Original Article

Application of real-time shear wave elastography in the assessment of torsional cervical dystonia

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Background: This study aimed to investigate the value of real-time shear wave elastography (SWE) in the assessment of torsional cervical dystonia (TCD).

Methods: Ninety healthy volunteers and 30 TCD patients were recruited, and elastography was performed at musculi sternocleidomastoideus (MSD) and musculi splenius capitis (MSC). Mean shear elastic modulus of right MSD and MSC in healthy controls and bilateral MSD and MSC in TCD patients was determined. The thickness of MSD and MSC of affected muscles was measured in TCD patients.

Results: In TCD patients, the mean shear elastic modulus of affected MSD and MSC was significantly higher than that of corresponding normal muscles ($P<0.01$) and that of controls ($P<0.01$). The diagnostic threshold was 24.9 kPa for MSD and 25.07 kPa for MSC (for MSD and MSC, the area under ROC was 0.979 and 0.979, with a sensitivity of 90% and 91.3%, and a specificity of 95.6% and 96.7%, respectively). The elastic modulus of neither affected nor normal MSD and MSC was significantly related to age and body mass index ($P>0.05$). The shear elastic modulus of affected MSD and MSC was positively related to the peak electromyography ($r=0.83$–0.73, $P<0.01$). The thickness of affected MSD and MSC was significantly thicker than that of corresponding normal muscles in TCD patients ($P<0.01$).

Conclusions: Real-time SWE can identify the difference in shear elastic modulus of MSD and MSC between the affected and normal side in TCD patients, indicating important diagnostic value in the assessment of muscular status for these patients.

Keywords: Shear wave elastography; real-time; torsional cervical dystonia; skeletal muscle; shear elastic modulus

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Introduction

Cervical dystonia (CD) is the most common type of focal dystonia and characterized by abnormal head and neck movement and abnormal posture due to intermittent or persistent involuntary contraction of neck muscles, causing a significant physical and psychological burden or even loss of working ability (1). Botulinum toxin type A is still the treatment of choice for CD (2). In the anti-dystonia treatment, objective and accurate assessment of muscular tension and monitoring of muscular function is crucial for the treatment, efficacy assessment and guidance for further treatment.

In clinical practice, clinicians usually assess the affected muscles by clinical symptoms and palpation, but this is subjective. Electromyography (EMG) as an effective tool can aid the clinical assessment of affected muscle for clinicians (3,4). EMG can be divided into needle EMG and surface EMG, of which needle EMG has been widely used in clinical practice (5). Needle EMG can reveal the function and pathophysiological status of spastic neck muscles and contralateral antagonistic muscles, but the morphology of spastic and hypertrophic muscles cannot be identified. It is also invasive and may cause discomfort to patients (5). Surface

EMG reflects the integrated myoelectric activity of muscles and is also non-invasive and easy to operate, but it cannot record the myoelectric activity of deep muscles and affected by some factors (6). Magnetic resonance elastography (MRE) is another method used for the assessment of spastic muscles and can detect muscular stiffness, but it is costly and time-consuming (7). Thus, it is necessary to develop non-invasive, intuitive, simple and convenient methods for observation of morphology, structure, and biology of muscles.

The muscular stiffness can objectively reflect the muscular status, and the spastic or twitching muscles have increased stiffness (8-10). Real-time shear wave elastography (SWE) is a new technique developed in recent years for measurement of tissue elasticity. This technique employs "Mach cone" principle and can collect the shear wave velocity by using ultra-fast imaging system for the calculation of elastic modulus of tissues, which can be used for the assessment of tissue stiffness. This technique has been a non-invasive, real-time, intuitive, simple and rapid one for assessment of muscular stiffness (11). It has been shown that SWE can be used for the measurement of shear elastic modulus of skeletal muscle (12-14). MSD stiffness was detected by using acoustic radiation force impulse in patients with congenital muscular torticollis (15). However, there was few studies reporting SWE applied in adult torsional cervical dystonia. In this study, (I) SWE was used for detection of shear elastic modulus of musculi sternocleidomastoideus (MSD) and musculi splenius capitis (MSC) in healthy controls; (II) the shear elastic modulus of MSD and MSC was compared between healthy controls and torsional CD (TCD) patients; (III) the relationship of shear elastic modulus of MSD and MSC with the degree muscular spasm determined by needle EMG parameters were assessed in CD patients. This study aimed to evaluate the value of SWE in the assessment of muscular status in TCD patients.

