Factors affecting passive muscle stiffness through shear wave elastography in children with spastic cerebral palsy

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ABSTRACT

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Background: In patients with spastic cerebral palsy (CP), both neural and non-neural components contribute to hypertonia. Children with CP have greater passive muscle stiffness as a non-neural component than typically developed children.

Objectives: This study aimed to investigate the factors affecting passive muscle stiffness using ultrasound shear wave elastography (SWE) in children with spastic CP and to determine the changes in SWE with therapeutic interventions.

Participants and Methods: We enrolled 32 children with spastic CP (21 boys and 11 girls; age range 2.5–10.6 years). The shear wave modulus was measured using SWE in the medial gastrocnemius at 0 degree plantar flexion (SWE-N) and resting position (SWE-R). Some children were treated with botulinum toxin injection (BoNT-A) with or without a short leg cast. SWE modified Ashworth scale and modified Tardieu scale were all evaluated before, 2 weeks, and 4 weeks after the intervention.

Results: Multiple regression analysis revealed that body mass index (BMI) had a significant negative effect on SWE-N. The Gross Motor Function Classification System (GMFCS) score was a positive factor, while age was a negative factor for SWE-R. Clinical spasticity assessments did not show a significant relationship with SWE. After the intervention, the SWE-N decreased, regardless of the treatment modality. SWE-R decreased after BoNT-A with or without a cast. The ratio of SWE-N to SWE-R decreased after BoNT-A with casts and physical therapy.

Conclusion: This study revealed that BMI, GMFCS score, and age were significantly associated with SWE. The significant changes in SWE after therapeutic intervention suggest that SWE may be a useful outcome measure for spastic management in children with CP.

Key words : cerebral palsy, muscle stiffness, elastography, shear wave

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I. INTRODUCTION

Spasticity is the most common symptom in children with cerebral palsy (CP). Spasticity is defined as increased muscle resistance caused by the velocity-dependent stretch reflex activation. The most common deformity in children with spastic CP is equinus foot, caused by ankle hypertonia. Ankle hypertonia is caused by both neural and non-neural factors.

The modified Ashworth scale (MAS) and Tardieu scale (TS) are the most commonly used tools for evaluating spasticity. These clinical assessments are insufficient for determining the contribution of non-neural components.[1]

Shear wave elastography (SWE) is a noninvasive imaging technique that measures tissue stiffness. SWE causes tissue stress by generating shear waves within the medium via an acoustic radiation force impulse. As tissue becomes harder, a shear wave moves faster. So measuring the shear wave speed can be used to determine the stiffness of the tissue.[2] These advancements in ultrasound elastic imaging techniques have enabled the quantification of passive muscle stiffness.[3]

Previous studies have reported that, when comparing the muscles of children with CP and typically developing children using SWE, SWE was significantly larger in children with CP than in typically developing children and showed a significant correlation with MAS.[4-6]

Few studies aimed to identify the factors related to SWE. According to a previous study,

SWE may vary depending on disease type, sex, age, anthropometry, muscle stretching, tissue compression, and operator-related reliability. However, a clear picture of the factors associated with SWE remains elusive due to different research protocols and heterogeneous study groups.[7] Moreover, there are only a few studies investigating the factors related to SWE in children with CP.[3,6,8-12]

Previous studies on changes in SWE after BoNT-A injection in children with spastic CP found a significant decrease in passive muscle stiffness measured with SWE.[10,12-16] Brandenburg et al. (2018) reported that BoNT-A injection resulted in significant changes in SWE but not in joint range of motion or spasticity in children with CP. These findings suggest that SWE can aid in treatment planning and monitoring effectiveness.[6]

The length of the spastic muscle or the relative muscle length is shortened in children with CP due to long-term stiffness and a difference in the speed of the muscle-tendon unit and bone growth, resulting in limitation of motion. Casting is a known efficacious therapeutic intervention for increasing the range of motion and decreasing spasticity.[17,18] However, to the best of our knowledge, changes in passive muscle stiffness after the intervention have rarely been studied.

This study aimed to investigate the factors affecting passive muscle stiffness using ultrasound SWE in children with spastic CP and to determine the changes in SWE with therapeutic interventions.

