



Quantitative Evaluation of Gastrocnemius Medialis Stiffness During Passive Stretching Using Shear Wave Elastography in Patients with Parkinson's Disease: A Prospective Preliminary Study

Lu Yin¹, Lijuan Du¹, Yuanzi Li¹, Yang Xiao², Shiquan Zhang², Huizi Ma³, Wen He¹

¹Department of Ultrasound, Beijing Tiantan Hospital, Capital Medical University, Beijing, China; ²Institute of Biomedical and Health Engineering, Shenzhen Institutes of Advanced Technology, Chinese Academy of Sciences, Shenzhen, China; ³Center for Movement Disorders, Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Objective: To prospectively investigate the feasibility of shear wave elastography (SWE) as a new quantitative and objective method for evaluating the stiffness of the gastrocnemius medialis (GM) muscle during passive stretching in patients with Parkinson's disease (PD).

Materials and Methods: SWE of the GM muscle was performed in 28 patients with PD [13 female and 15 male; mean age \pm standard deviation (SD): 63.0 ± 8.5 years] and 12 healthy controls (5 female and 7 male; mean age \pm SD: 59.3 ± 6.4 years) during passive ankle rotation. A Young's modulus-ankle angle curve was constructed. The GM slack angle and baseline Young's modulus (E_0) were compared between the markedly symptomatic and mildly symptomatic sides of patients with PD, and healthy controls. Additionally, the correlation between the GM slack angle and the severity of rigidity, and the observer reproducibility of SWE in determining the GM slack angle were evaluated.

Results: The GM slack angle was smaller on both the markedly and mildly symptomatic sides in patients with PD than in healthy controls (mean \pm SD of $-29.13^\circ \pm 3.79^\circ$ and $-25.65^\circ \pm 3.39^\circ$, respectively, vs. $-21.22^\circ \pm 3.52^\circ$; $p < 0.001$ and $p = 0.006$, respectively). Additionally, in patients with PD, the GM slack angle on the markedly symptomatic side was smaller than that on the mildly symptomatic side ($p = 0.003$). The E_0 value was lower on both the markedly and mildly symptomatic sides in patients with PD than in healthy controls (mean \pm SD of 10.11 ± 2.85 kPa and 10.08 ± 1.88 kPa, respectively, vs. 12.23 ± 1.02 kPa; $p = 0.012$ and $p < 0.001$, respectively). However, no significant difference was found between the markedly and mildly symptomatic sides in patients with PD ($p = 0.634$). A negative linear relationship was observed between the GM slack angle and lower limb rigidity score on the markedly symptomatic side in patients with PD ($r = -0.719$; $p < 0.001$). The intraclass correlation coefficients for observer reproducibility of SWE ranged from 0.880 to 0.951.

Conclusion: The slack angle determined by SWE may be a useful quantitative and reproducible method for evaluating muscle stiffness in patients with PD.

Keywords: Muscle stiffness; Slack angle; Shear wave elastography; Rigidity; Parkinson's disease

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Corresponding author: Wen He, MM, Department of Ultrasound, Beijing Tiantan Hospital, Capital Medical University, No.119 West Section of South 4th Ring Road, Fengtai District, Beijing 100070, China.

• E-mail: ttyyus@sina.com

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INTRODUCTION

Parkinson's disease (PD), the second most common neurodegenerative disorder after Alzheimer's disease, is characterized by rigidity, postural instability, resting tremor, and bradykinesia [1]. The prevalence of PD is estimated to be approximately 1% in people aged > 60 years in developed countries [2]. Rigidity, a cardinal motor sign of PD, is related to abnormal muscle extensibility and flexibility, and refers to the increased resistance of a muscle under passive stretching [3]. Passive muscular elastic properties, such as muscle stiffness, play major roles in musculoskeletal extensibility and flexibility [4]. However, the contribution of muscle stiffness to rigidity in patients with PD remains unclear.

Currently, the clinical assessment tools commonly used for evaluating the severity of rigidity in patients with PD include the Hoehn-Yahr Scale [5] and Unified Parkinson's Disease Rating Scale (UPDRS), part III [6]. However, these assessments require neurological professionals to move the joint, palpate the muscle, and determine the severity of PD. Thus, these assessments are subjective and non-quantitative. The error in diagnosing PD of neurologists specializing in neurodegenerative disorders can be up to 20% [7]. Therefore, the demand for noninvasive assessment tools for quantifying passive elastic properties and muscle stiffness in patients with PD has been increasing.

Myotonometry and magnetic resonance elastography (MRE) have been used to evaluate muscular compliance and resistance in patients with PD [8-10]. Myotonometry cannot reveal muscle structures in real time. Additionally, muscle morphology, particularly the orientation of muscle fibers, strongly affects its accuracy in evaluating muscle elastic properties [11]. The usefulness of MRE is limited because it is expensive, has some contraindications, takes a long time to perform, and requires patients with PD to remain stationary during the examination.

