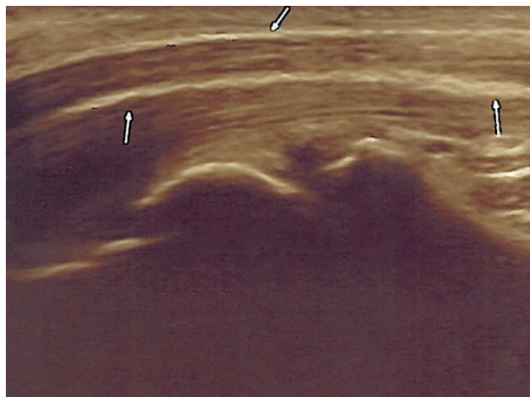
Figure 1. Cross- and longitudinal-section ultrasound images of normal median nerve. These arrows were the ultrasound image of the longitudinal section of normal median nerve, with linear parallelly-arranged noncontinuous trabs-like hypoechoic structures in the middle and hyperechoic epineurium on both sides.

the hamate bone hook was defined as the area located 1 cm on the inferior lateral side of the pisiform bone, which equated the extension line of the lateral edge of the ring ulnar bone.

Measurement parameters and methods

The diameter (D) and anteroposterior diameter (d) of the median nerve in the transverse plane of the carpal tunnel were measured towards the three planes, as values D1, D2, D3, d1, d2, and d3. Next, the cross-sectional area (CSA) of the median nerve was measured in these three planes, as CSA1, CSA2, and CSA3. The CSA ratio of the pisiform bone plane and radioulnar joint plane was further calculated, and the swelling rate (SR) was obtained. Subsequently, the flattening rate (FR) in each plane was calculated, namely D\d, as FR1, FR2, and FR3. The measurement of D and d corresponded to the distance within the inner edge of the euphotic zone of the median nerve edge. The median nerve CSA was measured using the method proposed by Yesildag et al. [17]. In the measurements, the formula of an ellipsoid area was used (D1×d1×3.14/4). The measurements were repeated three times and the average of the three was taken.

Statistical analysis

All measurement data are expressed as mean ± standard deviation, and were analyzed using SPSS 13.0 software. The intergroup means

were compared using the t-test. ROC analysis was performed for CSA, D, d and FR3 that had been validated as parameters with statistical difference.

Results

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) in CTS patients were obtained by determining the cut-off point using receiver operating characteristics (ROC) curve.

Ultrasonography

In the ultrasonograms of the normal control group, the median nerve appeared as an oval, low, or moderate echo in the transverse section, surrounded by hyperechoic ribbons, while in the longitudinal section, it appeared to be arranged in a cord-like fashion as non-continuous linear parallel hypoechoic structures. Strong echoes were observed on both sides, and were determined to represent the epineurium, under which the tendons were found, arranged in parallel. When the extremities moved, although the relative positions and thicknesses of the tendons and ligaments might have changed, the sizes and positions of the nerves remained relatively fixed, and no large displacements occurred, as shown in **Figure 1**.

In the study group, the nerve's thickness and CSA appeared increased, especially of the postular bone. The normal honeycomb structure observed on the cross-section appeared fuzzy, the longitudinal section was thickened, the internal wispy echo disappeared, and the flexor retinaculum was thickened. The median nerve was significantly enlarged in the postular bone plane, and significantly flatter in the hamate bone hook plane (**Figure 2**).

Measurement parameters

Comparison of the test results of the two groups is shown in **Table 1**. Significant differences in CSA, D, d, and FR3 were observed between the 2 groups, while the remaining results were comparable.

