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Research Article

Evaluation of Gastrocnemius Spasticity With Shear-Wave Elastography in Children with Cerebral Palsy after Botulinum Toxin Injection: Defining A Proper Position for Measurement

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Abstract

Aim: Cerebral Palsy (CP) is the most common neuromuscular disorder in children and it is characterized by a dysfunction in movement and posture. Botulinum toxin injection is a treatment method used for muscle spasticity in patients with CP. Elastography is a new method which is used for measuring muscle stiffness. This study aims to evaluate the gastrocnemius muscle stiffness in cerebral palsy patients before and after botulinum toxin injection by using the elastography method and contribute to the establishment of a treatment algorithm with a proper position for measurement.

Materials and Method: The participants of this study were chosen from the patients of our hospital's orthopaedics and traumatology department. Among the patients on whom botulinum injection to gastrocnemius muscle was planned, 30 patients were randomly selected. Elastography of both gastrocnemius muscles were taken before the injection of botulinum toxin, in the third week and third month after the injection. Simultaneously with the elastography, Modified Ashworth Scale (MAS) values were noted. In hemiparetic patients, contralateral legs were taken as the control group.

Results: The elastographic values of the medial head of gastrocnemius when the knee is in extension and ankle in passive dorsiflexion, were found to be statistically significantly related ($p<0.05$) to the MAS values before botulinum toxin injection, third week and third month post-injection.

Conclusion: Stiffness due to spasticity in gastrocnemius muscle in CP patients was demonstrated through elastographic evaluation. A correlation was found between clinical MAS values. The most proper position was in which the knee is fully extended and the ankle is passively dorsiflexed. Elastographic measurements may be able to be used in these patients as a method of diagnosis in the future and it will help to assess the effectiveness of the treatment after the injection of botulinum toxin.

Keywords: Elastography, sonoelastography, cerebral palsy, gastrocnemius spasticity

INTRODUCTION

Cerebral palsy (CP) is the most common neuromuscular disorder causing disability in children. The prevalence is estimated to be 2-3 per 1000 live births in the literature (1-5). The most frequent type of this condition is spastic CP which constitutes almost 80% of these children. Spasticity has been defined as a motor disorder which is characterized by a velocity-dependent increase in muscle tone, thus, causing abnormal active and passive muscle stiffness (2). Spasticity can be evaluated clinically by scales such as Modified Ashworth Scale (MAS); however, this examination is both a subjective method and may still lack reliability between physicians (3). While searching for a more reliable, objective and quantitative method in measuring spasticity, advances in the ultrasound techniques have led clinicians to find a solution to this problem in recent imaging modalities. Shear-wave elastography (SWE) is a new, cost-effective and noninvasive ultrasound modality, which provides a quantitative measurement of the passive stiffness of the muscles (6,7). There has been an increasing trend towards objective attempts trying to measure the spasticity of the muscles with SWE in children with CP, as an increased muscle stiffness has been found in this population than in healthy children (8-10).

Intramuscular botulinum toxin A (BoNT-A) injection to spastic muscles in CP has been widely used in the

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treatment of the spasticity and is found to be effective for these children in the literature (12). Some characteristics of BoNT-A injection such as the mechanism of action, application and lethal doses are well-known, while there is still no consensus in some of the characteristics such as application techniques and time to repeat the injection (13-16). Measuring the effect of BoNT-A in a quantitative way in CP patients is another important parameter in order to provide a suitable treatment plan and check the efficacy of the treatment. SWE could also be used in this area as a quantitative tool for both diagnosis and follow-up after treatment.

The motivation that prompted us to perform this study was to find out whether we could achieve a technique which could measure the effect of BoNT-A in children with CP and have a significant correlation with MAS. It would be ideal to combine the clinical and radiological means, providing a better understanding of the spasticity in CP patients, therefore the technique be used as a reliable tool in both diagnosis and checking the efficacy of spasticity treatments in this population. Our aim is to try to find the most appropriate position for measuring spasticity of gastrocnemius muscle before and after BoNT-A injection.