Methods

General characteristics

This study was approved by the Ethics Committee of Tongji Hospital of Tongji University. Written informed consent was obtained from each subject, and they understood the methods and examinations used in this study.

Patients with primary TCD were recruited from the Department of Neurology, Tongji University between March 2016 and March 2018, of whom simple TCD patients were recruited. Inclusion criteria were as follows: (I) patients were diagnosed with primary TCD; (II) simple TCD was confirmed. Exclusion criteria were as follows: (I) there were evident causes of TCD (such as brain trauma, spinal cord lesion, trauma, toxicity, perinatal injury, long term use of neuropsychiatric drugs); (II) there were comorbidities such as neurological diseases and systemic diseases; (III) there were nervous system positioning signs or cranial MRI showed abnormalities; (IV) patients received cranial or cervical surgery before recruitment; (V) patients received neck BTX-A treatment within the prior 3 months; (VI) patients were diagnosed with mixed TCD or simple TCD accompanied by continuous tremor.

In addition, healthy controls were recruited from the Center for Physical Examination of Tongji Hospital. There was no history of heart disease, diabetes mellitus, respiratory diseases, mental diseases, muscular dystrophy or head and neck pain in these patients.

Instrument and methods

Ultrasonography

SWE was performed by using the Aixplorer US system (SuperSonic Imagine, Aix-en-Provence, France) with an SL15–4 multifrequency linear probes operating at 4–15 MHz. MSD was superficial; thus the gen pattern was used in the general mode. MSC was relatively deeper than MSD, and superficial fascia was relatively compact. Thus pen pattern was adopted. The "penetration" mode was selected to deepen the penetration of the shear waves. The depth was 3 cm.

Patients were asked to sit on a chair with back leaning on the chair back. The neck was examined under pathological status, and patients should avoid the correction of head position. Some actions could induce pathological status. The probe was gently placed on the lateral neck to visualize the MSD with the depth of 3 cm and the elastic modulus of 0–600 kPa. On the cross-section, the thickness of MSD was measured at the middle of MSD. The MSD was examined along with the longitudinal axis up to the thoracic head and clavicular head. After examining the parallel muscle bundle, the examination was performed at elastography mode, and the lesion was determined in the area with the highest elastic modulus (*Figure 1A*). The region of interest (ROI) (10 mm × 10 mm) was determined, and the probe was maintained for several seconds. When the images became stable, the images were frozen, and round regions (diameter: 4 mm) were selected for the measurement of shear elastic modulus. The measurement was repeated 5 times. The system would automatically calculate mean Young's moduli,

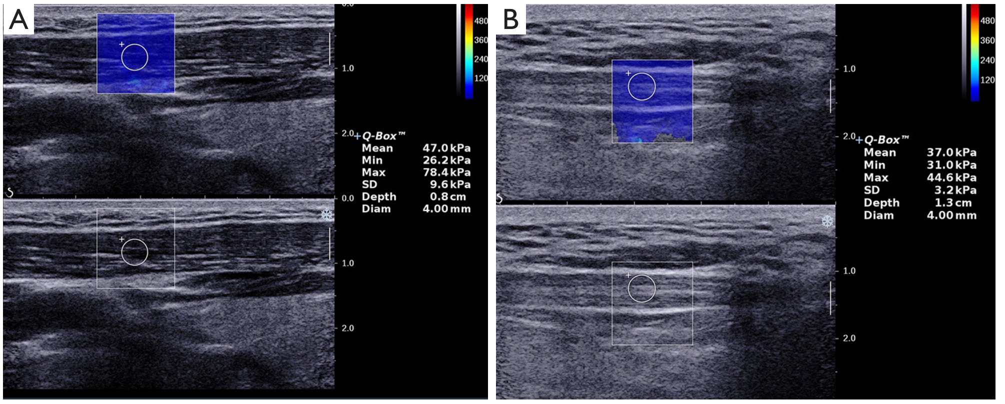

Figure 1 The lesion was determined in the area with the highest elastic modulus. (A) After examining the parallel muscle bundle, the examination was performed at elastography mode, and the lesion was determined in the area with the highest elastic modulus; (B) after examining the parallel muscle bundle along the longitudinal axis from the seventh cervical vertebra to the linea nuchae superior, the lesion was determined at the region with the highest elastic modulus.