II. MATERIALS AND METHODS

1. Participants

We enrolled children with spastic CP who met the inclusion criteria for this study. The inclusion criteria were as follows: 1) children with spastic CP between 2 and 13 years; 2) MAS at ankle plantar flexors with the knee extended ≥ 1+ with an R2 angle of Modified Tardieu Scale (MTS) (maximal ankle dorsiflexion angle) ≤ 15°; and 3) child and primary caregiver of the child agreed to participate in this study. The exclusion criteria were as

follows: 1) chemodenervation therapy in the gastrocnemius (GCM) or serial casting of the ankle within 3 months; 2) previous orthopedic surgery in the lower limb within 6 months; 3) history of allergy to the toxin; and 4) change in oral medications and dosing that might influence muscle tone within 30 days.

Ethical approval was granted by the Institutional Review Board and Ethics Committee of the Hospital (#4-2019-0590). The primary caregiver provided written informed consent according to the rules of the IRB of our hospital. Demographic information was recorded for each child, including age, sex, height, weight, and history of botulinum toxin injections.

2. Interventions

The children were treated with BoNT-alone (group A), BoNT-A with a short leg cast (group B), and no intervention (Group C).

Groups A and B received BoNT-A injections. A local anesthetic (lidocaine cream) was topically applied at the injection site 20 min before BoNT-A injection. Reconstituted vials containing 100 units of abobotulinum toxin A (Botox®, Allergan Inc., Irvine, CA, USA) and 2 mL of normal saline to provide a solution containing 50 units/mL were prepared for injection. BoNT-A was injected at two points at the medial and lateral heads of the GCM using ultrasonography guidance with the child in the prone position. The dose of the toxin ranged from 3.5 to 4.5 units/kg depending on the severity of spasticity (mean±SD = 3.86 ± 0.68 units/kg). The maximum dose was 20 units/kg and did not exceed 300 units.

In group B, short leg casting was applied for 1 to 2 weeks (depending on the degree of limitation of motion) to increase the passive range of motion (ROM) on the same day or the day after injection. Short leg casts were applied with the patient in a prone position with the knee flexed to 90° and the ankle dorsiflexed to maximal attainable dorsiflexion and held in the neutral hindfoot position.

Most children underwent intensive physical therapy, including stretching, strengthening,

and gait training during the study period (at least four sessions per week, 60 minutes per session).

3. Assessments

Clinical assessments and SWE were performed at baseline (T1), 2 weeks (T2), and 4 weeks (T3) post-intervention.

A. Clinical assessments

Throughout the study, the physiatrist assessed the muscle tone of the ankle plantar flexor using the MAS and MTS in the supine position, with the knee fully extended and flexed at 90°. The MAS is a 6-point rating scale ranging from 0 to 4, which is used to assess muscle tone. For statistical analysis, a MAS grade of 1 was regarded as 1, while a grade of 1(+) was regarded as 2, up to a score of 4, which was regarded as 5. For the MTS, two levels of the ankle dorsiflexion angle were measured using manual goniometry after slow and fast ankle joint stretches, referred to as the R2 and R1 angles, respectively.[19] The R1 angle was defined as the point in the ROM where a catch was first felt during quick, passive dorsiflexion of the ankle joint. In contrast, the R2 angle was defined as the maximum ankle dorsiflexion angle measured at the end of the movement. The difference between the two angles (R2-R1) represents the dynamic component of spasticity.[20]

B. Shear wave elastography

The medial GCM SWE was measured using a Samsung RS85 ultrasound scanner equipped with Prestige equipment (Samsung Medison Co. Ltd., Seoul, Korea) and a linear array transducer (LA2-9A; Samsung Medison Co. Ltd., Seoul, Korea). For SWE measurements, each child was positioned prone with one foot hanging over the edge of the examination table. The medial GCM was measured using B-mode and SW ultrasound elastography with the ankle in neutral (0-degree plantarflexion) (SWE-N) and resting (relaxed) positions (SWE-R). In the area with the most muscle bulk, the ultrasound transducer was

placed parallel to the long axis of the medial GCM. The distance from the fibular head to the proximal end of the ultrasound probe was measured and recorded to ensure the appropriate placement of the probe for repeated measurements. B-mode imaging was used to confirm the correct transducer placement. The transducer was placed with minimal pressure on the skin. We monitored whether muscle activation occurred using EMG signals (Dantec®, Natus, Middleton, WI, USA) to check the patient's muscle relaxation state (Figure 1. A).

