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Characterization of Carpal Tunnel Syndrome using High Frequency Ultrasound Imaging: a Comparison of Ultrasonic Features in the Median Nerve

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***Abstract*—Diagnosis of Carpal Tunnel Syndrome (CTS) is based on the medical history, clinical provocation test, and electrodiagnostic studies. However, electrodiagnostic studies can be uncomfortable for some patients, due to the invasiveness. Ultrasonography has been suggested to characterize the median nerve (MN) in patients with CTS as an aid in the initial assessment. The study aimed to compare the diagnostic performance of ultrasonic features from the MN in normal volunteers and patients with CTS using high frequency ultrasound. All participants were examined in the sitting position with a palm facing up using an Aplio i800 system (Cannon Medical Systems, Otawara, Japan). The cross-sectional area (CSA; in mm^2) and blood flow of MN were evaluated at the wrist using an i24LX8 probe (9-24 MHz). Blood flow was interrogated using Color Doppler Imaging, Power Doppler Imaging, Monochrome Superb Microvascular Imaging (mSMI), and Color Superb Microvascular Imaging with the same imaging settings for all participants. The maximum vascular area from each technique was quantified offline using Matlab (MathWorks, Natick, MA, USA). Shear wave elastography (SWE) images were acquired using the i18LX5 probe (4-18 MHz) at the wrist. The stiffness (in kPa) of the MN was quantified using a built-in software tool. To date, analysis included 20 hands in 10 normal volunteers and 14 hands in 9 patients with CTS. The CSA, vascular area, and stiffness of MN in patients with CTS were significantly different from those in normal volunteers ($p < 0.04$). The CSA, vascularity from mSMI, and stiffness showed high diagnostic performance independently, albeit based on a small sample size. Additionally, the combination of CSA, mSMI, and stiffness of SWE showed a specificity of 100% and a sensitivity of 93% with an overall accuracy of 95%.**

Keywords—Carpal Tunnel Syndrome, high frequency ultrasound, shear wave elastography, Superb Microvascular Imaging

I. Introduction

Carpal Tunnel Syndrome (CTS) is the most common entrapment neuropathy with a 3-6% prevalence in the general population [1, 2]. CTS causes pain, numbness, and tingling in the hand and arm due to the pressure on the median nerve at the level of wrist. There is no gold standard for the diagnosis of CTS and the current approaches are based on medical history, clinical provocation test, and electrodiagnostic studies [3]. However, electrodiagnostic studies are invasive and can be uncomfortable for some patients [4, 5]. Imaging methods such as ultrasonography and magnetic resonance (MR) imaging have been suggested to characterize the median nerve (MN) in patients with CTS as an aid in the initial assessment. However, MR imaging can be time-consuming, expensive, and not as accessible compared to ultrasonography [6]. Ultrasonography has improved its image quality with new technologies, leading to an increased use of ultrasound evaluation of nerve entrapment syndrome [5].

Previous studies have investigated many ultrasonic features as diagnostic criteria for CTS. The most commonly agreed criteria is the enlargement of the MN cross-sectional area (CSA) [3, 7]. It was reported that the CSA of the MN was significantly bigger in patients with CTS than in healthy volunteers with a considerable correlation with electrodiagnostic findings ($p<0.01$) [8]. However, the sensitivity and specificity of diagnosing CTS based on CSA have ranged from 60-100% and 22-100%, respectively, with an overall accuracy in the range of 68-97.2% [5].

In other studies, functional ultrasonic features such as Doppler (color and power) sonography, Superb Microvascular Imaging (SMI), and elastography (strain and shear) were evaluated to aid in the diagnosis of CTS. Conventional Doppler technologies remove clutter by suppressing low velocity flow components. However, SMI separates slow flow signals from overlaying tissue motion artifacts using an adaptive algorithm, allowing the visualization of slow microvascular flow that may not be seen with conventional Doppler imaging [9, 10]. Patients with CTS showed higher vascularity and stiffness in their MNs compared to healthy controls [2, 5, 7, 9]. The purpose of this study was to compare the diagnostic performance of these ultrasonic features as well as combined features from the MN in normal volunteers and patients with CTS using high frequency ultrasound.