MaxYoung's moduli, minimum Young's moduli of muscle in the region of interest, while mean Young's moduli were used for statistical analysis. In the examination of MSC, the probe was placed on the back neck, and the MSC was examined from the linea nuchae superior to the spinous process of a fifth cervical vertebra. The thickness of MSC was measured on the cross-section. After examining the parallel muscle bundle along the longitudinal axis from the seventh cervical vertebra to the linea nuchae superior, the lesion was determined at the region with the highest elastic modulus (*Figure 1B*). The measurement was repeated 5 times, and a mean was calculated. The shear elastic modulus of MSD and MSC was also examined in controls with similar methods. Because the severity of lesions at upper, middle and lower part of MSD and MSC were different in CD patients, indicating that sometimes lesions focused at a specific segment, the muscular stiffness of upper 1/3, middle, and lower 1/3 part of MSD and MSC were usually detected, the maximal stiffness was chosen as ROI, and elastic modulus was measured. Meanwhile, the results of elastic modulus and electromyography were run for correlation analysis. During the examination, pressure should not be administered via the probe, and examination was done in the same room at the room temperature of 24 ℃ by the same physician who had a 10-year experience on the ultrasound examination of skeletal muscles.

Exploration by needle EMG and infusion after localization

Subjects were asked to achieve good rest on the day of examination. In addition, oral drugs (such as Baclofen, clonazepam, benzoresin hydrochloride, etc.) and excitatory nerve drinks (such as wine, coffee, tea, etc.) were discontinued on the day of examination. In this study, electromyograph and evoked potential detector (NTZ-2000, Shanghai Nuocheng Electric Co., Ltd.) were used. Patients were asked to sit on a chair, and the examiner stood beside or back of the subject. Electrode placement: generally, the electrode was placed at the detection site and injection site. Localization of the muscle: the head turned to the opposite side, and the needle was placed at the upper, middle, thoracic head and clavicular head of the muscle, followed by EMG at 2–5 points; the skin and muscle were fixed with a hand of the examiner, and then the needle was inserted into the MSC, followed by EMG at 3–6 sites. Diagnostic criteria: subjects were asked to relax or keep the neck at the abnormal status. The involvement of the examined muscle in the abnormal movement was determined according to the motor unit action potential (MUAP) measured by EMG. The cluster release of EMG signals with the rhythmic sound of released action potential on EMG suggested the involvement of the muscle in the abnormal neck movement (16). After examination, Botox injection was performed once the involvement of the muscle was confirmed.

Statistical analysis

All the data are expressed as mean ± standard deviation and statistical analysis were performed with SPSS version 21.0. In this study, continuous variables (such

Table 1 General information

Demographic data	Healthy controls, n=90	Cervical dystonia, n=30	P value
Age	49.66±15.16	48.00±12.47	0.55
Gender	45/45	18/12	0.34
Handedness (R/L)	87/3	29/1	1.00
BMI, kg/m^2	23.86±2.22	23.90±2.19	0.93

BMI, body mass index.

as body weight, BMI, shear elastic modulus, muscular thickness) were compared with the independent t-test, and correlation analysis was done with the Pearson correlation analysis. Categorical variables (such as gender, left/right handedness) were compared with independent Chi-square test, and correlation analysis was done with the Spearman rank correlation test. A value of P<0.05 was considered statistically significant.

