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Short communication

Comparison of two ways of altering carpal tunnel pressure with ultrasound surface wave elastography

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ABSTRACT

Higher carpal tunnel pressure is related to the development of carpal tunnel syndrome. Currently, the measurement of carpal tunnel pressure is invasive and therefore, a noninvasive technique is needed. We previously demonstrated that speed of wave propagation through a tendon in the carpal tunnel measured by ultrasound elastography could be used as an indicator of carpal tunnel pressure in a cadaveric model, in which a balloon had to be inserted into the carpal tunnel to adjust the carpal tunnel pressure. However, the method for adjusting the carpal tunnel pressure in the cadaveric model is not applicable for the in vivo model. The objective of this study was to utilize a different technique to adjust carpal tunnel pressure via pressing the palm and to validate it with ultrasound surface wave elastography in a human cadaveric model. The outcome was also compared with a previous balloon insertion technique. Results showed that wave speed of intra-carpal tunnel tendon and the ratio of wave speed of intra-and outer-carpal tunnel tendons increased linearly with carpal tunnel pressure. Moreover, wave speed of intra carpal tunnel tendon via both ways of altering carpal tunnel pressure showed similar results with high correlation. Therefore, it was concluded that the technique of pressing the palm can be used to adjust carpal tunnel pressure, and pressure changes can be detected via ultrasound surface wave elastography in an ex vivo model. Future studies will utilize this technique in vivo to validate the usefulness of ultrasound surface wave elastography for measuring carpal tunnel pressure.

1. Introduction

Carpal tunnel syndrome (CTS) is a common disorder of median nerve (MN) compression, which accounts for most of all entrapment neuropathies in upper extremity (Ghasemi-rad et al., 2014; Ibrahim et al., 2012). CTS pathophysiology has become commonly recognized to be highly related to carpal tunnel pressure (CTP). In average, normal CTP, at rest, ranges from 3 to 24 mmHg and a possible obstruction of blood flow and nerve paresthesia might occur, as a sign of median nerve disorder when it exceeds 30 mmHg (Coppieters et al., 2012; Gelberman et al., 1981; Goss and Agee, 2010; Hamanaka et al., 1995; Luchetti et al., 1989; Seradge et al., 1995).

Aside from repetitive wrist and finger movement, high CTP could also come from externally applied force. One particular study looked into the results of CTP when applying a force of 1 kg on different locations of the palm and wrist (Cobb et al., 1995). A total of 16 points were selected and they discovered that those points directly on the central line of carpal tunnel and both radial and ulnar points near the carpal tunnel outlet, were sensitive to externally applied force. In addition, the relationship of a single point compression near the outlet of carpal tunnel was investigated in a preliminary study and the results shown that the CTP was linearly proportional with the applied force (Kubo et al., 2017a).

Currently, invasively inserting a catheter sensor is the only way to measure carpal tunnel pressure. On the other hand, ultrasound has been used extensively to help diagnose CTS as a non-invasive tool. A method utilizing ultrasound surface wave elastography (USWE) was developed to measure CTP (Kubo et al., 2017b; Wang et al., 2012). By measuring the shear wave speed propagating through the third flexor digitorum superficialis (FDS) in the carpal tunnel, this technique has been applied to a cadaver model simulating CTS in a pilot study and CTP was highly correlated to wave speed.

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Before entering the next phase of collecting data from CTS patients, it would be more convincing and would further solidify the reliability of USWE if we could detect the pressure change in carpal tunnel in healthy subjects. However, previously, a balloon was inserted into the carpal tunnel of a cadaver model to create different pressure conditions, as it is invasive to do it in vivo (Kubo et al., 2017b; Wang et al., 2012). Since applying force on the palmar area was confirmed to be an effective and simple way of altering CTP, we intended to apply different magnitude of forces on the palm and combine USWE to look into the correlation of wave speed of tendon and CTP in two different ways of increasing CTP. This study was conducted on human cadaver hands to verify the feasibility of USWE prior to performing it on normal human controls to gain more evidence that the USWE would be useful to deduce CTP accurately and noninvasively. This study hypothesized that the wave speed would increase with higher CTP and the wave speed results from two ways of increasing CTP would be highly correlated with each other.