Shear wave elastography (SWE) is an emerging ultrasound technique that allows quantitative measurement of biomechanical properties under pathological or physiological conditions in real time [12]. It tracks shear waves generated by acoustic radiation forces as they propagate through muscle tissues. Shear waves travel faster through stiffer tissues than through more lax tissues [13]. Some studies have indicated that SWE and MRE have good agreement in the assessment of soft tissues [14-16]. Previous studies have reported that compared with healthy subjects, patients

with PD exhibit increased passive muscle stiffness (i.e., a larger elastic modulus) in a relaxed or fixed position on ultrasound elastography [17-19]; however, skeletal muscle is a dynamic tissue, and its biomechanical properties cannot be comprehensively evaluated using a single image frame or a single static elastic parameter at rest or in a fixed position. Moreover, in patients with PD, the relationship between muscle stiffness and the joint angle during passive stretching is not fully understood. SWE allows dynamic assessment of passive muscle stiffness throughout the functional range of motion (ROM) in patients with PD by determining the slack angle, which is defined as the angle at which passive muscle tension begins to increase [20-22]. Therefore, this study aimed to investigate the feasibility of SWE as a new quantitative and objective method to evaluate the stiffness of the gastrocnemius medialis (GM) muscle in patients with PD during passive stretching.

MATERIALS AND METHODS

This prospective study was approved by the Institutional Review Board of our hospital and was conducted in accordance with the Declaration of Helsinki (IRB No. KYSQ 2019-039-01). Written informed consent was obtained from all subjects.

Participants

Twenty-eight patients with PD with lower limb rigidity were recruited between October 2019 and February 2020. The inclusion criteria were as follows: 1) meeting the standards of the Movement Disorder Society Clinical Diagnostic Criteria for Parkinson's disease [23], 2) Hoehn-Yahr stage I-II, 3) age between 45 and 80 years, 4) a duration since the diagnosis of at most 10 years, and 5) no neuromuscular diseases (e.g., motor neuron disease) other than PD. To minimize the influence of muscular activity on the measurement of passive elastic properties, the patients were asked to continue their medications for PD (e.g., Madopar). The exclusion criteria were as follows: 1) resting tremor as the main manifestation of PD, 2) lower extremity dystonia caused by stroke or other conditions, 3) a history of lower limb trauma or surgery, and 4) serious cardiopulmonary or other systemic diseases. Additionally, 12 sex- and age-matched healthy participants with no history of trauma to the legs or neuromuscular disorders were selected as the control group. Clinical information, including age, sex, height, weight, duration of PD, and UPDRS lower limb

rigidity score, of all participants was recorded.

Grouping

For each patient with PD, the markedly symptomatic and mildly symptomatic lower limb was identified according to the severity of rigidity evaluated by the UPDRS lower limb rigidity score (0 = no rigidity, 1 = slight rigidity, 2 = mild rigidity, 3 = moderate rigidity, 4 = severe rigidity) [6]. The side with a higher score was considered to be markedly symptomatic. If the scores were the same, the side with the first onset was considered to be the markedly symptomatic side for evaluation. For healthy subjects, the right leg was used as the control. Thus, our study included three groups: the markedly symptomatic side of patients with PD, the mildly symptomatic side of patients with PD, and healthy controls.

Muscle Length and Thickness Measurement

GM muscle thickness was measured as the distance between the anterior and posterior muscle membranes at the center of the GM muscle on a transverse grayscale ultrasonogram. We calculated the average of three measurements [24]. GM muscle length was measured as the distance between the internal epicondyle of the femur and the distal musculotendinous junction using a tape measure. The musculotendinous junction was confirmed using ultrasonography (US). We calculated the average of three measurements [25].

Dynamic SWE Acquisition

The patient was placed in the supine position with one foot tightly fastened to the footplate of an isokinetic dynamometer, which could stretch the GM muscle passively by automatically rotating the ankle. The ankle was passively rotated from 40° plantar flexion to the end-ROM (the angle at which the subjects felt pain) with a constant velocity of 2°/s. The neutral position was defined as 0°, with a negative value for plantar flexion and a positive value for dorsal flexion. Simultaneously, the Young's modulus of the GM was measured using an Aixplorer US scanner in the SWE mode with a linear array probe (SL15-4; SuperSonic Imagine). A schematic diagram of the experimental process is shown in Figure 1.

The US probe was manually adhered to the middle and upper third of the posteromedial side of the lower leg (marked by a skin marker for fixed measurement after identifying the thickest part of the GM muscle on a

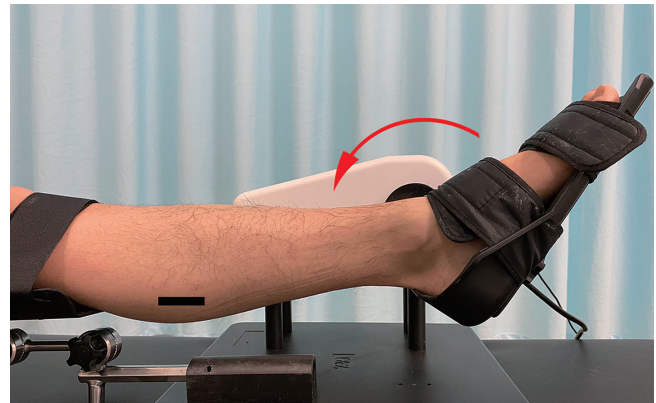


Fig. 1. Schematic diagram of the experimental setup. The red arrow represents the direction of movement of the ankle joint. The ultrasound probe is adhered to the skin and is parallel to the muscular fibers to provide a clear view of the gastrocnemius medialis muscle belly with minimal pressure during the entire examination.

conventional), and a region of interest with a size of 10 x 10 mm was chosen at the center of the GM muscle. The probe was positioned parallel to the myofibers to maximize the reliability of the measurements with minimal pressure during the whole examination because extra pressure from the probe could have resulted in overestimation of muscle stiffness [26]. Oral instructions were provided to the subjects to relax completely and avoid active muscle contractions or movements throughout the process. Surface electrodes were used to obtain electromyography signals of the GM muscle and detect any undesired active contractions. Electromyography activity of < 1% is required during passive stretching [27].