Results

General characteristics

Among these 120 patients with primary CD, 33 patients were diagnosed with simple TCD, and finally, 30 patients received ultrasound examination of the muscles after exclusion of 3 patients with continuous tremor. Right torsion was found in 18 patients, left torsion in 12 patients, and 11 patients had concomitant should elevation. The longest course of disease was 125 months, and the shortest one was 1 month (mean: 29.27±31.55 months). According to the Tsui scale (17), the score of these patients was 3–10 (mean: 6.47±2.76). The spasm mainly involved ipsilateral MSC, musculi levator scapulae, contralateral MSD, and cucullaris. 90 healthy controls were divided into 3 groups according to the age: 20–39 years group, 40–59 years group and 60–79 years group (n=30 per group). The age, gender, BMI and handedness of subjects are shown in *Table 1*.

In 7 patients, the shear elastic modulus was undetectable due to thick MSC. In TCD patients, the thickness of affected MSD was 1.49±1.53 cm thicker than that of intact MSD (max: 6.10 cm) (P<0.01); the thickness of affected MSC was 2.87±2.67 cm thicker than that of intact MSC (range: 0.10–8.70 cm) (P<0.01). In addition, the thickness of affected MSC and MSD in TCD patients was also significantly different from that in controls (P<0.01). The elastic modulus was comparable between MSD and MSC (P>0.05). The elastic modulus of intact MSD and MSC in TCD patients was also similar to that in controls (P>0.05). SD value was relatively high in the affected group, which was associated with disease severity according to Tsui scale. The difference of Young's moduli between severing and the mild lesion was big, leading to high SD value with a maximum >30 kPa, while the difference of mean Young's moduli in normal muscle tissues, leading to low SD value with a maximum >4 kPa (*Table 2*).

In healthy controls, the shear elastic modulus of MSC and MSD had no relationship with age (r=0.08 and 0.08, respectively; P=0.48 and 0.46, respectively; *Figure 2*). In TCD patients, the shear elastic modulus of affected MSD and MSC had no relationship with age (r=0.20 and 0.10, respectively; P=0.29 and 0.66, respectively; *Figure 3*). In TCD patients, the shear elastic modulus of affected MSD and MSC was positively related to the increased amplitude of involuntary waves (r=0.83 and 0.73; P<0.01). The shear elastic modulus of affected MSD and MSC in TCD patients and that of MSD and MSC in healthy controls had no relationship with BMI (r=0.04 and –0.07; P>0.05).

The elastic modulus of affected MSD and MSC in TCD patients was significantly different from that in healthy controls (P<0.01) (*Figure 4*). ROC analysis showed the diagnostic threshold of MSD and MSC was 24.90 kPa and 25.07 kPa, respectively (area under ROC: 0.979 and 0.979; sensitivity: 90.0% and 91.3%; specificity: 95.6% and 96.7%) (*Figure 5*).

The intraclass correlation coefficient of MSD and MSC elastic moduli in the normal control group was 0.92 and 0.91 respectively. The intraclass correlation coefficient of contralateral MSD and MSC elastic moduli was 0.90 and 0.91 respectively. The intraclass correlation coefficient of affected MSD and MSC elastic moduli was 0.89 and 0.88 respectively (*Table 3*).

Discussion

TCD is the most common type of CD (18) and mainly involves contralateral MSD, cucullaris, ipsilateral MSC and musculi levator scapulae. Especially, the MSC and MSD are the most susceptible to CD (18). Thus, in the present study, MSD and MSC were examined by SWE, and the shear elastic modulus of both muscles was determined, aiming to assess the features and muscular tension of both muscles in TCD patients.

The cause of CD remains still poorly understood (19). It has been widely accepted that the occurrence of CD is as

Table 2 MSD and MSC in three groups

Group	Thickness of MSD (cm)	Mean shear elastic modulus (kPa)	Thickness of MSC (cm)	Mean shear elastic modulus (kPa)
Affected (n=30/23)				
x̄±S	10.95±1.98[ac]	55.42±36.38[ab]	9.33±3.06[ac]	62.10±34.88[ab]
Min	7.70	21.83	5.20	21.07
Max	13.80	162.83	17.10	122.60
Contralateral (n=30)				
x̄±S	9.46±1.60[c]	20.93±4.52	6.45±1.55[c]	20.45±4.01
Min	6.80	13.50	3.60	12.87
Max	12.20	32.13	9.90	26.77
Controls (n=90)				
x̄±S		19.57±2.93		19.48±2.81
Min		12.87		12.86
Max		26.80		25.89

[a], TCD patients: muscles at affected side *vs.* intact side; [b], muscles at the affected side in TCD patients *vs.* corresponding muscles in controls; [c], TCD patients: MSC *vs.* MSD at the affected side and intact side. MSD, musculisternocleidomastoideus; MSC, musculi splenius capitis.