2. Materials and methods

Eight human fresh, frozen cadaveric specimens from the forearm to finger were collected from the Anatomy Department at Mayo Clinic approved by the Institutional Review Board (4 males and 4 females; 3 left and 5 right hands; aged 20–80 years were included). None of them had a prior disease history that could potentially jeopardize the carpal tunnel intactness.

All specimens were prepared with the distal forearm bones fixed in a supinated position, wrist neutral, and fingers extended by using Velcro straps, as in Kubo, et al's study (Kubo et al., 2017a). The median nerve and each of the flexor tendons were attached to a suture and given 50 g of pre-load except the third FDS by hanging weights gliding through pulleys. For the third FDS, multiple weights were applied to simulate different tendon tensions. Next, the prepared specimen was fixed and put on a base plate for external force application and CTP sensor insertion (Fig. 1). Setup details were referenced from a previous preliminary study, as well as confirmation of the linear relationship between applied force and CTP with a high R^2 of 0.9998 (Kubo et al., 2017a).

For measuring the ultrasound surface wave elastography, a 0.1 s harmonic vibration at 100 Hz was generated by a function generator (Model: FG33120A, Hewlett Packard, Palo Alto, CA), amplified by an audio amplifier and transmitted through an electromagnetic shaker (Model:FG-142, Labworks Inc., Costa Mesa, CA) applied to the skin. The tip of the shaker was a spherical (4 mm in diameter) indenter and was placed onto the third FDS through the skin. The propagated shear wave was then detected by a linear array ultrasound probe L11-4 with central frequency of 6.4 MHz (Verasonics, Inc, Kirkland, WA). The probe was positioned longitudinally on the central line of carpal tunnel width and half of it lies outside the proximal border of the carpal tunnel and the other half lies inside (Fig. 1). Therefore, we were able to measure the wave propagation simultaneously both inside and outside of carpal tunnel. Eight ultrasound tracking lines inside and outside the tunnel, respectively were used to measure the wave propagation at each pressure and at each tension level (Fig. 2). Measurements were performed and recorded three times at each condition. Surface wave speed (SWS) in the tendon was estimated using a phase gradient method

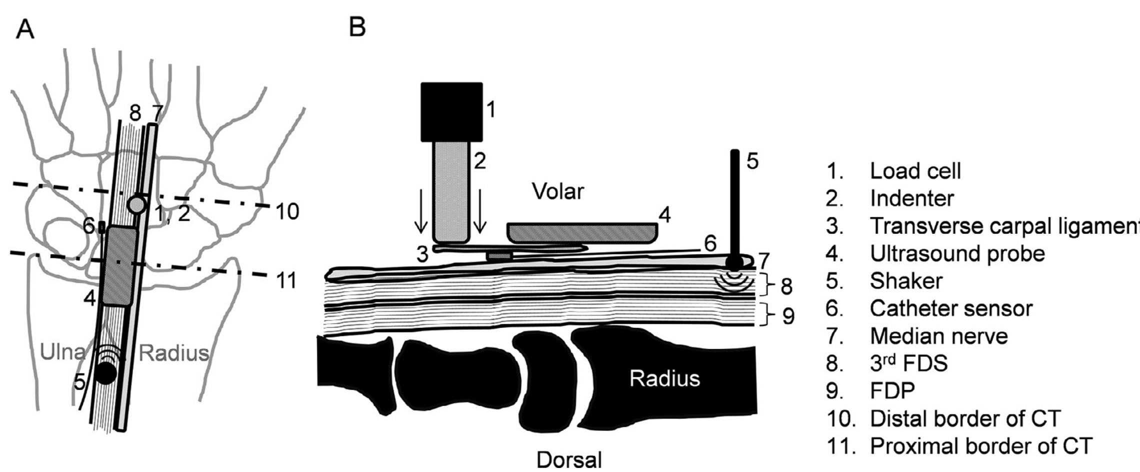

Fig. 1. (A) Coronal view and (B) sagittal view of experimental setup.