The first cycle was considered preconditioning, and the next three cycles were considered for analysis. The same measurement process was applied to both legs of each patient with PD and to the right legs of healthy volunteers.

Slack Angle and Baseline Young's Modulus Determination

The ankle angle corresponds to the Young's modulus value. A Young's modulus-ankle angle curve was constructed. The GM slack angle was defined as the angle at which passive GM muscle tension began to increase and was determined visually by an experienced observer. This visual observation was similar to that of the exponential model and exhibited good intra- and inter-observer reliabilities [28-30]. The average Young's modulus before the slack angle was defined as the baseline Young's modulus (E_0).

Reliability Evaluation

The intra- and inter-observer reproducibility of SWE in

determining the GM slack angle were assessed. For inter-observer reliability, all participants were examined by two observers on the same day. For intra-observer reliability, observer A took two independent measurements on two consecutive days at approximately the same time. Observer A had 5 years of experience in ultrasonic elastography, and observer B had one year of experience in ultrasonic elastography. Each observer was blinded to the data of the other operator and the initial information of the enrolled subjects. The data from the first examination by observer A were used for further statistical analyses.

Statistical Analysis

Quantitative parameters are reported as mean \pm standard deviation (SD). The normality of the data distribution was assessed using the Shapiro-Wilk test. The differences in age, weight, height, and sex between patients with PD and healthy subjects were analyzed using independent-samples *t* test or Fisher's exact test. The Kruskal-Wallis test was used to compare the muscle length, muscle thickness, slack angle, and E_0 among the markedly symptomatic side of patients with PD, the mildly symptomatic side of patients with PD, and healthy controls. Post hoc tests were performed when appropriate, using the Mann-Whitney U test with Bonferroni correction. The correlation between the GM slack angle and UPDRS lower limb rigidity score was analyzed for the markedly symptomatic side of patients with PD using Spearman's correlation coefficient. The reliability of the measurements of the slack angle was tested using the intraclass correlation coefficient (ICC). The 95% confidence intervals (CIs) and *p* values were calculated. Statistical significance was set at *p* < 0.05. All data were analyzed using IBM SPSS Statistics for Windows (version 21.0; IBM Corp.).

RESULTS

Demographics

Twenty-eight patients with PD (13 female and 15 male; mean age \pm SD: 63.0 \pm 8.5 years) and 12 healthy subjects (5 female and 7 male; mean age \pm SD: 59.3 \pm 6.4 years) were enrolled in our study. The clinical information of all subjects is listed in Table 1. No significant differences were observed in age (*p* = 0.186), height (*p* = 0.328), weight (*p* = 0.609), or sex (*p* = 1.000) between patients with PD and healthy subjects.

Comparison of the Muscle Length and Thickness among the Three Groups

No significant differences were found in the GM muscle length among the markedly symptomatic side of patients with PD, mildly symptomatic side of patients with PD, and healthy controls (22.11 \pm 1.81 cm vs. 22.11 \pm 1.99 cm vs. 21.33 \pm 2.34 cm; *p* = 0.360); similarly, no significant differences were found in the GM muscle thickness (1.51 \pm 0.27 cm vs. 1.53 \pm 0.30 cm vs. 1.59 \pm 0.25 cm; *p* = 0.498) (Table 2).

Comparison of the Slack Angle and E_0 among the Three Groups

Typical examples of the Young's modulus of the muscle at different positions are shown in Figure 2. Young's modulus-angle curves were constructed. Figure 3 shows representative Young's modulus-angle curves for the markedly symptomatic side of patients with PD, mildly

Table 1. Characteristics of Study Participants

	Parkinson's Disease (n = 28)	Control (n = 12)	<i>P</i>
Age, years	63.0 \pm 8.5	59.3 \pm 6.4	0.186
Height, m	165.0 \pm 7.4	167.4 \pm 6.3	0.328
Weight, kg	69.1 \pm 11.7	70.9 \pm 4.7	0.609
Sex, male:female	15:13	7:5	1.000
Duration, years	5.2 \pm 2.7		
UPDRS lower limb score (markedly symptomatic side), point			
1	3		
2	17		
3	8		

Data are mean \pm standard deviation or patient numbers. UPDRS = Unified Parkinson's Disease Rating Scale

Table 2. Parameters of the Gastrocnemius Medialis Muscle on the Markedly Symptomatic and Mildly Symptomatic Sides in Patients with PD, and Healthy Controls

	Markedly Symptomatic Side in PD (n = 28)	Mildly Symptomatic Side in PD (n = 28)	Healthy Controls (n = 12)
Length, cm	22.11 \pm 1.81	22.11 \pm 1.99	21.33 \pm 2.34
Thickness, cm	1.51 \pm 0.27	1.53 \pm 0.30	1.59 \pm 0.25
Slack angle, $^\circ$	-29.13 \pm 3.79* [†]	-25.65 \pm 3.39*	-21.22 \pm 3.52
E_0 , kPa	10.11 \pm 2.85 [‡]	10.08 \pm 1.88 [‡]	12.23 \pm 1.02