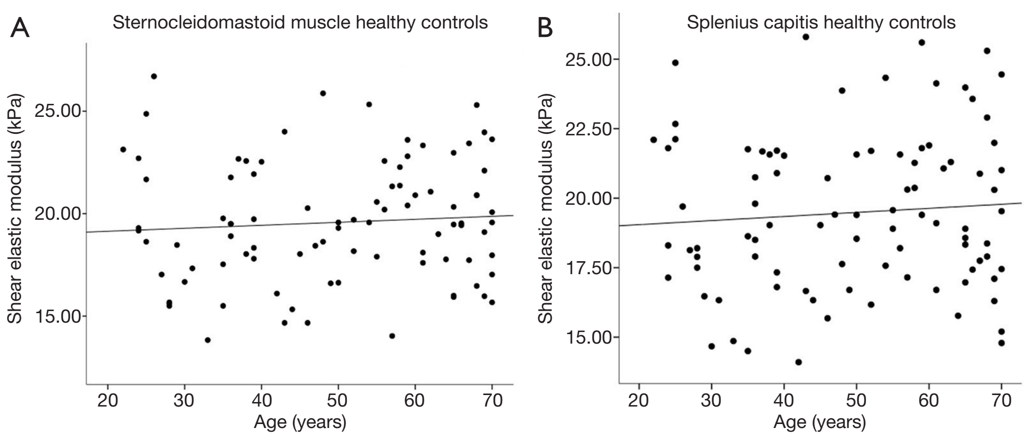

Figure 2 In healthy controls, the shear elastic modulus of MSD (A) and MSC (B) had no relationship with age. MSD, musculisternocleidomastoideus; MSC, musculi splenius capitis.

a result of interaction between genetic and environmental factors. In the early phase of CD, the spastic muscles have weak strength and the corresponding contralateral muscles may counteract with it, and thus there is no significant difference in the muscular volume. The progression of CD may significantly increase the difference in the muscular strength between the intact side and affected side. The volume of spastic muscles may progressively increase due to the long-term uncontrollable movement, resulting in hypertrophy and stiffness of affected muscles. There is evidence showing that the distribution of spastic and hypertrophic muscles on CT is closely related to the type of CD (20). Generally, the hypertrophic muscles are mainly distributed in the posterior 1/4 region of rotator capitis side (such as MSC, musculi semispinalis capitis, musculus semispinalis cervicis, and musculi levator scapulae). In the present study, routine ultrasonography was done to measure the thickness of related muscles. Currently, there is no

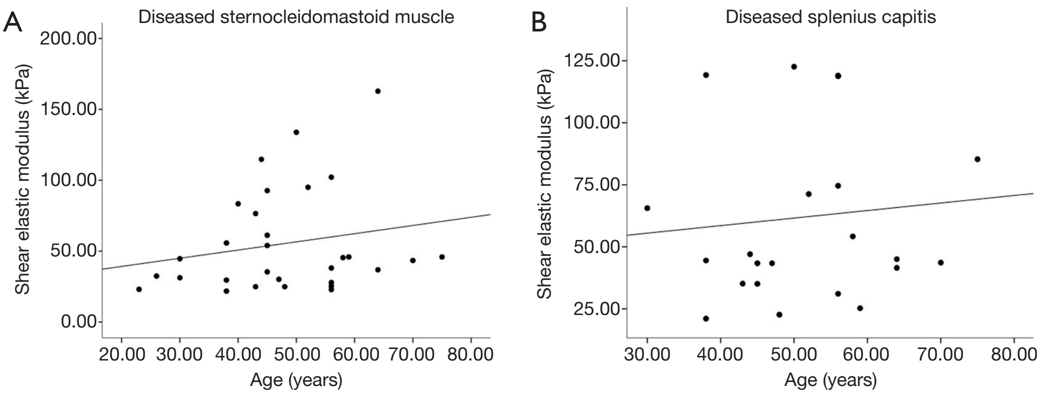

Figure 3 In TCD patients, the shear elastic modulus of affected MSD (A) and MSC (B) had no relationship with age. TCD, torsional cervical dystonia; MSD, musculisternocleidomastoideus; MSC, musculi splenius capitis.