For SWE measurement, a region of interest (ROI) was placed in the middle region of the medial GCM so that the muscle fascia that borders tendons and blood vessels did not overlap. Finally, the ROI of the correct position was calculated using the "reliability measurement index" (RMI), calculated as the weighted sum of the magnitude of the shear wave and residual of the wave equation. According to the manufacturer, the RMI ranges from 0.0 ± 1.0, with a standardized value of 0.5, when characterizing diffuse liver disease is considered acceptable and correlates with reproducible measurements. Because no standardized RMI value recommended for musculoskeletal applications exists, the same condition of ≥ 0.5 was chosen. SWE was measured five times, for each ankle position and the average of these values was used for analysis (Figure 1. B).

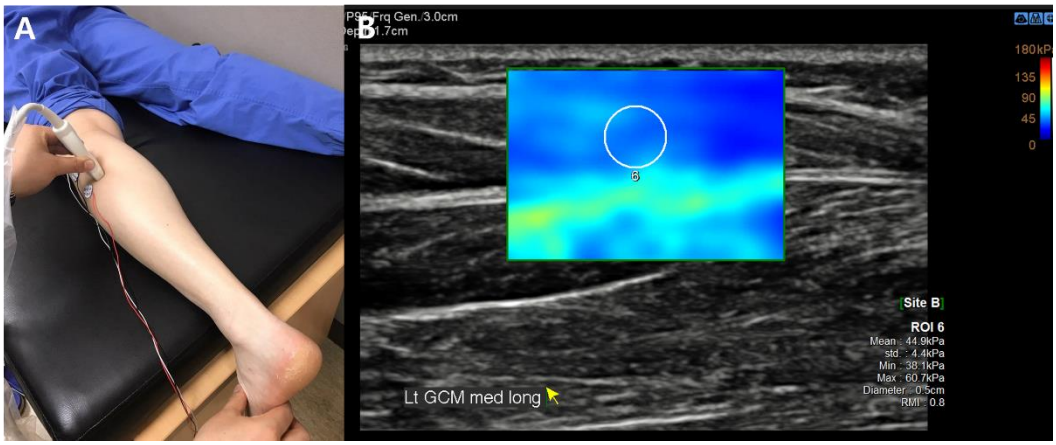

Figure 1. Shear wave elastography. (A) Placement of the transducer on the medial gastrocnemius (GCM) muscle. (B) Shear wave elastography imaging assessed on the GCM. The white circle (center) represents the shear wave measurement area.

4. Statistical analysis

Quantitative variables are expressed as medians and interquartile ranges [25th and 75th percentiles]. The distribution of these variables was compared using the Mann–Whitney U test and Kruskal–Wallis test because the data were not normally distributed. The proportions of these variable categories were compared between the groups using the chi-squared test. The correlations between SWE, patient characteristics, and clinical assessment at baseline were investigated using Spearman correlation analysis. Spearman's correlation $\geq$0.80 was defined as very strong, 0.80–0.60 as strong, 0.60–0.40 as moderate, 0.40–0.20 as weak, and 0.20 as very weak.[21] Stepwise regression analysis was used to determine the effect of several variables on SWE. The generalized estimating equation (GEE) method, which extends the generalized linear model accounting for within-subject correlations across repeated measurements, was used to analyze the change in SWE over time for each group and to estimate factors affecting SWE.[22] Bonferroni post hoc tests were used to analyze the time factor further. SPSS version 25 for Windows (SPSS Inc., Chicago, IL, USA) was used for all the statistical analyses. $p < 0.05$ was considered to be statistically significant.

III. RESULTS

1. Participant characteristics and baseline assessments

We enrolled 32 children with spastic CP (7 unilateral CP, 25 bilateral CP), and 57 legs (one leg with seven unilateral CP and two legs with 25 bilateral CP) were analyzed in this study. The participants included 21 boys and 11 girls with a median age of 5.5 years old (Q1, 3.4; Q3, 6.5; age range 2.5-10.6 years). The children were classified as Gross Motor Function Classification System (GMFCS) levels I to V (8/7/6/10/1). The median number of previous BoNT injections into the GCM in all children was two (Q1, 0; Q3, 4). The median body mass index (BMI) of all children was 15.4 kg/m^2 (Q1, 14.1; Q3, 16.2). No differences in sex, CP type, or BMI among the three groups. However, age, history of

BoNT injections, and distribution of GMFCS levels were significantly different among the three groups. Groups C, B, and A had the oldest members, and groups B, C, and A had the most history of BoNT injections. Each group's height and weight were not significantly different.