Evaluation of diagnostic indicators

The partial diagnostic criteria for evaluating the median nerve parameters are shown in **Table**
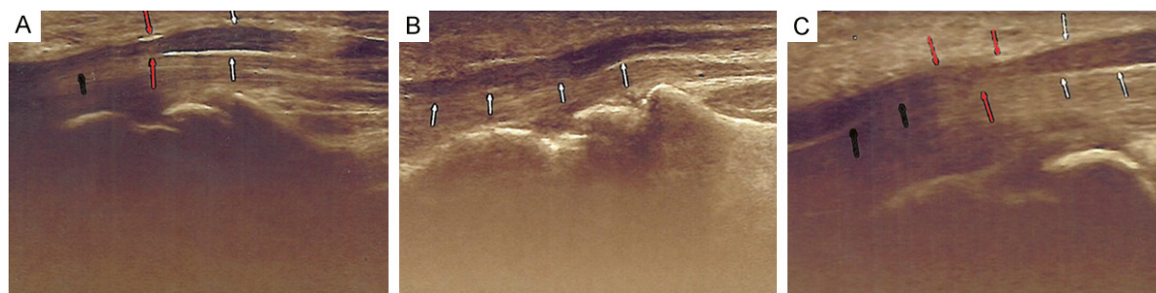
Figure 2. Cross- and longitudinal-section ultrasound images of median nerve lesions. The Figure was the ultrasound image of the longitudinal section of diseased median nerve, in which the intra-nerve sarciniform echo disappeared and the compressed proximal end appeared thickening. A: The median nerve was compressed by the transverse carpal ligament, and the red arrow pointed at the compression site; the above red arrow pointed at the transverse carpal ligament. The black arrow indicated the distal end of the compressed nerve, and the white arrow indicated the proximal end of the compressed nerve. B: The distal end of the compressed diseased median nerve, the nerve degenerated and showed irregular shape, uneven thickness, and vague border. C: The carpal tunnel of the median nerve was obviously compressed (red arrow). Black arrow indicated the distal end of the compressed nerve, white arrow indicated the proximal end of the compressed nerve. The both ends of the compressed nerve were thickened due to edema.

Table 1. Median nerve ultrasound measurement parameters

Group	n	CSA (cm²)	D (cm)	D (cm)	FR1	FR2	FR3	SR
Study Group	63	0.11±0.03	0.23±0.04	0.3±0.06	2.83±0.85	2.57±0.68	3.52±0.86	1.33±0.27
Control group	43	0.07±0.01	0.17±0.02	0.20±0.03	2.81±0.67	2.50±0.54	3.21±0.26	1.31±0.21
P		<0.01	<0.01	<0.01	>0.05	>0.05	<0.01	0.67

Note: CSA: cross-sectional area of the median nerve on the postular bone plane; D, d: transverse and anterior diameter of the median nerve on the postular bone plane; FR1, FR2, FR3: D/d of the median nerve of radioulnar joint, postular bone and hamate bone planes; SR: CSA ration of median nerve postular bone plane and radioulnar joint; $P<0.01$, significant difference, $P>0.05$ no significant difference.

Table 2. Evaluation of partial diagnostic criteria of median nerve

Parameter	Diagnostic criteria	Sensitivity	Specificity	Positive predictive value	Negative predictive value
CSA	≥0.1 cm²	92%	86%	91%	88%
FR3	≥3.32	33.3%	88%	81%	47.5%
D	≥0.195 cm	82.5%	69.7%	80%	73%

CSA: cross-sectional area of median nerve on the postular bone plane; FR3: D/d on the hamate bone hook plane; D: transverse diameter of median nerve on the postular bone.

2. We selected the indicators with significant differences, namely CSA, D, and FR3, and used their mean values for further analyses. The average median nerve CSA on the postular bone plane of the control group was set as 0.1 cm², the average median nerve FR3 on the hamate bone hook plane was set as 3.32, and the average median nerve diameter D on the postular bone plane was set as 0.195 cm. The above values were assumed as the ultrasound

criteria of CTS, and the diagnostic sensitivity, specificity, PPV, and NPV were calculated in order to evaluate the diagnostic value of these three criteria.

HFU was found to be able to clearly show the median nerve. Intergroup comparison of the CT test results is shown in **Table 1**. The median nerve of the study group was found to be significantly thicker in all three planes, and the CSA was increased, especially on the postular bone plane, compared with the control group ($P<0.01$). Moreover, the median nerve of the study group was under pressure on the hamate bone hook plane and the FR was increased compared with the control group ($P<0.01$). The comparisons of the median nerve FR on the radioulnar joint and postular bone plane of the 2 groups did not show any significant differences ($P>0.05$). Similarly, the medi-

an nerve SR of the 2 groups showed no significant difference, and was hence not considered a diagnostic factor. When the threshold of the median nerve CSA on the postular bone plane was set as 0.1 cm^2, the diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of HFU for CTS were 92%, 86%, 91%, and 88%, respectively, indicating a good diagnostic value. However, when the median nerve FR3 on the hamate bone hook plane was used as the diagnostic indicator (set as 3.32), the diagnostic sensitivity, specificity, PPV, and NPV of HFU for CTS were reduced to 33.3%, 88%, 81%, and 47.5%, respectively, indicating a poor diagnostic value. When the median nerve D on the postular bone plane was used (set as 0.195 cm), the corresponding values were 82.5%, 69.7%, 80% and 73%, respectively, indicating a fair diagnostic value.