Data are mean \pm standard deviation. *Compared with the healthy controls (*p* < 0.001 and *p* = 0.006, respectively), [†]Compared with the mildly symptomatic side in patients with PD (*p* = 0.003), [‡]Compared with the healthy controls (*p* = 0.012 and *p* < 0.001, respectively). E_0 = the baseline Young's modulus, PD = Parkinson's disease

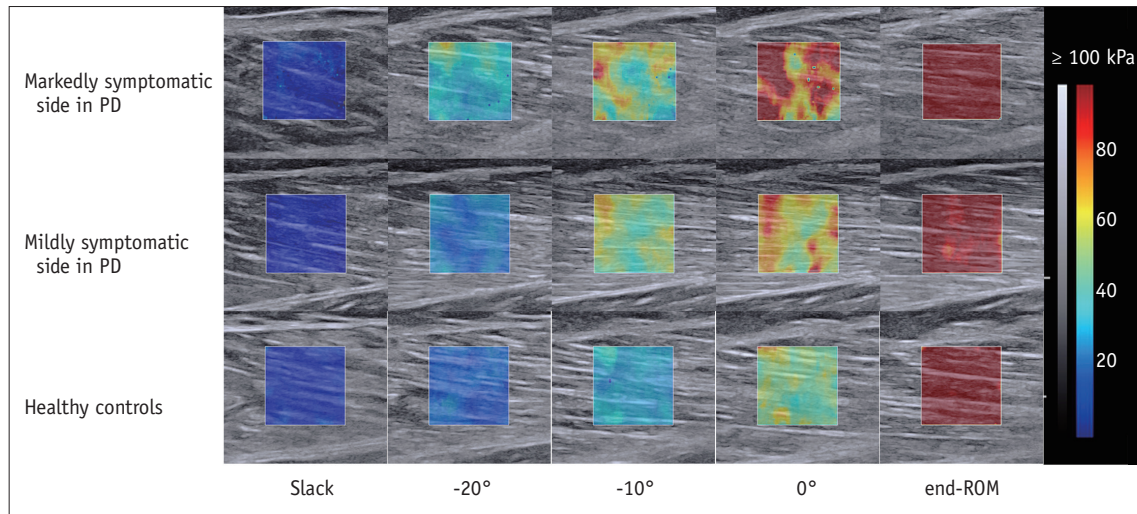


Fig. 2. SWE of the GM muscle at different positions. A typical example of ultrasound SWE used to measure the slack angle of the GM muscle at 20° of plantar flexion, 10° of plantar flexion, 0°, and at the end-ROM on the markedly symptomatic side in patients with PD, mildly symptomatic side in patients with PD, and healthy controls. Negative values indicate plantar flexion of the ankle joint. The colored regions represent the Young's modulus map, and the color spectrum is located on the lower right from blue (soft) to red (hard). The SWE images of the markedly and mildly symptomatic sides of a 69-year-old male patient with PD with a UPDRS score of 3 and 1 on the markedly and mildly symptomatic sides, respectively, are presented. The SWE images of a 69-year-old healthy male participant with a UPDRS score of 0 are presented as a healthy control. end-ROM = end of the range of motion, GM = gastrocnemius medialis, PD = Parkinson's disease, SWE = shear wave elastography, UPDRS = Unified Parkinson's Disease Rating Scale

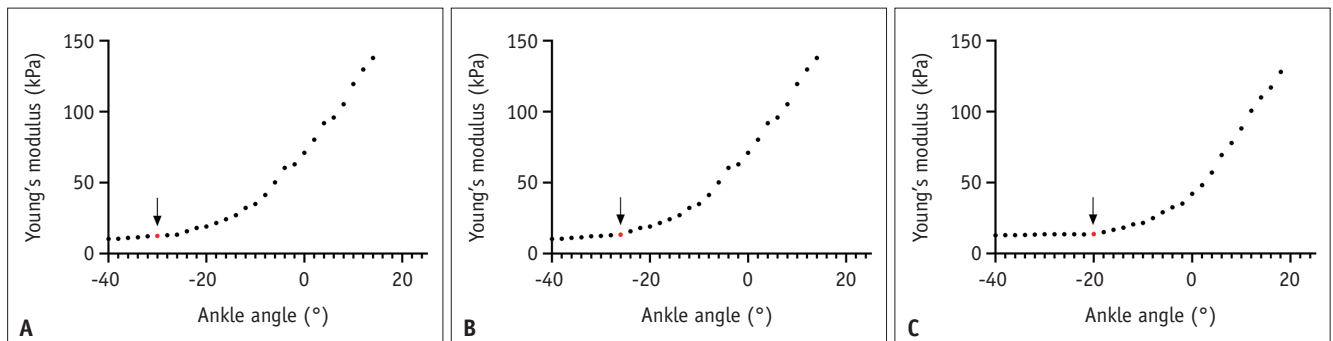


Fig. 3. Representative Young's modulus-ankle angle curves.