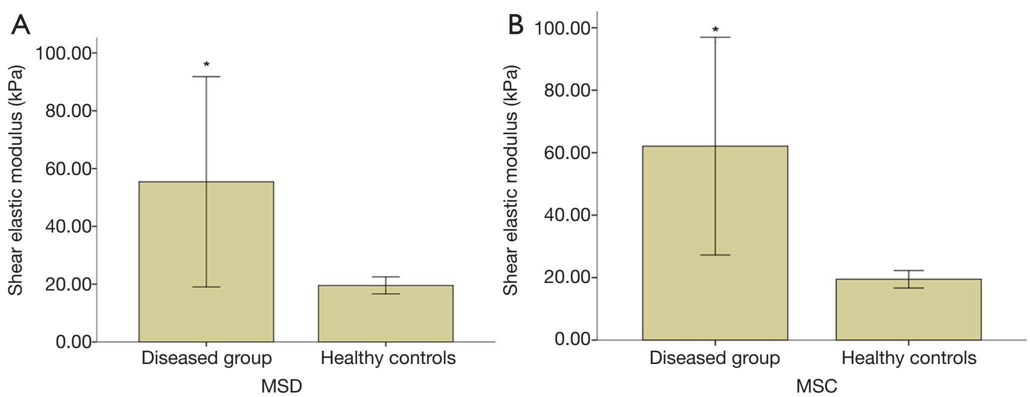

Figure 4 The elastic modulus of affected MSD (A) and MSC (B) in TCD patients was significantly different from that in healthy controls. MSD, musculisternocleidomastoideus; MSC, musculi splenius capitis; TCD, torsional cervical dystonia.

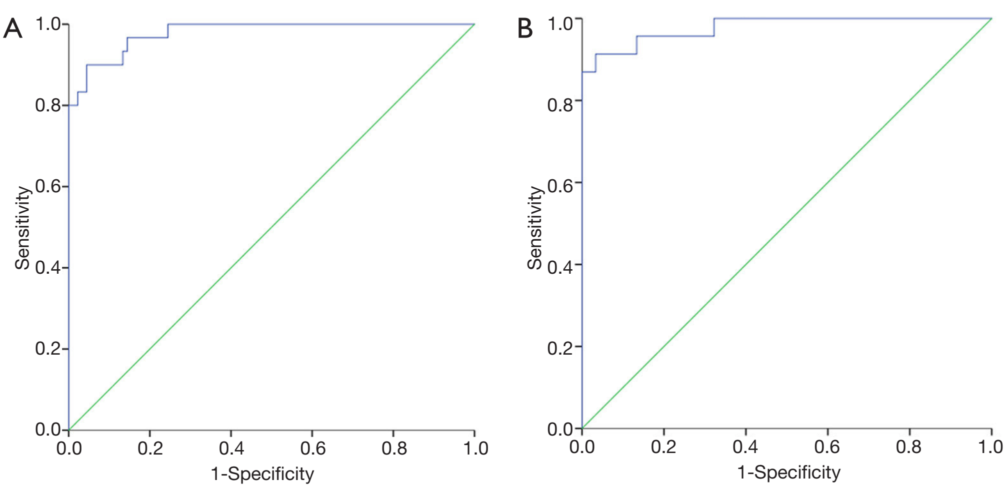

Figure 5 ROC analysis showed the diagnostic threshold of MSD (A) and MSC (B) was 24.90 and 25.07 kPa, respectively. MSD, musculisternocleidomastoideus; MSC, musculi splenius capitis.