MATERIALS AND METHOD

A total of 30 patients, 15 boys and 15 girls were included in this study. These patients were randomly selected from the patients who were admitted to our hospital's department of orthopaedics and traumatology, diagnosed with CP, had lower extremity spasticity on physical examination, and were scheduled for BoNT-A injection for the gastrocnemius muscle. Parents were informed about the study and their consent was obtained. Ethical approval was also obtained from the faculty, before starting the study (Approval No: 83045809-604.01/02-77203). GMFCS IV and V patients who did not have the ability to sit and walk independently, or patients who had previously undergone surgical intervention for their lower extremities were not included in the study. Patients who had static deformity or joint contracture on the ankle were also excluded. In addition, patients who had difficulty in elastographic examination because they were agitated were also excluded from the study, with the prediction that the measurements could be affected due to the possible increase in spasticity. Families who did not want to participate in the study or come to the follow-up were also excluded.

All of the elastographic measurements were made by the same radiologist who had ten years of musculoskeletal radiology and three years of elastography experience and did not know the severity of the disease of children, while the physical examination and BoNT-A injections of the children were all performed by the same orthopedic and traumatology surgeon.

Clinical Evaluation

The patients were evaluated clinically and elastographically preoperatively, in the third postoperative week and in the third postoperative month. GMFCS and MAS were noted in the clinical examination.

Elastographic Evaluation

Elastography was performed on both lower extremities of all patients participating in the study; 14 days prior to botulinum toxin injection, in the third week and third month after the injection. SWE USG (Aixplorer; Supersonic Imagine, Ltd., Aix-en-provence, France) and 4-15-MHz transducer (Supersonic Imagine, Ltd.) were used for elastographic examination. After the ultrasound was set to the musculoskeletal mode, measurements were made separately on the medial and lateral heads of the gastrocnemius muscle. Ten measurements were taken for each leg at different positions of the ankle and knee joint and the values were recorded as kilopascal (kPa). Measurement positions are given in Table 1. Each measurement was taken twice. In cases where inconsistency was detected between two measurements, a new measurement was made and the average of the two measurements that were consistent with each other was taken. The contralateral leg in hemiplegic patients was considered as the control group, and elastographic measurements were also performed on the healthy legs.

Table 1. Elastographic Positions and Numbers

NO	PATIENT POSITION	KNEE	ANKLE	GASTROCNEMIUS HEAD
1	PRONE	EXTENSION	45° PLANTAR FLEXION	MEDIAL
2	PRONE	EXTENSION	45° PLANTAR FLEXION	LATERAL
3	PRONE	EXTENSION	30° DORSIFLEXION	MEDIAL
4	PRONE	EXTENSION	30° DORSIFLEXION	LATERAL
5	PRONE	FLEXION	45° PLANTAR FLEXION	MEDIAL
6	PRONE	FLEXION	45o PLANTAR FLEXION	LATERAL
7	PRONE	FLEXION	30° DORSIFLEXION	MEDIAL
8	PRONE	FLEXION	30° DORSIFLEXION	LATERAL
9	STANDING	EXTENSION	NEUTRAL	MEDIAL
10	STANDING	EXTENSION	NEUTRAL	LATERAL

Elastographic evaluation was performed while the ultrasound probe was in the transverse position, the myotendinous junction of the gastrocnemius muscle was identified and the probe was ascended from distal to proximal. After identifying the medial and lateral heads of the muscle posteriorly, the ultrasound probe was adjusted to the longitudinal axis, parallel to the muscle fibers and the measurement was taken when the clearest image was obtained. Knee flexion and ankle dorsiflexion movements were performed passively by the same physician. While the knee was in 90 degrees of flexion, the ankle was passively supported and fixed at the point where it reached maximum dorsiflexion. While recording the spasticity values, the measurements were made by taking the region between the superficial and deep fascia of the muscle, which is considered to be the most homogeneous ultrasonographically by the radiologist, in a rectangle (Q-Box) created by the software of the elastography device. A circle with a diameter of 5mm (ROI, range of interest) was created in the region of the color scale of the different spasticity values in the formed rectangle, and the average of the spasticity calculated by the software in this circle was recorded (Figure 1). Care was taken that the circle did not touch the hyperechoic muscle fascia. According to the color scale created by the software, the softest and ost loose part of the muscle appears blue, while as the spasticity increases, the color turns into green and yellow; and red color is formed in the most spastic areas.