A-C. A typical example of visual determination of the slack angle from the Young's modulus-ankle angle curve in the **(A)** markedly symptomatic side of patients with PD, **(B)** mildly symptomatic side of patients with PD, and **(C)** healthy controls. The black arrow and red dot show the slack angle at which passive gastrocnemius medialis muscle tension begins to increase. **(A)** and **(B)** are obtained from a 66-year-old male PD patient with a UPDRS score of 2 on the markedly symptomatic side and a score of 1 on the mildly symptomatic side. **(C)** has been obtained from a 56-year-old healthy male participant with a UPDRS score of 0. PD = Parkinson's disease, UPDRS = Unified Parkinson's Disease Rating Scale

symptomatic side of patients with PD, and healthy controls.

The GM slack angles for the markedly symptomatic side of patients with PD, mildly symptomatic side of patients with PD, and healthy controls were $-29.13^\circ \pm 3.79^\circ$, $-25.65^\circ \pm 3.39^\circ$, and $-21.22^\circ \pm 3.52^\circ$, respectively. Significant differences were observed among the markedly symptomatic side of patients with PD, mildly symptomatic side of patients with PD, and healthy controls ($p < 0.001$) (Fig. 4). The GM slack angles on both the marked and mildly symptomatic sides in patients with PD were smaller than those in healthy controls ($p < 0.001$ and $p = 0.006$,

respectively). Additionally, for patients with PD, the GM slack angle for the markedly symptomatic side was smaller than that for the mildly symptomatic side ($p = 0.003$) (Table 2).

The GM E_0 values for the markedly symptomatic side of patients with PD, mildly symptomatic side of patients with PD, and healthy controls were 10.11 ± 2.85 kPa, 10.08 ± 1.88 kPa, and 12.23 ± 1.02 kPa, respectively. The GM E_0 values for both the markedly and mildly symptomatic sides of patients with PD were lower than those for healthy controls ($p = 0.012$ and $p < 0.001$, respectively). However, no significant difference was observed in the GM E_0 values

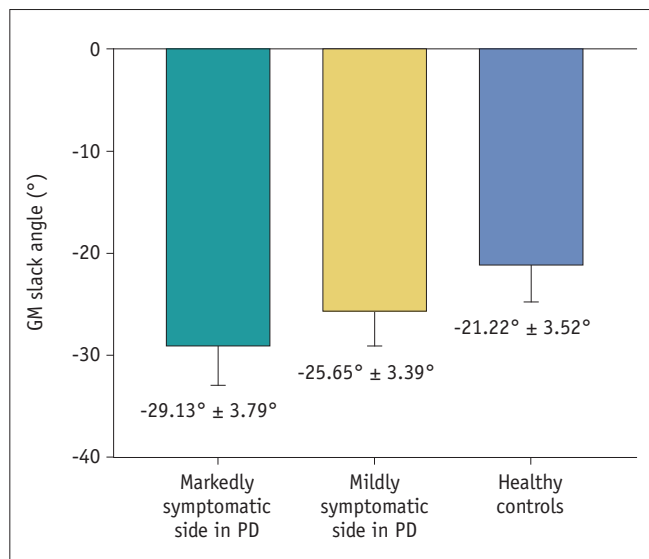


Fig. 4. Bar diagram of the GM slack angle in patients with PD and healthy controls. The bar diagram illustrates that the GM slack angle is increased in the order of markedly symptomatic side of patients with PD, mildly symptomatic side of patients with PD, and healthy controls. GM = gastrocnemius medialis, PD = Parkinson’s disease

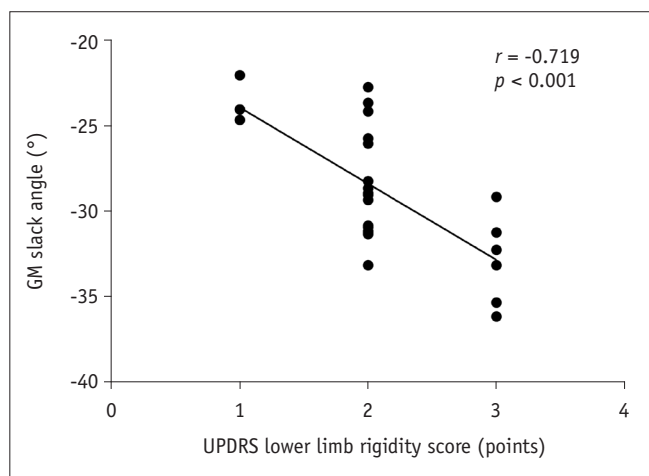


Fig. 5. Correlation between the GM slack angle and UPDRS lower limb rigidity score in patients with PD. A highly negative linear relationship is observed between the GM slack angle and UPDRS lower limb rigidity score on the markedly symptomatic side in patients with PD. GM = gastrocnemius medialis, PD = Parkinson’s disease, UPDRS = Unified Parkinson’s Disease Rating Scale

between the markedly and mildly symptomatic sides in patients with PD ($p = 0.634$) (Table 2).

Correlation Analysis

A negative linear relationship was observed between the GM slack angle and UPDRS lower limb rigidity score on the markedly symptomatic side in patients with PD ($r = -0.719$; $p < 0.001$) (Fig. 5).