Discussion

CTS is caused by increased pressure within the carpal tunnel, which leads to pressure on the median nerve. Increased and decreased carpal tunnel volume can lead to increased pressure within the carpal tunnel. The diagnosis of CTS is generally based on clinical symptoms and characteristic physical findings, and electrical diagnostic examination is typically required for accurate diagnosis. Some CTS patients do not exhibit typical symptoms and signs; hence, improved objective examination is needed and factors that can distinguish CTS from the other neurological disorders need to be identified.

The preferred examination in cases of suspected CTS is EMG. Nerve conduction examination along with EMG can help in the accurate diagnosis of CTS, exclude other neurological disorders, and determine the severity of nerve injury. Therefore, EMG has significant value for clinical diagnosis; however, it has several limitations, including the fact that it is relatively invasive, and is hence not accepted by all patients, and the fact that electrophysiological examination by itself cannot directly and accurately assess the nature, extent, and changes of nerve injury, and cannot dynamically observe these developments and changes.

On the other hand, MRI can visualize soft tissues at high resolution, and represents an effective imaging method for visualization of ligaments, tendons, muscles, nerves, blood vessels, and other wrist morphological structures. Compared to electrophysiological examination, MRI can provide more information for the differentiation and diagnosis of CTS [11-14]; however, its clinical application is limited because of its high cost.

The establishment of a standard effective and relatively inexpensive diagnostic imaging method for CTS has become increasingly important. With development and progress in technology, new diagnostic tools and methods have been developed. Among these, HFU has been demonstrated to be capable of both dynamically and statically displaying the traveling directions of the upper peripheral nerves, and to fill the gaps of other diagnostic tools. HFU has been recently reported as a new technique in orthopedic clinical practice for the diagnosis of peripheral nerve entrapment syndrome. Ultrasonography is intuitive and associated with accurate positioning, and can easily show changes in nerve thickening, edema, and nerve continuity, thereby revealing the cause, location, and extent of entrapment. In a meta-analysis, Fowler et al. [18] concluded that ultrasound has a sensitivity and specificity of 77.6% and 86.8%, respectively, for the diagnosis of CTS. However, Fowler et al. [19] reported that ultrasound may not be more accurate than electrophysiological testing in complicated cases or cases in which the diagnosis is unclear.

HFU can clearly distinguish between anatomical carpal tunnel structures and identify the causes of many conditions, such as ganglion cysts, tendinous cysts, hematomas, lipomas, and thickening of radial transverse carpal ligament lesions [20, 21]; our study supports the diagnostic value of HFU for CTS.

This study showed that the median nerve CSA and FR in the hamate bone hook plane of the study group were significantly higher than those in the normal control group, which was consistent with other studies [22-26]. Although there are no widely accepted ultrasound diagnostic standards, previous studies on the quantitative determination of CTS by ultrasonography have reported that the median nerve CSA measured on the postular bone plane had the most significant diagnostic value [27]. In one previous study, when the threshold of the CSA on the postular bone plane was set as 9.0-15.0 mm^2,

the sensitivity and specificity for CTS were 70-97% and 57-100%, respectively [28]. Similarly, the present study showed that when the threshold of CSA in the postular bone plane was set as 0.1 cm^2, the sensitivity and specificity for CTS were 92% and 86%, respectively, indicating a high diagnostic value.

Presently, HFU is not widely used for the diagnosis of peripheral nervous system diseases, as most clinicians and doctors are not fully aware of its clinical value. With the development of ultrasound equipment and technology, more valuable information towards the CTS diagnosis, surgical method selection, and postoperative nerve blood supply situations can be obtained, and dynamic monitoring of the changes of the arterial and venous blood flow along the median nerve can be conducted.

To improve the clinical value and application of HFU for CTS diagnosis, further multi-center large-sample studies on its diagnostic value must be performed, measurements and diagnostic criteria must be unified, and operation procedures must be standardized, in order to allow specialization in clinical application for ultrasound doctors.

Conclusion

As a novel technique for the diagnosis of peripheral neuropathy, HFU can produce real-time dynamic images and clearly elucidate carpal tunnel structures and their relationships with the adjacent tendons. In addition, this method is simple and non-invasive, and the results are instant, suggesting that this technique is helpful for determining the cause of CTS, selecting appropriate treatment and surgical methods, reducing treatment costs, and improving the efficacy of CTS diagnosis. However, the limitations of our study are the single-center design and the small number of patients.

Our results showed that when the threshold of the median nerve CSA in the postular bone plane was set as 0.1 cm^2, the sensitivity and specificity were high; thus, we believe that CSA is a good clinical indicator of CTS.

Disclosure of conflict of interest

None.

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