Table 1 shows the spasticity and SWE values of the subjects at baseline (T1). At T1, there were significant differences between the three groups in MAS in knee extended (KE), MTS in knee flexed (KF), and KE, except for MAS in KF and R2-R1 angles of MTS in KF and KE. In the post hoc analysis, R1 (angle of spastic catch) and R2 (maximum angle when slowly stretched) of MTS in KF were smaller in group B than in groups A and C. Groups A and B had higher MAS scores in KE than group C. Group B had a smaller R1 of MTS in the KE than Group C. Group B had a lower R2 of MTS in KE than groups A and C. The median values of the SWE-N (SWE in the neutral ankle position), SWE-R (SWE in the resting ankle position) and SWE ratio (= ratio of SWE-N to SWE-R) of all participants were 82.5 kPa, 40.9 kPa, and 2.10, respectively, and there was no significant difference between the three groups.

Table 1. Demographic characteristics, spasticity evaluation, and shear wave elastography at baseline

		Total participants (N=32)		Group A (BoNT alone) (19 legs)		Group B (BoNT+Cast) (15 legs)		Group C (No intervention) (23 legs)		Between-group comparisons
		N	%	N	%	N	%	N	%	*p*-value†
Sex	male	21	63.6%	12	63.2%	10	66.7%	15	65.2%	0.977
	female	11	34.4%	7	36.8%	5	33.3%	8	34.8%	
CP type	unilateral	7	21.9%	3	15.8%	2	13.3%	2	8.7%	0.880
	bilateral	25	78.1%	16	84.2%	13	86.7%	21	91.3%	
GMFCS	I	8	25.0%	8	42.1%	2	13.3%	1	4.3%	0.005
	II	7	21.9%	4	21.1%	6	40.0%	3	13.0%	
	III	6	18.8%	1	5.3%	5	33.3%	5	21.7%	
	IV	10	31.3%	6	31.6%	2	13.3%	12	52.2%	
	V	1	3.1%	0	0.0%	0	0.0%	2	8.7%	

	Median	(Q1, Q3)	Median	(Q1, Q3)	Median	(Q1, Q3)	Median	(Q1, Q3)	*p*-value‡
Age (year)	5.5	(3.4, 6.5)	3.8	(2.7, 5.5)	5.5	(5.0, 6.0)	6.2	(4.4, 7.3)	0.012
BoNT history (frequency)	2.0	(0, 4)	0.0	(0, 2)	4.0	(1, 5)	2.0	(1, 3)	0.002
Height (cm)	101.5	(95.1, 111.5)	98.0	(92.3, 105.0)	103.0	(101.0, 106.1)	106.1	(94.2, 116.0)	0.078
Weight (kg)	15.9	(13.6, 19.1)	14.3	(13.0, 17.3)	17.8	(14.3, 18.8)	18.7	(13.6, 22.7)	0.060
BMI (kg/m^2)	15.4	(14.1, 16.2)	14.9	(13.8, 15.5)	16.3	(14.0, 16.7)	15.5	(14.9, 16.1)	0.083
MAS in KF	2	(2, 3)	2	(2, 3)	2	(2, 3)	2	(2, 3)	0.838
R1 in KF (°)	-5.0	(-10, 5)	-5.0	(-10, 5)	-10.0	(-20, -5)	0.0	(-10, 10)	0.019
R2 in KF (°)	20	(12.5, 25)	25	(20, 25)	15	(5, 20)	25	(20, 25)	<0.001
R2-R1 in KF (°)	20	(15, 30)	30	(20, 35)	20	(15, 25)	20	(15, 25)	0.075
MAS in KE	3	(2, 3)	3	(2, 3)	3	(2, 3)	2	(2, 3)	0.044
R1 in KE (°)	-15	(-25, -10)	-15	(-20, -10)	-20	(-30, -15)	-10	(-25, 0)	0.026
R2 in KE (°)	5	(0, 10)	5	(5, 15)	0	(-5, 0)	10	(5, 15)	<0.001
R2-R1 in KE (°)	20	(15, 25)	25	(20, 25)	20	(10, 25)	20	(10, 25)	0.070
SWE-N (kPa)	82.5	(64.4, 114.5)	82.5	(55.5, 120.26)	76.2	(68.1, 141.8)	83.9	(56.8, 112.35)	0.780
SWE-R (kPa)	40.9	(31.4, 49.9)	43.77	(31.4, 49.9)	39.2	(30.4, 55.4)	39.1	(30.75, 55.25)	0.979
SWE ratio	2.10	(1.48, 2.80)	2.09	(1.405, 2.88)	2.12	(1.69, 2.73)	2.13	(1.44, 2.93)	0.757