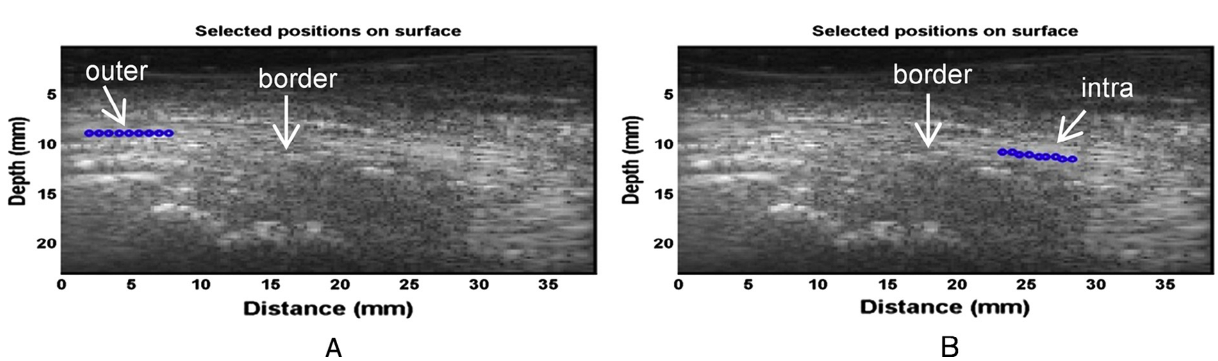

Fig. 2. In-situ human tendon testing, eight locations over a length of 8 mm in the tendon were selected to measure the outer (A) and intra (B) carpal tunnel tendon using ultrasound tracking beams.

$$v = \left| \frac{2\pi f}{\alpha} \right| \quad (1)$$

where v is the wave speed to be determined, f is the excitation frequency in Hz, and α is the slope of the linear regression between phase delay and distance (Zhang et al., 2017a; 2017b; Zhou et al., 2017; Zhang et al., 2018).

After preparation of the cadaveric specimens and setup of all the equipment, measurement was conducted starting from CTP of 0 mmHg and gradually increased the independent variable CTP to 10, 20, 30, 60, 90, 120, and 150 mmHg through the palmar pressing by the indentation system and collected data under each condition. Then we increased the independent variable tendon tension of the third FDS (50, 200, 500, 1000, 1500 g) and repeated the same procedure. A total of 35 conditions (7 pressures $*$ 5 tensions) were tested. After finishing all the conditions in palmar pressing, the indentation system was removed and replaced with a balloon inserted into the carpal tunnel guided by a Kirschner wire (Kubo et al., 2017b). A balloon was gradually inflated by injecting normal saline to increase CTP. The same procedures were repeated, as the palmar pressing mentioned above.

3. Statistical analysis

Mean and standard deviation of intra-, outer- and the ratio of intra- and outer-carpal tunnel SWS (i-SWS, o-SWS and r-SWS) at each tendon tension and CTP conditions were calculated. Two-way ANOVA with repeated measures was carried out and the critical p value was set at 0.05. In addition, coefficient of determination (R^2) was calculated with CTP versus i-SWS and r-SWS, respectively. Linear equation was also computed by regression to further establish the relationship between CTP and SWS. These data reduction procedures were done on the results of both palmar pressing and balloon inflation, respectively. Pearson's correlation coefficient was used to evaluate the relationship between palmar pressing and balloon inflation on both i-SWS and r-SWS.

4. Results

For the palmar pressing method, mean values with standard deviation of i-SWS, o-SWS, r-SWS, and the linearly fitted lines under each of the five tendon tensions are shown in Fig. 3. The statistical outcomes showed that there was no interaction between CTP and tendon tension (i-SWS: $p = 0.557$, o-SWS: $p = 0.639$, r-SWS: $p = 0.708$). There was a significant main effect of CTP on both i-SWS ($p = 0.000$) and r-SWS ($p = 0.000$) but not o-SWS ($p = 0.375$). However, no significant main effect of tendon tensions was found in i-SWS, o-SWS, and r-SWS (i-SWS: $p = 0.144$, o-SWS: $p = 0.285$, r-SWS: $p = 0.329$). Similar results were found in the balloon method, as well as with i-SWS and r-SWS and both increased with CTP but not o-SWS. In addition, the computed equations of the linearly fitted lines with R^2 values all higher than 0.85 from both palmar pressing and balloon inflation methods are shown in Table 1. Moreover, results from both methods of increasing CTP were displayed to be highly correlated with each other. Pearson's correlation r values are all higher than 0.9.