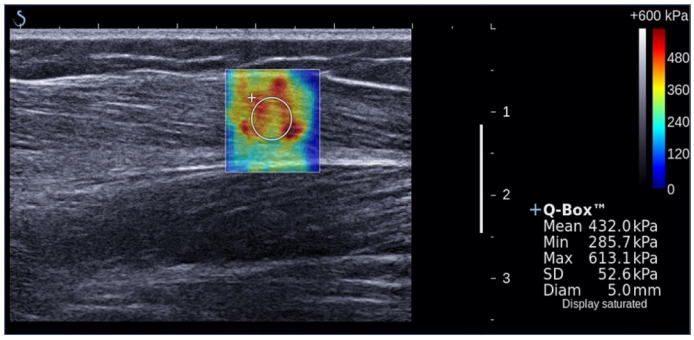

Figure 1. Elastographic appearance and the calculation of the increased spasticity in the gastrocnemius muscle

Botulinum Toxin A (BoNT-A) Injection

BoNT-A was injected into one or both gastrocnemius muscles of the patients whose preoperative clinical and elastographic evaluations were completed, under operating room conditions. Injections were administered (onabotulinum toxin A, Botox, Allergan, Inc. CA, USA) at 5 IU (international unit) per kilogram (kg) after the necessary sterility conditions were met while the patients were under sedation. The injection was technically made from two medial points, namely the medial head of the gastrocnemius muscle and the muscle body. After crossing the muscle fascia with a black tip injector, dorsiflexion and plantar flexion movements of the ankle were made and checking that the injector moves (inside the muscle), 1/3 of the total dose is transferred to the medial head, and the remaining part to the proximal, middle and distal of the muscle body from the second and third points (Figure 2).

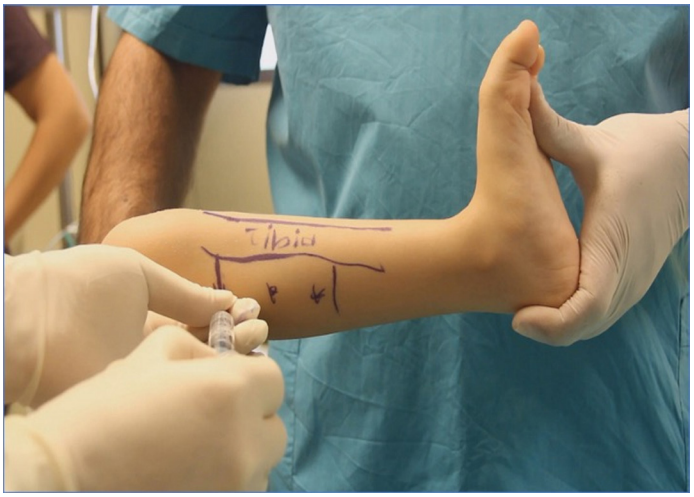

Figure 2. Application technique of botulinum toxin A (BoNT-A) injection to the medial head of the gastrocnemius muscle

Post-injection Care

The patients who were discharged from the hospital at the fourth hour after the injection were kept nonweightbearing for a maximum of one day to relieve their pain and agitation, then they were mobilized on the second day with full weight-bearing, and they were allowed to continue their routine physiotherapy programs.

Statistical Analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. While evaluating the study data, descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) as well as the conformity of quantitative data to normal distribution were tested with the Shapiro-Wilk test and graphical examinations. One-way ANOVA was used for comparisons between groups of more than two normally distributed quantitative variables, and Tukey test was used for post-hoc pairwise evaluations. The Kruskal Wallis test was used for comparisons between groups of more than two quantitative variables that did not show normal distribution, and the Mann-Whitney U test was used for post-hoc pairwise evaluations. Student's t test was used for two-group comparisons of normally distributed quantitative variables, and the Mann Whitney U test was used for two-group comparisons of non-normally-distributed quantitative variables. Paired t test was used for the in-group pairwise evaluations of normally distributed quantitative variables. Wilcoxon Signed Ranks test was used for the pairwise evaluation of quantitative variables that did not show normal distribution. Spearman correlation analysis was used to evaluate the relationships between quantitative variables. Statistical significance was accepted as $p<0.05$.