II. Methods

A. Subjects

This ongoing study was approved by IRB of Thomas Jefferson University and all participants provided written

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informed consent. The patient group was composed of patients who had been referred for the electrodiagnostic testing and diagnosed with CTS, both clinically and electrodiagnostically.

B. Ultrasound studies

The participants were examined in the sitting position with a palm facing up on the examination table using an Aplio i800 system (Cannon Medical Systems, Otawara, Japan). The CSA and blood flow of MN were evaluated at the wrist using an i24LX8 probe (9-24 MHz) with the highest center frequency allowed by the imaging system. The CSA (in mm^2) was obtained from the maximum nerve area at the pisiform level using the free-form measurement tool implemented on the scanner. The blood flow was interrogated from a sagittal view using Color Doppler Imaging (CDI), Power Doppler Imaging (PDI), Monochrome Superb Microvascular Imaging (mSMI), and Color Superb Microvascular Imaging (cSMI) with the same imaging settings for all participants. The maximum vascular area from each technique was quantified offline by counting colored pixels (arbitrary unit; a.u.) using Matlab (MathWorks, Natick, MA, USA).

Shear wave elastography (SWE) images were acquired using i18LX5 probe (4-18 MHz) at the level of proximal carpal row in a sagittal view. To avoid compression by the transducer, extra gel or an aqueous standoff pad (Parker Laboratories, Inc. Fairfield, NJ, USA) was used (Fig. 1(b)). The mean stiffness (in kPa) in the MN was quantified using a built-in software tool with a circular region of interest (ROI) selection. Each ROI size was adjusted to fit to the size of MN. The propagation map displayed with SWE was utilized to identify the two most reliable (smooth and parallel contour lines) measurements for each case (right side of Fig. 1). The final mean stiffness of the MN was obtained by averaging those two measurements.

C. Statistical analysis

Student's t-test (with a significance level of 5%) and receiver operating characteristic (ROC) analysis were performed for the ultrasonic features using Matlab. Additionally, ROC analysis was applied for the predictors created by combining the ultrasonic features using a generalized linear model.

III. Results

To date, the analysis includes 20 hands in 10 normal volunteers (6 women and 4 men) and 14 hands in 9 patients (7 women and 2 men) with CTS. The CSA, vascular area, and stiffness of MN in patients with CTS were significantly different from those in normal volunteers ($p < 0.04$). The results are summarized in Tables 1 and 2. Examples of stiffness from SWE, CSA, and vascularity from CDI, PDI, mSMI, cSMI measurements in CTS patient and normal volunteer are presented in the Figs. 1-4, respectively. In addition, the example shown in Fig. 3 demonstrates the difference in vascularity detection for the same MN region by various tools.

The CSA showed the highest accuracy and specificity for predicting CTS, while the stiffness from shear wave elastography achieved the highest sensitivity. The diagnostic cut-off point was determined where the Youden's index was maximum [11]. The combination of CSA and stiffness using a generalized linear regression showed the overall accuracy of 94% with a specificity and sensitivity of 100% and 86%, respectively. The CSA, stiffness, and mSMI combination improved the overall accuracy to 95% with specificity and sensitivity of 100% and 93%, respectively (cf., Fig. 5).

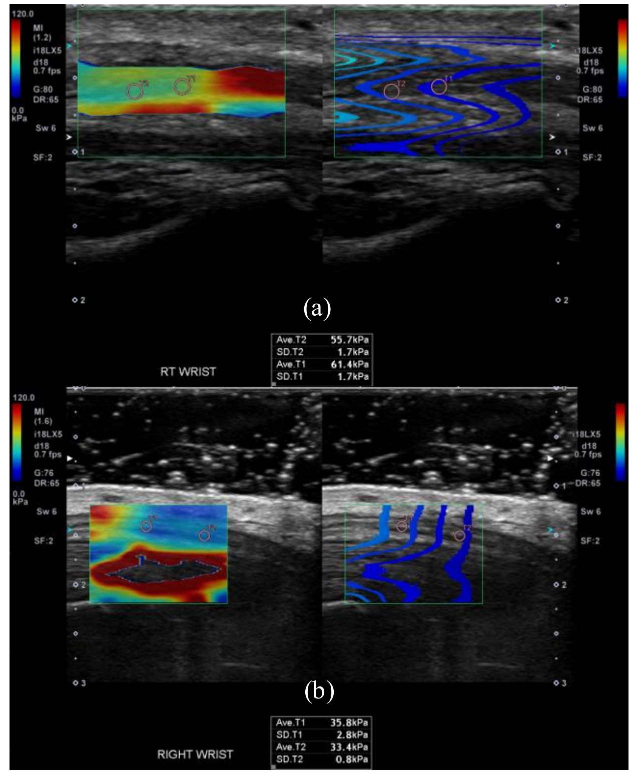

Fig. 1. Examples of stiffness measurement with shear wave elastography. (a) CTS patient (b) normal volunteer.