5. Discussion

From our results, it was clear that the higher CTP, the higher i-SWS. On the other hand, for the portion outside the carpal tunnel, o-SWS held nearly constant with the increased CTP. These results indicated that pressure increase may alter the elastic properties of the tendon within carpal tunnel but not the one outside of carpal tunnel. This was further elucidated by the statistical results with no significant difference in o-SWS. Due to the consistency of o-SWS, the ratio of i-SWS to o-SWS, namely r-SWS, displayed the same trend as i-SWS and increased proportionally with CTP with significant difference. Through obtaining the linear equations of CTP versus SWS, it enabled us to indirectly infer the CTP by simply calculating the SWS in a non-invasive manner.

As for higher tendon tension, it did not increase the CTP significantly. This might be related to the anisotropic attribute of tendon. The load we applied to tendon as a tension was in the longitudinal direction. However, the effect of CTP change was more in a trans-

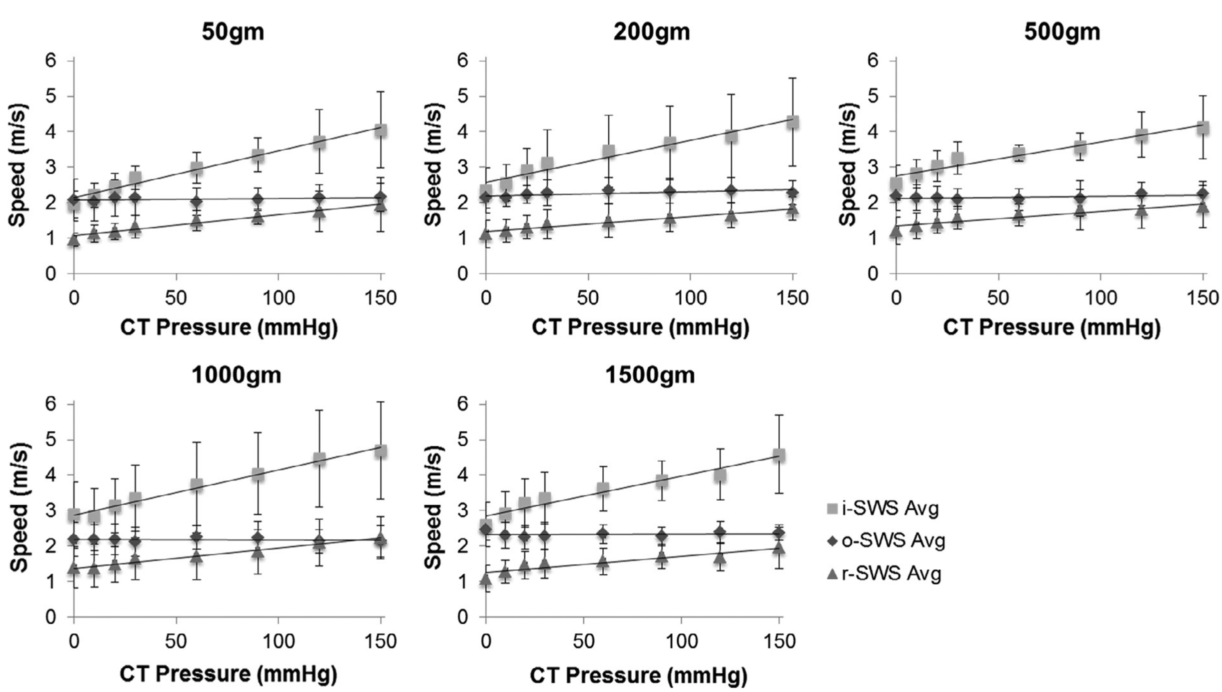

Fig. 3. i-SWS, o-SWS and r-SWS under different CTP (increased by palmar pressing) and tendon tension.

Table 1
Linear fitted equation and R^2 values are shown as well as Pearson's correlation coefficient of i-SWS and r-SWS to show the relationship between two methods using palmar pressing and balloon inflation to increase CTP.