RESULTS

The mean age was 4.87±1.63 years. The demographics of the patients and characteristics of the disease were described in Table 2. There were no patients with any side effects or complications related to the injection. The change in the decrease in the postoperative (post-injection) third week values according to the preoperative MAS values of the cases was found to be statistically significant ($p<0.001$). It was determined that the change in the direction of decrease observed in the postoperative third month values according to the preoperative MAS values of the cases was statistically significant ($p<0.001$). In addition, it was determined that the change in the increase in the postoperative third month values compared to the postoperative third week MAS values was statistically significant ($p=0.023$) (Figure 3).

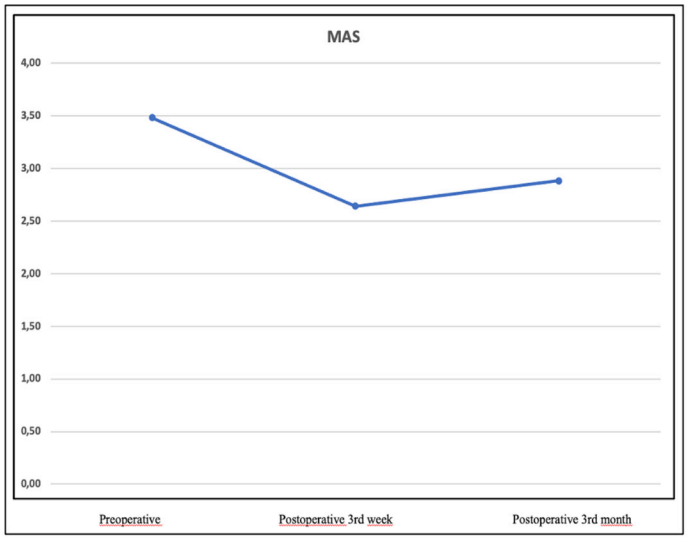

Figure 3. The distribution of Modified Ashworth Scales (MAS) preoperative and postoperatively

Fifty legs of thirty patients in total were evaluated elastographically and clinically in ten different positions. The relationship between these evaluations and MAS values in the preoperative period, postoperative third week, and postoperative third month was examined. As a result of the statistical analysis, the MAS value was found to be correlated with positions 1, 3, 4, 5, 7, 8, 9, and 10, preoperatively. In the evaluations after botulinum toxin application, there was a significant correlation between the 3rd, 9th and 10th positions of these positions and MAS in the postoperative third week ($p<0.001$, $p<0.003$, $p<0.007$); 3rd, 4th, 7th, 8th and 9th positions were found to have a significant correlation with MAS at the postoperative third month ($p<0.001$, $p<0.006$, $p<0.002$, $p<0.007$, $p<0.015$, respectively). When the effect of BoNT-A injection on elastographic measurements was evaluated, there were two positions (3 and 7) out of a total of 10 positions, with statistically significant results both in the third week and third month after the injection.

Table 2. Demographics of the patients and characteristics of the disease

(n=30)		Min-Max	Mean±ss
Age (years)		2-8	4.87±1.63
		n	**%**
Sex	Female	15	50.0
	Male	15	50.0
Diagnosis	Hemiparetic	10	33.3
	Diparetic	20	66.7
MAS	1	1	3.3
	1+	3	10.0
	2	9	30.0
	3	17	56.7
GMFCS	1	10	33.3
	2	16	53.3
	3	4	13.3
Side	Right	5	16.7
	Left	5	16.7
	Bilateral	20	66.7
History of BoNT-A injection	-	18	60.0
	+	6	20.0
	++	5	16.7
	+++	1	3.3

Two positions (3 and 7) with statistical significance were determined in terms of the relationship between the pre-injection period and the elastography values in the third week and third month after the injection. The change observed in the postoperative third week values compared to the preoperative position 3 elastographic values was found to be statistically significant ($p=0.001$). When compared to the preoperative position 3 elastographic values of the cases, the change observed in the postoperative third month values was found to be statistically significant ($p=0.001$). It was determined that the change observed in the postoperative 3rd month values according to the 3rd week position 3 elastographic values of the cases was not statistically significant ($p>0.05$).

There was no statistically significant difference between the cases with and without a history of BoNT-A injection in terms of the changes observed in the postoperative third week values according to the preoperative MAS values ($p>0.05$). Neither was there a statistically significant difference between the cases with and without a history of injection in terms of the changes observed in the postoperative third month values, when compared to the preoperative MAS values ($p>0.05$). The increase observed in the postoperative third month values compared to the preoperative MAS values in cases with a history of injection was found to be statistically significantly larger than the increase observed in this period in cases without a history of injection ($p=0.018$).