TABLE I. QUANTIFIED ULTRASONIC FEATURES (MEAN ± STANDARD DEVIATION)

Predictor	Normal volunteers	CTS patients
CSA	7.5 ± 1.2 mm^2	12.7 ± 4.2 mm^2
CDI	342.2 ± 867.2 a.u.	1701.3 ± 1918.2 a.u.
PDI	272.4 ± 687.6 a.u.	1249.0 ± 1843.7 a.u.
mSMI	490.1 ± 848.5 a.u.	1234.1 ± 955.0 a.u.
cSMI	251.4 ± 438.5 a.u.	2209.0 ± 2784.5 a.u.
Stiffness	56.4 ± 32.1 kPa	105.3 ± 35.9 kPa

IV. Discussion

The findings from this ongoing study agreed with previous studies [2, 3, 5, 7]. The patients with CTS showed a bigger CSA, greater vascularity and stiffness of the MN than normal volunteers. Although the CSA of MN has been reported to be the most consistent ultrasonic feature to predict CTS in previous studies, a lack of consensus on its threshold value

TABLE II. DIAGNOSTIC PERFORMANCE OF ULTRASONIC FEATURES

Predictor	T-test p value	Area under the ROC curve	Specificity	Sensitivity
CSA	<0.001	0.94	100%	79%
CDI	0.009	0.81	85%	79%
PDI	0.037	0.73	80%	64%
cSMI	0.004	0.83	95%	57%
Stiffness	<0.001	0.85	80%	93%

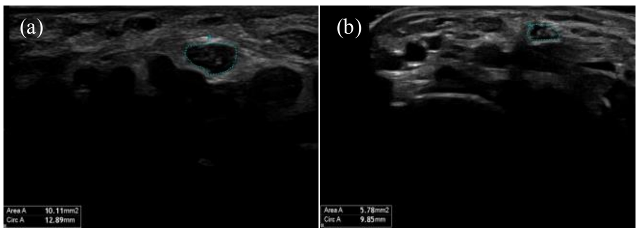

Fig. 2. Examples of CSA measurements. (a) CTS patient (b) normal volunteer.

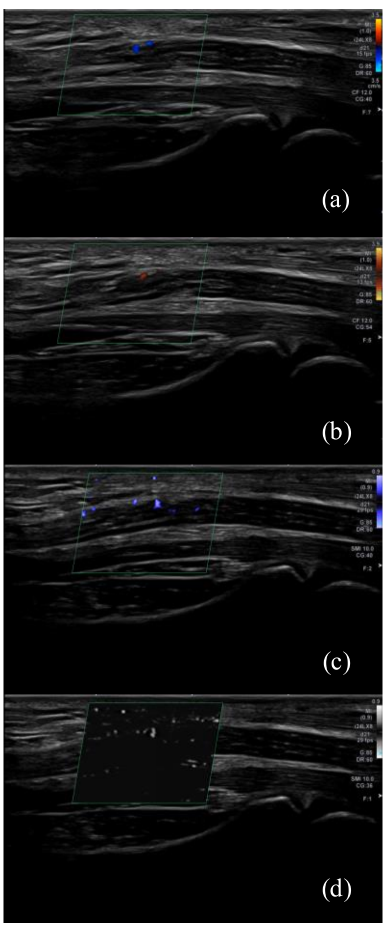

Fig. 3. Evaluation of vascular features for a CTS patient using (a) Color Doppler Imaging (b) Power Doppler Imaging (c) Monochrome Superb Microvascular Imaging (d) Color Superb Microvascular Imaging.