Table 3. Reliability Assessment of Shear Wave Elastography in Determining the Slack Angle of the Gastrocnemius Medialis Muscle

Observer and Participant Group	Slack Angle (°)	ICC (95% CI)*
Observer A, observation 1		
Markedly symptomatic side in PD	-29.13 ± 3.79	
Mildly symptomatic side in PD	-25.65 ± 3.39	
Healthy controls	-21.22 ± 3.52	
Observer A, observation 2 (for intraobserver reliability)		
Markedly symptomatic side in PD	-28.55 ± 4.04	0.896 (0.785–0.951)
Mildly symptomatic side in PD	-25.85 ± 3.73	0.880 (0.759–0.943)
Healthy controls	-21.67 ± 3.56	0.951 (0.810–0.986)
Observer B (for interobserver reliability)		
Markedly symptomatic side in PD	-28.97 ± 3.97	0.924 (0.843–0.964)
Mildly symptomatic side in PD	-25.62 ± 3.33	0.910 (0.815–0.957)
Healthy controls	-21.90 ± 3.97	0.880 (0.594–0.965)

Data are mean ± standard deviation. *In comparison with the data from observation 1 by observer A. CI = confidence interval, ICC = intraclass correlation coefficient, PD = Parkinson’s disease

Reliability Evaluation

The intra- and inter-observer reliability of dynamic SWE in determining the GM slack angle was excellent. The ICC ranged from 0.880 to 0.951. The detailed ICCs and 95% CIs are listed in Table 3.

DISCUSSION

To the best of our knowledge, the present study is the first to verify the relationship between passive muscle stiffness and rigidity in patients with PD using dynamic SWE. The main findings of our study are that the GM slack angle in patients with PD was smaller than that in healthy controls and negatively associated with the severity of rigidity.

The GM muscle was chosen as the target muscle because of its superficial position and large volume to facilitate SWE examination; additionally, it is the dominant muscle for passive dorsiflexion among the muscles in the triceps surae complex [30]. In PD, rigidity refers to the abnormal muscle tone resulting from abnormal interactions among passive connective tissues and aberrant reflex responses

to stretching and shortening [31]. In the present study, we set a velocity of 2°/s, which seldom causes reflex responses to stretching [20]. In our study, the GM slack angle in patients with PD was smaller than that in healthy controls. Furthermore, the GM slack angle for the markedly symptomatic side was smaller than that for the mildly symptomatic side in patients with PD. These findings indicated that during passive ankle stretching, the GM muscle began to tense earlier on the markedly symptomatic side in patients with PD, and earlier in patients with PD than in healthy controls. The SWE protocol used in our study partially simulated the clinical process by which neurologists assess rigidity in PD. These results are consistent with the clinical characteristics of increased muscle tone in patients with PD.

The E_0 of the GM indirectly reflects its ability to resist deformation [29]. The E_0 of healthy elderly people was approximately 12 kPa in our study, which is different from the Young's modulus of 17–18 kPa in the relaxed position in some previous studies [32,33]. These studies focused on young adults. In contrast, we examined elderly patients with PD and age-matched healthy elderly individuals. Some studies have reported that muscle stiffness tends to decrease with advancing age and is significantly lower in elderly subjects than in young subjects [34–36].

Our study revealed that E_0 was lower in patients with PD than in healthy controls. This finding is inconsistent with those of previous studies in which patients with PD exhibited increased muscle stiffness in a relaxed or fixed position compared with healthy controls [17–19]. However, those studies focused on muscles of the upper extremities, such as the biceps brachii or triceps brachii. The selectivity of rigidity in different limbs may partially explain the conflicting results.

Muscle stiffness has recently been shown to be related to the number of muscular fibers in the muscle itself and the level of fat infiltration [37]. Studies have shown that the elastic modulus of skeletal muscles is negatively correlated with muscle fat infiltration and muscle atrophy [38,39]. Unlike healthy elderly people, patients with PD exhibit fat loss as their illness progresses [40] and should show a higher Young's modulus. However, in our study, ignoring the effect of fat loss, the E_0 of the GM muscle in patients with PD was lower than that in healthy controls. This indicates that patients with PD may have more severe muscle atrophy than healthy elderly individuals, although no significant change was found in basic muscle parameters (such as

muscle length and muscle thickness) between patients with PD and healthy controls.

A negative linear relationship was observed between the GM slack angle and UPDRS lower limb rigidity score on the markedly symptomatic side in patients with PD, indicating that the GM slack angle was negatively associated with the severity of rigidity. A higher level of rigidity resulted in a lower measured slack angle, which was expected to decrease the motor function of the lower limbs.

To date, one of the limitations for the clinical use of SWE in the field of musculoskeletal evaluation is variable reliability. In previous studies, the intra- and inter-observer ICCs varied from 0.33 to 0.87 [41]. Standardization of SWE measurement helps improve reliability. In our study the body posture and ROM of the ankle were standardized to ensure intra- and inter-observer reliability. Consequently, the reliability and reproducibility of SWE in the evaluation of passive elastic properties by determining the GM slack angle was satisfactory.

Our study has some limitations. First, the sample size was small. Additional studies with a larger group of patients with PD are required. Second, although SWE was useful in determining the GM slack angle during passive stretching in 28 consecutively enrolled patients with PD presenting with Hoehn and Yahr stage I–II symptoms (mild cases), it remains unknown whether similar results can be obtained in patients with PD presenting with Hoehn and Yahr stage III–V symptoms (severe cases). Additional studies with various Hoehn and Yahr stages are warranted.

