Clinical Imaging 40 (2016) 1075–1080

Contents lists available at ScienceDirect

Clinical Imaging

journal homepage: http://www.clinicalimaging.org

Ultrasound shear wave elastography in assessment of muscle stiffness in patients with Parkinson's disease: a primary observation

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ARTICLE INFO

Article history:
Received 18 September 2015
Received in revised form 14 May 2016
Accepted 25 May 2016
Available online xxxx

Keywords:
Biceps brachii muscle
Parkinson's disease
Shear wave elastography
Young's modulus

ABSTRACT

Objective: The aim of this study was to assess the capability of ultrasound shear wave elastography (SWE) in evaluating the muscle stiffness in patients with Parkinson's diseases (PD).
Methods: Ultrasound SWE of the longitudinal biceps brachii was performed on 46 patients with PD and 31 healthy controls from May 2013 to October 2013. The stiffness of the biceps brachii muscles measured with quantitative Young's modulus (kPa) was compared between the remarkably symptomatic arms and mildly symptomatic arms in the PD and between PD and controls with unpaired *t* test. The correlation between the Young's modulus of the biceps brachii measured by SWE and motion scores assessed by unified Parkinson's disease rating scale (UPDRS) part III was analyzed by Pearson's correlation coefficient. The reliability of SWE in assessment of biceps brachii stiffness was tested using intraclass correlation coefficient (ICC).
Results: The mean Young's modulus of biceps brachii in remarkably symptomatic arms, mildly symptomatic arms, and healthy controls was 59.94 ± 20.91 kPa, 47.77 ± 24.00 kPa, and 24.28 ± 5.09 kPa, respectively. A significant difference in Young's modulus of biceps brachii was found between healthy controls and all PD patients (all $P<.05$); however, it was not between remarkably symptomatic and mildly symptomatic arms. A positive linear correlation was found between the Young's modulus of the biceps brachii and the motion score by UPDRS in patients with PD ($r = 0.646$, $P = .000$). The ICC for interobserver and intraobserver variation in measuring Young's modulus of the biceps brachii with SWE was 0.74 (95% confidence interval 0.68–0.78) and 0.78 (95% confidence interval 0.75–0.82), respectively.
Conclusions: SWE of the biceps brachii can be used as a quantitative assessment of muscle stiffness in the patients with PD.

1. Introduction

Parkinson's disease (PD) is a chronic progressive neurological disorder that is characterized by rest tremor, bradykinesia, rigidity, and postural instability [1]. The symptoms in the patients with PD are unequivocally produced by the rigidity of the muscles. As a clinical symptom, however, the rigidity refers to the phenomenon of an increased muscular resistance when passively stretching the muscle. Currently, main clinical examination methods for the evaluation of motor abilities in the patients with PD include the unified Parkinson's disease rating scale (UPDRS) [2] and the Hoehn and the Yahr Scale [3]. However, these methods in assessment of stage and/or scale of the PD are complex and require a neurological professional to manually pressing on the muscle or moving the joint [2]. In addition, they are not subjective methods. Therefore, the demand of noninvasive technique for quantifying mechanical characteristics of the muscles in the patients with PD has been increasing. Recently, magnetic resonance elastography with external vibration on the muscle has been applied to assess muscular disorders [4–6] (e.g., the increase of muscle tension and shear wave length). However, its utility is limited by its high cost and the contraindications for the patients having claustrophobia or a pacemaker [5,6].

Shear wave elastography (SWE) is a 2D shear wave imaging technique, using acoustic radiation force to generate shear waves that are tracked with an ultrafast plane wave insonification technique [7]. Ultrasound scanner generates a remote radiation force through focused ultrasonic beams that induce the propagation of transient shear waves. An ultrafast echographic imaging sequence is subsequently performed to acquire successive raw radiofrequency data at an extremely high frame rate (≤20,000 frames/s) [8]. In muscle biomechanical applications, SWE has been used to measure passive [9], load-dependent muscle elasticity [10] and elasticity changes in healing muscle [11]. However, we have not found any report of using SWE in assessment of muscle stiffness in the patients with PD during our reference review.

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http://dx.doi.org/10.1016/j.clinimag.2016.05.008
0899-7071/

Given that the muscle rigidity in PD alters the muscle stiffness and the SWE assesses tissue stiffness (e.g., muscle), our hypothesis was that the value of muscle Young's modulus representing the muscle stiffness in the patients with PD differed from that in healthy subjects. Alternatively, SWE can be used as a quantitative marker in evaluating muscle stiffness in the patients with PD.

2. Materials and methods

2.1. Patients

This study included 46 patients (27 men and 19 women, mean age of 47.9 ± 2.8 years) who were diagnosed with PD according to British Brain Bank clinical criteria [2] (Table 1). Subjects had no other current or past neuromuscular disorders (e.g., motor neuron disease, dystrophies, peripheral neuropathy), besides PD. The duration of PD was less than 10 years and patients were in Hoehn–Yahr stage I-II [3]. All the patients had one arm remarkable and the other mild in symptom. Sixteen of the patients were taking medication for PD (Table 2).