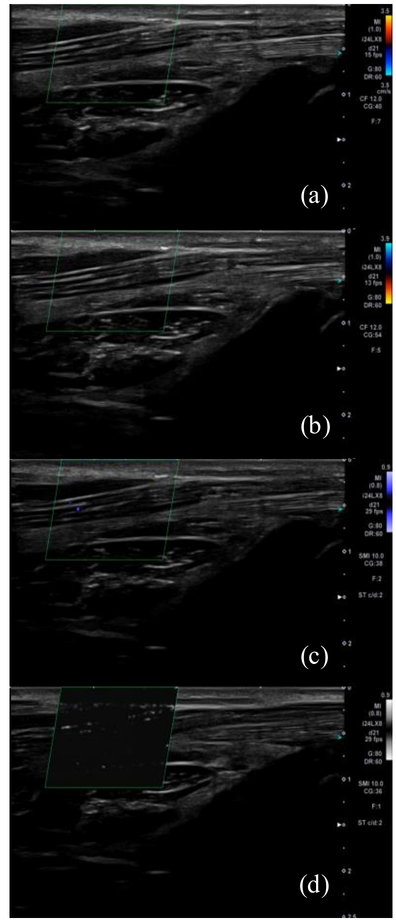

Fig. 4. Evaluation of vascular features for a normal volunteer using (a) Color Doppler Imaging (b) Power Doppler Imaging (note, the color bar is the same as CDI) (c) Monochrome Superb Microvascular Imaging (d) Color Superb Microvascular Imaging.

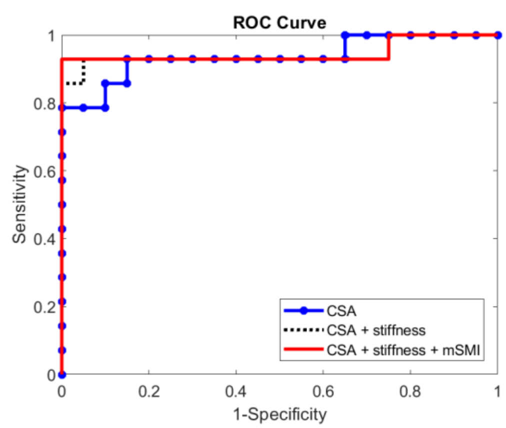

Fig. 5. Comparison of ROC curves from CSA only vs. combination of CSA and stiffness vs. combination of CSA, stiffness, and mSMI.

diminished its clinical reliability [6, 12, 13, 14]. The cut-off value for the CSA varied from 9 - 14 mm^2 in the previous studies [14] and the cut-off value ranged between 9.5 and 10.1 mm^2 (due to the discrete CSA values from the participants) to achieve 93% accuracy for this study.

Among the parameters evaluating the vascularity (i.e., CDI, PDI, mSMI, and cSMI), all showed similar accuracy except for PDI whose accuracy was a bit lower. Compared to the other ultrasonic features, the vascularity parameters showed a lower accuracy for diagnosing CTS in this study.

Previous studies evaluating the stiffness obtained from strain elastography as a biomarker to predict CTS showed specificities and sensitivities of 45-88% and 82-88%, respectively [3, 15]. The stiffness from SWE measurements showed higher diagnostic values, where the specificity and sensitivity ranges were 89-91%, 83-93%, respectively [16, 17]. Except for the study by Zhang et al., these studies revealed a higher sensitivity than specificity based on MN stiffness. In this study, we also found a higher sensitivity than specificity based on MN stiffness. Thus, the combined predictor using CSA and stiffness improved the sensitivity for diagnosing CTS over CSA alone. By adding a vascularity parameter to this combined predictor, only mSMI improved the sensitivity, while CDI, PDI, and cSMI did not.

This study has limitations. The current sample size is small and it needs further validation with a larger study. The quantification of stiffness was not objectively standardized. The reliable stiffness values were selected by referring to the propagation map subjectively. Also, the inter-observer agreement was not assessed.

V. Conclusion

The CSA, vascularity from mSMI, and stiffness showed high diagnostic performance independently, albeit based on a small sample size. The combination of these three predictors using generalized linear regression showed a specificity of 100% and a sensitivity of 93% with an overall accuracy of 95% indicating this could become a new diagnostic tool for evaluating patients with suspected CTS.

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