Abbreviations: CP, cerebral palsy; GMFCS, gross motor function classification system; BoNT, botulinum toxin; BMI, body mass index; MAS, modified Ashworth scale; KF, knee flexed; KE, knee extended; SWE, shear wave elastography; N, neutral ankle position; R, resting ankle position
R1 is defined as the angle in which a catch is found during a quick stretch.
R2 is defined as the maximum dorsiflexion angle.
†, The P value was calculated by chi-square test
‡, The P value was calculated by Kruskal-Wallis test

Of the 57 legs, 56 (98.2%) completed clinical assessments at 2 weeks (T2), while 39 (68.4%) completed clinical assessments at 4 weeks (T3). The elastography completion rates were 86.0%, 94.7%, and 68.4% (SWE-N and SWE ratios) and 96.5%, 98.2%, and 68.4% (SWE-R) at T1, T2, and T3, respectively (Table 2). The reasons for the incomplete evaluation were follow-up loss, and the patient's lack of cooperation, which prevented elastography evaluation or resulted in a partial evaluation led to the incomplete evaluation.

Table 2. Number of legs that completed the assessment.

		Group A (total 19 legs)		Group B (total 15 legs)		Group C (total 23 legs)		Total (total 57 legs)	
		N	%	N	%	N	%	N	%
Clinical assessment (MAS, MTS)	T1	19	100.0%	15	100.0%	23	100.0%	57	100.0%
	T2	18	94.7%	15	100.0%	23	100.0%	56	98.2%
	T3	15	78.9%	7	46.7%	17	73.9%	39	68.4%
SWE-N SWE ratio	T1	17	89.5%	15	100.0%	17	73.9%	49	86.0%
	T2	18	94.7%	15	100.0%	21	91.3%	54	94.7%
	T3	15	78.9%	7	46.7%	17	73.9%	39	68.4%
SWE-R	T1	19	100.0%	15	100.0%	21	91.3%	55	96.5%
	T2	18	94.7%	15	100.0%	23	100.0%	56	98.2%
	T3	15	78.9%	7	46.7%	17	73.9%	39	68.4%

Abbreviations: MAS, modified Ashworth scale; MTS, modified Tardieu scale; SWE, shear wave elastography; N, neutral ankle position; R, resting ankle position

2. Factors affecting shear wave elastography

In the correlation analysis, SWE-N showed a significant moderately negative correlation with BMI and a nonsignificant association with GMFCS. The SWE-R demonstrated a significantly weak correlation with the GMFCS and BMI and there was no correlation between the variables and the SWE ratio (Table 3).

Multiple regression analysis showed that BMI was negatively associated with SWE-N, and age was negatively associated with SWE-R. Conversely, GMFCS was positively associated with SWE-R (Table 4).

Table 3. The correlation between shear wave elastography and parameters

	SWE-N		SWE-R		SWE ratio	
	rho	*p*	rho	*p*	rho	*p*
Sex	0.12	0.422	0.22	0.108	-0.17	0.234
Age	-0.10	0.482	-0.04	0.755	0.01	0.942