When hemiparetic cases were considered as a separate group, statistically significant results were obtained in positions 3, 4, 9 and 10 from the elastographic evaluations made in ten different positions compared with the opposite leg (control group).

To summarize the statistical analysis, only one position (3) achieved statistically significant meaning both in hemiplegic and diplejic patients, in terms of the changes in the MAS, elastographic values and the effect of BoNT-A injection preoperatively, in the third week and third month postoperatively.

DISCUSSION

The main finding of our study claims that spasticity of the gastrocnemius muscle could be measured consistently with sonoelastographic examination in children with cerebral palsy. While the knee is fully extended and the ankle is positioned in passive dorsiflexion, the changes on the medial head of the gastrocnemius muscle are measurable with a statistically significant difference preoperatively and postoperatively. This position has been also correlated with MAS values and the effect of botulinum toxin injection.

In a study conducted by Vasilescu et al. in 2010, the use of sonoelastography was examined in 7 patients with cerebral palsy who received botulinum toxin injection indication due to muscle spasticity, and elastographic examination was performed (9). In the control measurements made after botulinum toxin injection in these patients, it was stated that the stiffness and contraction of the injected muscles decreased in five out of seven children. The small number of patients studied and the lack of homogenization in terms of CP types were the limitations of that study. The use of elastography for gastrocnemius spasticity in CP patients was also approved by the study of Maisetti et al. in 2012 and it was stated that elastography can provide an indirect calculation of passive muscle strength (10).

In a study by Kwon et al. in 27 legs of 15 CP patients in 2012, 12 healthy children were evaluated as the control group and shear wave velocities at the medial gastrocnemius head in CP patients were found to be faster than the control group (11). In addition, it was stated that the results obtained were correlated with the MAS scores in the clinic. In a letter to the editor of this study, the work was appreciated, but some parts of it were criticized (17). The first of these criticisms was about elastography positions. In the study where it was stated that the patients were placed in the prone position and the ankles were hung from the examination bed, the study was criticized for not providing information about the ankle position. Since the gastrocnemius is a double-jointed muscle, muscle stiffness may increase while the ankle is in dorsiflexion and may decrease while in plantar flexion and it was stated that this could affect the measurements. Considering this fact in our study, it was thought that the measurements could change with the knee position as well as that of ankle.

Other studies have shown that the stiffness of the gastrocnemius muscle changes in certain positions of the ankle. In the study published by Chino et al. in 2012, the stiffness in the gastrocnemius decreased in plantar flexion; in the study of Akagi et al., it was reported that this stiffness increased with ankle dorsiflexion (18,19). In our study, the stiffness in the gastrocnemius muscle decreased when the ankle was plantar flexed; and increased when the ankle was dorsiflexed. The majority of elastographic examinations that resulted in statistically significant results in our study were the measurements made in positions where the ankle was passively dorsiflexed.

In a study by Gi-Young Park et al., BoNT-A was injected into the gastrocnemius muscle of 17 CP patients and physiotherapy was performed after the injection (20). The results were evaluated elastographically in the preoperative period and postoperative fourth week. At the end of the study, it was determined that there was a decrease in muscle spasticity in the short-term in patients who received physiotherapy with botulinum toxin injection and MAS scores decreased significantly, both of which could be demonstrated by elastographic methods. In our study, the correlation of elastographic values with clinical MAS at baseline could be demonstrated in eight out of ten different positions. However, considering the values in the third week and third month after BoNT-A injection, this correlation disappeared in most of the positions. There were two positions (3 and 9) where the correlation could be shown. A high correlation was found between elastographic measurements in these two positions and clinical MAS values. A statistically significant relationship was also found between the elastography values in the period before BoNT-A injection and the values in the third week and third month after the injection in two positions (3 and 7). One and only position that has statistically significant changes in terms all MAS and botulinum toxin effect preoperatively and postoperatively was the position 3, where the stiffness of the medial gastrocnemius head is measured when the knee is fully extended and the ankle is in passive dorsiflexion.