Tendon Tension	Parameters	Methods	Linear equation	R^2	Pearson correlation (r)
50 g	i-SWS	Palmar pressing	y = 0.0133x + 2.1372	0.9794	0.999
		Balloon inflation	y = 0.011x + 2.3795	0.9765	
	r-SWS	Palmar pressing	y = 0.006x + 1.0716	0.9737	0.996
		Balloon inflation	y = 0.0048x + 1.0339	0.9795	
200 g	i-SWS	Palmar pressing	y = 0.0118x + 2.5786	0.9472	0.995
		Balloon inflation	y = 0.0067x + 2.4807	0.9672	
	r-SWS	Palmar pressing	y = 0.0042x + 1.1964	0.9574	0.991
		Balloon inflation	y = 0.0033x + 1.1532	0.9258	
500 g	i-SWS	Palmar pressing	y = 0.0095x + 2.7717	0.9476	0.993
		Balloon inflation	y = 0.0098 + 2.8218	0.9387	
	r-SWS	Palmar pressing	y = 0.0041x + 1.351	0.8807	0.978
		Balloon inflation	y = 0.0038x + 1.2108	0.9138	
1000 g	i-SWS	Palmar pressing	y = 0.0127x + 2.881	0.9828	0.979
		Balloon inflation	y = 0.0091x + 2.9742	0.9444	
	r-SWS	Palmar pressing	y = 0.0058x + 1.3758	0.9755	0.947
		Balloon inflation	y = 0.0033x + 1.1754	0.9135	
1500 g	i-SWS	Palmar pressing	y = 0.0112x + 2.8457	0.9464	0.981
		Balloon inflation	y = 0.0099x + 3.3261	0.9346	
	r-SWS	Palmar pressing	y = 0.0046x + 1.2611	0.8667	0.936
		Balloon inflation	y = 0.0034x + 1.3694	0.9581	

i-SWS: Intra-carpal tunnel shear wave speed; r-SWS: Ratio of intra- and outer-carpal tunnel shear wave speed.
For linear equations, y is shear wave speed and x is carpal tunnel pressure.

verse direction. In addition, this could also be because the tensions applied and the elongation response were mostly in the linear zone. Therefore, the stiffness was similar leading to no significant increase in SWS when we increase the tendon tension. However, applying tension out of this range could pose an effect on SWS. In future studies, as long as the tendon tension would be controlled in this range, a non-biased deduction of CTP could be obtained. In this study, we also compared the results from two different methods of increasing CTP. They both displayed a linear relationship with high R^2 values under multiple tendon tensions. Moreover, from the results in Table 1, high correlation was found between the two methods, indicating that the trends of CTP induced by both methods were considered to be identical. USWE could pick up the same pressure change within the carpal tunnel in both methods.

In this study, we calculated the ratio of i-SWS and o-SWS (r-SWS) instead of the difference between i-SWS and o-SWS (d-SWS), as a previous study suggested (Kubo et al., 2017b). These two parameters both aimed to normalize and eliminate the variability among different individuals. For d-SWS, it still consisted of the same and relatively large deviation, as in i-SWS. However, it was found that there was lower deviation in r-SWS compared to d-SWS, especially in higher CTP conditions. Therefore, we believe that taking the ratio of i-SWS and o-SWS to normalize it and using r-SWS as an indicator of indirect measurement of CTP, would be more accurate and appropriate for further examination on CTS patients to reduce individual differences.

This study was done on human cadavers so the original internal property and environment of carpal tunnel might not be the same, as in living human. In addition, the methods we proposed to increase CTP neglected the pathological changes of the soft tissue in CTS but simply focused on the pressure increase. Further studies should be carried out to apply USWE on living humans, including both the normal and CTS patients, to eliminate the limitations encountered in this study. Despite the limitations, several important discoveries have been made. i-SWS and r-SWS were found to increase in proportion with elevated CTP. More importantly, whether the elevated pressure was induced by palmar pressing or balloon inflation, i-SWS and r-SWS both showed similar results with high correlation. This suggested that as long as there is a change in CTP, we would be able to indirectly detect it through USWE in a non-biased manner based on the non-significant main effect in this tendon tension range. We believe that this non-invasive technology could serve as a useful tool in helping the diagnosis of CTS for clinicians.

Conflict of interest statement

There are no conflicts of interest for all authors.

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