GMFCS score	0.26	0.072	0.29	0.031	-0.04	0.771
BoNT history	-0.05	0.716	-0.10	0.448	0.13	0.364
BMI	-0.48	0.001	-0.32	0.016	-0.12	0.402
MAS in KF	-0.11	0.433	0.00	0.995	-0.13	0.389
R1 in KF	-0.10	0.494	0.14	0.304	-0.26	0.072
R2 in KF	0.19	0.194	0.21	0.119	-0.08	0.583
R2-R1 in KF	0.21	0.144	-0.06	0.656	0.20	0.168
MAS in KE	0.18	0.220	0.11	0.436	0.07	0.649
R1 in KE	-0.08	0.595	0.03	0.824	-0.09	0.523
R2 in KE	-0.05	0.728	0.08	0.575	-0.21	0.140
R2-R1 in KE	0.00	0.990	0.00	0.981	-0.08	0.607

Abbreviations: GMFCS, gross motor function classification system; BoNT, botulinum toxin; BMI, body mass index; MAS, modified Ashworth scale; SWE, shear wave elastography; N, neutral ankle position; R, resting ankle position
R1 is defined as the angle in which a catch is found during a quick stretch.
R2 is defined as the maximum dorsiflexion angle.
Statistics were analyzed by Spearman correlation

Table 4. Factors affecting shear wave elastography

	Stepwise regression analysis				
	B (SE)	β	*p*-value	F (p)	Adjusted R^2
SWE-N				7.03 (0.011)	0.112
BMI	-7.93 (2.99)	-0.36	0.011		
SWE-R				5.58 (0.006)	0.145
GMFCS score	7.12 (2.22)	0.44	0.002		
Age	-2.96 (1.41)	-0.29	0.040		
SWE ratio					
	No variable entered.				

Abbreviations: B, unstandardized coefficients; SE, standard error; β, standardized coefficients; SWE, shear wave elastography; N, neutral ankle position; R, resting ankle position; BMI, body mass index; GMFCS, gross motor function classification system

3. Changes after interventions

A. Changes in clinical assessments after interventions

The MAS and MTS scores of all groups changed significantly between T2 and T3 compared with T1. Group A significantly improved MTS and MAS at T2 and T3 relative to T1, except R2 in KE at T3. Group B demonstrated significant improvements in R1 and R2 of MTS at T2 and T3, and R2-R1 angles at T2 than at T1 (Table 5).

B. Changes in shear wave elastography after interventions

All groups' SWE-N decreased over time relative to their baseline values. In group A, SWE-N decreased significantly only at T3 compared to T1 only. In group B, SWE-N significantly decreased at T2 and T3 compared with that at T1; however, SWE-N increased significantly at T3 compared with that at T2. In group C, there were no significant differences between the T1, T2, and T3 SWE-N assessments. In groups A and B, SWE-R was significantly lower at T3 than at T1. The SWE ratio was significantly reduced at T2 compared with that at T1 in group B. In Group C, the SWE ratio significantly decreased at T3 (Table 6).