Healthy children were not included in our study, but the healthy sides of the hemiparetic patients were examined as the control group. It was observed that the affected leg was statistically significantly stiffer than the healthy leg in the preoperative period, this stiffness statistically approached the stiffness in the intact leg in the third week after BoNT-A injection, and this effect continued in the postoperative third month.

In a study published by Arda et al. in 2011, the elasticity values of normal soft tissues were tried to be defined by elastography method and a standardization established (21). In this study, regardless of age, the average elasticity of the gastrocnemius muscle was 11.4±4.1 kPa in men and 11.0±4 in women. Since all of the patients in our study were hemiplegic or diplegic a value range could not be determined in terms of gastrocnemius muscle stiffness in normal individuals. Although elastographic examination

has been performed on the intact legs of hemiplegic patients, it is known that the legs that are considered to be healthy in hemiplegic type CP patients may also be slightly affected by spasticity. In this respect, these values should not be perceived as the values of a normal individual.

In our study, patients who had botulinum toxin injections before and those who did not have a history of injection were also compared in terms of MAS values. In the examinations, it was observed that the increase in the MAS values in the postoperative third month was higher in patients who had previously received botulinum toxin injection compared to the MAS values in the preoperative period compared to the patients who did not have a previous injection history. This can be interpreted as an indication of the fact that the effect of botulinum toxin may disappear faster in patients with a previous injection history. This effect has been described in the literature as the development of resistance to repeated botulinum toxin injections (22).

There are some restricting factors and limitations of our study. Although it is the largest patient group, as far as we can determine, in which CP and elastography methods have been studied together in the literature, the number of legs that can be taken as a control group has been limited, especially due to the small number of hemiparetic patients. At this point, it should be noted that in hemiparetic patients, both lower extremities are affected by spasticity, and the other leg is usually assumed to be normal since the effect on one leg is dominant in the clinic. Therefore, conducting similar studies in the future with healthy groups will provide useful information to the literature. In addition, the fact that our patient follow-up period is limited to three months is another limiting factor. Long-term follow-up and elastographic examinations of these patients are important, especially in order to investigate the long-term effects of botulinum toxin injection. One of the limitations of our study is that during the elastographic evaluations, it was not detected by the superficial EMG method whether the patients actually were calm with the correct muscles relaxed and measured. Another limiting factor is the amount of passive dorsiflexion applied especially to the ankles of the patients during the extractions. Although passive dorsiflexion is performed by the same physician each time, it is obvious that there may be variations in this amount from time to time. Adjusting the dorsiflexion force with the help of a device to apply the same force to each patient each time would have contributed significantly to the standardization of the study.

Another limitation regarding the botulinum toxin injection we applied in our study is that we did not receive ultrasound support during the BoNT-A injections. However, in a study conducted by Chin et al. in 2005, it was reported that manual injections had given satisfactory results (over 75%) only in gastro-soleus applications after a total of 1372 separate botulinum toxin injections made manually in the upper and lower extremities of 226 CP patients (22). In our study, the applications were directed only to the gastrocnemius muscle. In addition, all of the injections were made by the same orthopedic surgeon who was experienced in botulinum toxin injection and the limitation of this factor was tried to be eliminated.

CONCLUSION

In conclusion, shear wave elastography is a non-invasive, inexpensive, easy-to-apply and effective imaging method that has been increasingly used in the musculoskeletal area in recent years. In addition to the diagnosis of many diseases, studies are ongoing to control and follow-up the efficacy of treatment with elastography. CP is a pathology that elastographic examination may be used due to the spasticity and muscle stiffness. Since the evaluation of muscle spasticity with MAS in clinical examination differs from physician to physician, an effort has been made to demonstrate spasticity with imaging methods in order to provide standardization in this regard. Increased spasticity in the gastrocnemius muscle can be objectively demonstrated by elastographic examination. Elastography can be used as a diagnostic method in this context, as well as to evaluate the effectiveness of botulinum toxin and similar spasticity reduction interventions. In our study, one position was found to be statistically significant and clinically correlated with MAS across the measurements. This was the measurement of the medial head of the gastrocnemius, where the knee is fully extended and the ankle is passively dorsiflexed.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Ethical approval was also obtained from the faculty, before starting the study (Approval No: 83045809-604.01/02-77203).*

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