In conclusion, the slack angle determined by dynamic SWE may be a useful quantitative and reproducible method for evaluating muscle stiffness in patients with PD.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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Author Contributions

Conceptualization: Wen He, Lijuan Du. Data curation: Lu Yin, Yuanzi Li. Formal analysis: Lu Yin, Lijuan Du, Yuanzi Li. Funding acquisition: Wen He, Lijuan Du. Investigation: Lu Yin, Yuanzi Li, Shiquan Zhang. Methodology: Lu Yin, Lijuan Du, Yuanzi Li, Xiao Yang. Project administration: Wen He, Lu

Yin, Lijuan Du. Resources: Huizi Ma, Lijuan Du. Validation: Lu Yin, Yuanzi Li. Writing—original draft: Lu Yin. Writing—review & editing: Wen He, Lijuan Du, Lu Yin.

ORCID iDs

Lu Yin

<https://orcid.org/0000-0002-0357-2595>

Lijuan Du

<https://orcid.org/0000-0002-0153-6136>

Yuanzi Li

<https://orcid.org/0000-0002-2468-2988>

Yang Xiao

<https://orcid.org/0000-0002-0516-0543>

Shiquan Zhang

<https://orcid.org/0000-0003-3747-0842>

Huizi Ma

<https://orcid.org/0000-0002-3845-8020>

Wen He

<https://orcid.org/0000-0002-7177-4498>

REFERENCES

- Jankovic J. Parkinson's disease: clinical features and diagnosis. *J Neurol Neurosurg Psychiatry* 2008;79:368-376
- Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. *Lancet Neurol* 2016;15:1257-1272
- Berardelli A, Sabra AF, Hallett M. Physiological mechanisms of rigidity in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1983;46:45-53
- Gajdosik RL. Passive extensibility of skeletal muscle: review of the literature with clinical implications. *Clin Biomech (Bristol, Avon)* 2001;16:87-101
- Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology* 1967;17:427-442
- Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, et al. Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): scale presentation and clinimetric testing results. *Mov Disord* 2008;23:2129-2170
- Rizzo G, Copetti M, Arcuti S, Martino D, Fontana A, Logroscino G. Accuracy of clinical diagnosis of Parkinson disease: a systematic review and meta-analysis. *Neurology* 2016;86:566-576
- Marusiak J, Jaskólska A, Budrewicz S, Koszewicz M, Jaskólski A. Increased muscle belly and tendon stiffness in patients with Parkinson's disease, as measured by myotonometry. *Mov Disord* 2011;26:2119-2122
- Creze M, Soubeyrand M, Yue JL, Gagey O, Maître X, Bellin MF. Magnetic resonance elastography of the lumbar back muscles: a preliminary study. *Clin Anat* 2018;31:514-520
- Wang CK, Fang YD, Lin LC, Lin CF, Kuo LC, Chiu FM, et al. Magnetic resonance elastography in the assessment of acute effects of kinesio taping on lumbar paraspinal muscles. *J Magn Reson Imaging* 2019;49:1039-1045
- Gao J, He W, Du LJ, Li S, Cheng LG, Shih G, et al. Ultrasound strain elastography in assessment of resting biceps brachii muscle stiffness in patients with Parkinson's disease: a primary observation. *Clin Imaging* 2016;40:440-444
- Klauser AS, Miyamoto H, Bellmann-Weiler R, Feuchtner GM, Wick MC, Jaschke WR. Sonoelastography: musculoskeletal applications. *Radiology* 2014;272:622-633
- Liu J, Ji Y, Ai H, Ning B, Zhao J, Zhang Y, et al. Liver shear-wave velocity and serum fibrosis markers to diagnose hepatic fibrosis in patients with chronic viral hepatitis B. *Korean J Radiol* 2016;17:396-404
- Bensamoun SF, Wang L, Robert L, Charleux F, Latrive JP, Ho Ba Tho MC. Measurement of liver stiffness with two imaging techniques: magnetic resonance elastography and ultrasound elastometry. *J Magn Reson Imaging* 2008;28:1287-1292
- Yoon JH, Lee JM, Woo HS, Yu MH, Joo I, Lee ES, et al. Staging of hepatic fibrosis: comparison of magnetic resonance elastography and shear wave elastography in the same individuals. *Korean J Radiol* 2013;14:202-212
- Oudry J, Chen J, Glaser KJ, Miette V, Sandrin L, Ehman RL. Cross-validation of magnetic resonance elastography and ultrasound-based transient elastography: a preliminary phantom study. *J Magn Reson Imaging* 2009;30:1145-1150
- Watts RL, Wiegner AW, Young RR. Elastic properties of muscles measured at the elbow in man: II. Patients with parkinsonian rigidity. *J Neurol Neurosurg Psychiatry* 1986;49:1177-1181
- Marusiak J, Kisiel-Sajewicz K, Jaskólska A, Jaskólski A. Higher muscle passive stiffness in Parkinson's disease patients than in controls measured by myotonometry. *Arch Phys Med Rehabil* 2010;91:800-802
- Du LJ, He W, Cheng LG, Li S, Pan YS, Gao J. Ultrasound shear wave elastography in assessment of muscle stiffness in patients with Parkinson's disease: a primary observation. *Clin Imaging* 2016;40:1075-1080
- Le Sant G, Nordez A, Hug F, Andrade R, Lecharte T, McNair PJ, et al. Effects of stroke injury on the shear modulus of the lower leg muscle during passive dorsiflexion. *J Appl Physiol (1985)* 2019;126:11-22
- Miyamoto N, Hirata K, Miyamoto-Mikami E, Yasuda O, Kanehisa H. Associations of passive muscle stiffness, muscle stretch tolerance, and muscle slack angle with range of motion: individual and sex differences. *Sci Rep* 2018;8:8274
- Xu J, Hug F, Fu SN. Stiffness of individual quadriceps muscle assessed using ultrasound shear wave elastography during passive stretching. *J Sport Health Sci* 2018;7:245-249
- Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, et al. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord* 2015;30:1591-1601
- Nasirzade A, Ehsanbakhsh A, Ilbeygi S, Sobhkhiz A, Argavani H, Aliakbari M. Relationship between sprint performance of