Table 3 The intraclasscorrelationcoefficient of MSD and MSC elastic moduli

Group	Correlation coefficient	95% CI
Normal MSD (n=90)	0.92	0.89–0.94
Normal MSC (n=90)	0.91	0.87–0.93
Affected MSD (n=30)	0.89	0.80–0.95
Affected MSC (n=23)	0.88	0.79–0.94
Contralateral MSD (n=30)	0.90	0.82–0.95
Contralateral MSC (n=30)	0.91	0.85–0.95

MSD, musculisternocleidomastoideus, MSC, musculi splenius capitis; CI, confidence interval.

normal range for neck muscles on the cross-section. Thus, it is crucial to compare the muscles of both sides. Our results showed the thickness of spastic muscles increased significantly as compared to corresponding contralateral muscles in TCD patients, and the increase was more evident in the MSC of rotator capitis side.

As compared to other elastographic techniques, SWE does not require manual compression, which reduces the operation error and increases the repeatability (21-23). In addition, it determines the shear elastic modulus which represents the biological characteristic of muscles, and thus it is applicable in the quantification of muscular tissues. Examiner intraclass repetitive researches were also conducted in this study. Results showed that ICC was over 0.75, indicating that elastic moduli measure with SWE was reliable and repeatable. Muscular tissues have anisotropy. It is speculated that during the measurement of shear elastic modulus, the measurement will be more accurate and have better repeatability when the acoustic beam plane is parallel to that of muscular fibers (24). In the present study, the probe was parallel to the muscular fibers in the measurement of MSC and MSD. SWE can quantify the shear elastic modulus of neck muscles in a non-invasive manner. Our results showed there was a significant difference in the shear elastic modulus of MSC and MSD between healthy controls and CD patients, and the diagnostic threshold was 24.92 and 25.22 kPa, respectively, with high sensitivity and high specificity. In our study, the subjects were asked to keep calm during the measurement because MSD was superficial, and thus the results were stable. However, the elastic modulus of MSC was undetectable in 7 subjects. This might be ascribed to that the MSC is deep (under the cucullaris), the muscles in back neck became thicker, and the vibration amplitude of tissues in back neck reduces because the connective tissues in the back neck are dense and the probe frequency is limited (4–15 MHz). In the present study, only simple TCD patients were included, and those with continuous tremor were excluded because our previous findings showed the shear elastic modulus on SWE was unstable in patients with continuous tremor.

Arda *et al.* (25) speculated that the mean elastic modulus of normal masseter, gastrocnemius, and supraspinatus had no relationship with age, and there was no significant difference in the elastic modulus among different muscular tissues. Our results showed the shear elastic modulus of affected MSD and MSC in TCD patients, and that of MSD and MSC in healthy controls had no relationship with age, and there was no significant difference in the shear elastic modulus between MSC and MSD in healthy controls.

Nordez *et al.* (26) applied SWE in the assessment of shear elastic modulus of musculus biceps brachii during the isometric contraction, and results showed the shear elastic modulus was positively related to the myoelectric activity during the isometric contraction and linearly associated with the myoelectric activity in a specific range of isometric contraction. Our results showed the elastic modulus of spastic muscles was significantly higher than that of contralateral muscles, which suggests that the stiffness of affected muscles is higher than that of intact muscles. In addition, it was positively related to the myoelectric activity on needle EMG.

There are still several limitations to this study. Although the patients were blind to examination, the double-blind examination was difficult for the examiner, which may cause bias in the explanation of results. Moreover, the sample size was small, and a single center was involved, which may cause subjective errors. Thus, our results should be further validated in more multicentered studies with large sample size.

Taken together, SWE is a simple and convenient method for the assessment of muscular strength. The measurement of muscular mechanical properties is helpful for the understanding of the interaction between muscular structure and function, and for quantification of muscular elasticity, which provide scientific evidence for the diagnosis of spastic muscles and following assessment of prognosis. Thus, SWE has applicable good value in clinical practice. Of note, there are several limitations to SWE which is also muscle selective, and more clinical trials with large sample size are warranted to confirm our findings.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The study was conducted in accordance with the Committee for Human Research at our institution and followed all regulations. Informed consent was obtained before scans.

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