The motion ability of all patients was examined with the UPDRS subscale III (Table 3).

In addition, 31 healthy volunteers (18 men and 13 women, mean age of 46.7 ± 3.2 years) were enrolled as control group. All volunteers underwent neurological examination before their SWE examinations. They had no history of neuromuscular disorders of any kind or taking any medication.

The Institutional Ethics Committee approved the study and written informed consent was obtained from all subjects. This study was conducted in the accordance with the declaration of Helsinki.

2.2. Ultrasound SWE

All subjects were placed in supine position and kept their limbs in full relaxation. SWE was performed with an AixPlorer ultrasound scanner (Supersonic Imagine, Aix en-Provence, France) equipped with a linear array transducer (4–15 MHz). We started with grayscale images with musculoskeletal setting. The ultrasound transducer was gently placed on the arm skin where the biceps brachii is located without any compression.

The Young's modulus was measured at the middle portion of the biceps brachii muscle belly where the maximal muscle bundle was located. A color-coded box superimposed on the grayscale image represents the region of interest (ROI) (Fig. 1). The ROI was placed near the center of the muscle belly where the maximum thickness of the muscle was present. The color scale of blue (soft) and red (hard) in color-coded box represents the value of Young's modulus in the ROI, when the color distribution appears homogeneous for at least 3 s. In addition, a 5-mm-diameter circle was placed around the center of the ROI for quantitative analysis [12]. Subsequently, the maximal, minimal, and the mean Young's modulus in the selected circular areas was measured using Q-Box software installed in the ultrasound scanner (Fig. 1).

Three measurements in each muscle were obtained in every subject and the mean Young's modulus was the average of the three Young's modulus measurements.

The same standard measurement of Young's modulus was applied in all subjects with PD and healthy controls.

Table 1
Clinical characteristics of the PD and control groups

Item	Control	PD
Number of cases	31	46
Mean age (years)	46.7 ± 3.2	47.9 ± 2.8
Female/male	13/18	19/27

PD: Parkinson's disease.

Table 2
Characteristics of medication in subjects with PD

Patient No.	Sex	Duration of medication	Medication
1	M	3 years	1
2	M	1 year	2 + 3
3	M	3 years	2
4	F	3.2 years	2
5	F	5 years	3
6	M	3.5 years	3 + 4
7	F	10 years	2 + 5
8	F	1 month	2
9	M	2 years	5
10	M	4 months	3
11	M	4 months	6
12	M	3 years	2
13	F	1 month	2
14	F	2 years	2 + 5
15	M	1 year	4 + 7
16	M	1 year	7

1: Hydrochloric acid benserazide (Madopar); 2: Pramipexole hydrochloride (Sifrol); 3: Hydrochloric acid benserazide (Madopar); 4: Valproic acid sodium (Amantadine); 5: Amantadine hydrochloride (Amantadine); 6: Traditional drug; 7: Arotinolol hydrochloride (Carbamazepine).

Nine controls were randomly selected to be scanned twice by one observer. These controls were also scanned by two observers separately for testing the repeatability and reproducibility of SWE in measuring Young's modulus of the muscles.

2.3. Statistical analysis

All quantitative variables including Young's modulus of the muscle in the patients with PD and healthy controls, and motion scores by UPDRS were expressed as mean and standard deviation. An unpaired 2-tailed *t* test was used to analyze the difference in mean Young's modulus of the biceps brachii between the remarkably symptomatic arms and the mildly symptomatic arms in patients with PD, as well as between the patient with PD and healthy controls. The correlations between the Young's modulus and the motion scores in remarkably symptomatic arms in PD patients were analyzed with Pearson's correlation coefficient. The repeatability and reproducibility of Young's modulus measurements were tested using the intraclass correlation coefficient (ICC, two-way mixed, single measures). A *P* value of less than .05 was considered to indicate a statistical significance. All data were analyzed by SPSS 19.0 software (SPSS, Chicago, IL, USA).

3. Results

All clinical information of the patients with PD and healthy volunteers were listed in Table 1.The name and dose of mediations for PD were listed in Table 2. The Young's modulus of longitudinal biceps brachii in remarkably symptomatic arms, mildly symptomatic arms in the patients with PD, and healthy controls was 59.94 ± 20.91 kPa, 47.77 ± 24.00 kPa, and 24.28 ± 5.09 kPa, respectively (Fig. 1). There was a significant difference in Young's modulus of the biceps brachii between PD and controls (all $P<.05$) and no significant difference between remarkably and mildly symptomatic arms (Table 4).

A positive linear correlation was found between the Young's modulus of longitudinal biceps brachii and the motion scores ($r=.646$, $P=.000$) in the patients with PD (Fig. 2). The ICC for interobserver and intraobserver variation in measuring Young's modulus of the biceps brachii with SWE was 0.74 (95% confidence interval 0.68–0.78) and 0.78 (95% confidence interval 0.75–0.82), respectively.

4. Discussion

Our results have demonstrated that the Young's modulus of the longitudinal biceps brachii in patients with PD was higher than healthy