- front crawl swimming and muscle fascicle length in young swimmers. *J Sports Sci Med* 2014;13:550-556
25. Kruse A, Schranz C, Tilp M, Svehlik M. Muscle and tendon morphology alterations in children and adolescents with mild forms of spastic cerebral palsy. *BMC Pediatr* 2018;18:156
 26. Gao J, He W, Du LJ, Chen J, Park D, Wells M, et al. Quantitative ultrasound imaging to assess the biceps brachii muscle in chronic post-stroke spasticity: preliminary observation. *Ultrasound Med Biol* 2018;44:1931-1940
 27. Xiao Y, Wang C, Sun Y, Zhang X, Cui L, Yu J, et al. Quantitative estimation of passive elastic properties of individual skeletal muscle in vivo using normalized elastic modulus-length curve. *IEEE Trans Biomed Eng* 2020;67:3371-3379
 28. Hug F, Lacourpaille L, Maïsetti O, Nordez A. Slack length of gastrocnemius medialis and Achilles tendon occurs at different ankle angles. *J Biomech* 2013;46:2534-2538
 29. Maïsetti O, Hug F, Bouillard K, Nordez A. Characterization of passive elastic properties of the human medial gastrocnemius muscle belly using supersonic shear imaging. *J Biomech* 2012;45:978-984
 30. Hirata K, Kanehisa H, Miyamoto-Mikami E, Miyamoto N. Evidence for intermuscle difference in slack angle in human triceps surae. *J Biomech* 2015;48:1210-1213
 31. Powell D, Muthumani A, Xia R. A comparison of the effects of continuous versus discontinuous movement patterns on parkinsonian rigidity and reflex responses to passive stretch and shortening. *J Nat Sci* 2016;2:e201
 32. Zhou J, Yu J, Liu C, Tang C, Zhang Z. Regional elastic properties of the Achilles tendon is heterogeneously influenced by individual muscle of the gastrocnemius. *Appl Bionics Biomech* 2019;2019:8452717
 33. Kelly JP, Koppenhaver SL, Michener LA, Proulx L, Bisagni F, Cleland JA. Characterization of tissue stiffness of the infraspinatus, erector spinae, and gastrocnemius muscle using ultrasound shear wave elastography and superficial mechanical deformation. *J Electromyogr Kinesiol* 2018;38:73-80
 34. Şendur HN, Cindil E, Cerit MN, Kılıç P, Gültekin İİ, Oktar SÖ. Evaluation of effects of aging on skeletal muscle elasticity using shear wave elastography. *Eur J Radiol* 2020;128:109038
 35. Akagi R, Yamashita Y, Ueyasu Y. Age-related differences in muscle shear moduli in the lower extremity. *Ultrasound Med Biol* 2015;41:2906-2912
 36. Alfuraih AM, Tan AL, O'Connor P, Emery P, Wakefield RJ. The effect of ageing on shear wave elastography muscle stiffness in adults. *Aging Clin Exp Res* 2019;31:1755-1763
 37. Sun Y, Xiao Y, Li F, Wang C, Wu T, Zhou M, et al. Diagnosing muscle atrophy by use of a comprehensive method of assessing the elastic properties of muscle during passive stretching. *AJR Am J Roentgenol* 2020;214:862-870
 38. Roskopf AB, Ehrmann C, Buck FM, Gerber C, Flück M, Pfirrmann CW. Quantitative shear-wave US elastography of the supraspinatus muscle: reliability of the method and relation to tendon integrity and muscle quality. *Radiology* 2016;278:465-474
 39. Botar-Jid C, Damian L, Dudea SM, Vasilescu D, Rednic S, Badea R. The contribution of ultrasonography and sonoelastography in assessment of myositis. *Med Ultrason* 2010;12:120-126
 40. Tan AH, Hew YC, Lim SY, Ramli NM, Kamaruzzaman SB, Tan MP, et al. Altered body composition, sarcopenia, frailty, and their clinico-biological correlates, in Parkinson's disease. *Parkinsonism Relat Disord* 2018;56:58-64
 41. Baumer TG, Davis L, Dischler J, Siegal DS, van Holsbeeck M, Moutzouros V, et al. Shear wave elastography of the supraspinatus muscle and tendon: repeatability and preliminary findings. *J Biomech* 2017;53:201-204