Table 5. Changes in spasticity of ankle plantar flexor after interventions

		Group A (BoNT alone)			Group B (BoNT + Cast)			Group C (Control)			between-group comparisons	post hoc analysis*,‡		
		Median	(Q1, Q3)	p^*	Median	(Q1, Q3)	p^*	Median	(Q1, Q3)	p^*	$p^\dagger$	A vs C	B vs C	A vs B
with knee flexed														
MAS	Δ1	0.0	(-1, 0)	0.025	0.0	(-1, 0)	0.063	0.0	(-1, 0)	0.008	0.980			
	Δ2	-1.0	(-1, 0)	0.005	0.0	(-2, 0)	0.102	0.0	(-1, 0)	0.102	0.287			
R1 of MTS	Δ1	5.0	(5, 10)	0.000	15.0	(10, 20)	0.001	5.0	(0, 10)	0.001	<0.001	0.936	0.001	0.006
	Δ2	10.0	(0, 15)	0.004	10.0	(5, 30)	0.027	5.0	(0, 10)	0.005	0.238			
R2 of MTS	Δ1	0.0	(0, 5)	0.034	10.0	(5, 10)	0.001	0.0	(0, 5)	0.021	<0.001	>0.999	0.001	0.001
	Δ2	0.0	(0, 5)	0.033	5.0	(5, 10)	0.026	0.0	(0, 5)	0.008	0.092			
R2-R1 of MTS	Δ1	-5.0	(-6.25, 0)	0.002	-5.0	(-10, -5)	0.001	-5.0	(-5, 0)	0.015	0.252			
	Δ2	-5.0	(-10, 0)	0.026	0.0	(-20, 0)	0.197	-5.0	(-7.5, 5)	0.263	0.703			
with knee extended														
MAS	Δ1	-0.5	(-1, 0)	0.005	-1.0	(-2, 0)	0.003	0.0	(0, 0)	0.317	<0.001	0.002	<0.001	0.286
	Δ2	-1.0	(-1, 0)	0.002	-1.0	(-2, -1)	0.024	0.0	(0, 0)	0.564	<0.001	0.001	0.001	0.256
R1 of MTS	Δ1	7.5	(3.75, 15)	0.001	20.0	(10, 25)	0.001	0.0	(0, 10)	0.010	<0.001	0.125	<0.001	0.013
	Δ2	10.0	(5, 15)	0.002	15.0	(10, 25)	0.018	5.0	(0, 10)	0.061	0.007	0.069	0.015	0.733
R2 of MTS	Δ1	0.0	(0, 5)	0.058	5.0	(5, 10)	0.001	0.0	(0, 5)	0.026	0.001	>0.999	0.001	0.013
	Δ2	5.0	(0, 10)	0.008	5.0	(0, 5)	0.034	0.0	(0, 5)	0.010	0.598			
R2-R1 of MTS	Δ1	-5.0	(-10, 0)	0.006	-10.0	(-15, -5)	0.004	0.0	(-5, 0)	0.213	0.016	0.236	0.019	0.602
	Δ2	-5.0	(-10, 0)	0.017	-10.0	(-15, -5)	0.017	0.0	(-7.5, 7.5)	0.971	0.024	0.231	0.036	0.618

Abbreviations: BoNT, botulinum toxin; MAS, modified Ashworth scale; MTS, modified Tardieu scale; Δ1, difference between baseline and at 2 weeks; Δ2, difference between baseline and at 4 weeks
R1 is defined as the angle in which a catch is found during a quick stretch.
R2 is defined as the maximum dorsiflexion angle.
*, The P value was calculated by Mann-Whitney test.
†, The P value was calculated by Kruskal-Wallis test.
‡, The Bonferroni correction was used to adjust for multiple post-hoc comparisons.

Table 6. Generalized estimating equation regression models of intervention effects on SWE

		T1		T2		T3		*p*-value (time)	*p*-value			*p*-value (time x group)
		Mean	[95% CI]	Mean	[95% CI]	Mean	[95% CI]		T1 vs T2	T1 vs T3	T2 vs T3	
SWE-N	Group A	82.55	[66.12, 103.08]	69.92	[54.62, 89.52]	61.10	[50.50, 73.93]	0.001	0.102	0.001	0.223	0.026
	Group B	95.33	[74.55, 121.90]	55.89	[44.81, 69.72]	69.28	[55.97, 85.75]	<0.001	0.001	0.001	0.033	
	Group C	83.95	[61.33, 114.93]	71.41	[55.97, 91.1]	61.77	[48.89, 78.04]	0.021	0.348	0.052	0.108	
SWE-R	Group A	40.08	[34.65, 46.35]	35.12	[30.09, 40.99]	32.22	[27.84, 37.28]	<0.001	0.137	<0.001	0.109	0.885
	Group B	45.58	[36.77, 56.49]	36.47	[26.32, 50.55]	30.65	[22.44, 41.86]	0.007	0.134	0.001	0.097	
	Group C	43.53	[35.49, 53.4]	42.05	[34.62, 51.08]	36.55	[30.59, 43.66]	0.242	0.175	0.103	0.548	
SWE ratio	Group A	2.18	[1.65, 2.89]	2.17	[1.57, 3.00]	2.13	[1.65, 2.75]	0.915	0.785	0.693	0.924	<0.001
	Group B	2.30	[1.92, 2.75]	1.48	[1.32, 1.66]	2.38	[1.87, 3.03]	<0.001	<0.001	0.794	<0.001	
	Group C	2.17	[1.78, 2.64]	1.96	[1.36, 2.83]	1.76	[1.55, 2.00]	0.029	0.531	0.018	0.475	

Values are presented as estimated mean [95% confidence interval].
Abbreviations: SWE, shear wave elastography; N, neutral ankle position; R, resting ankle position

IV. DISCUSSION

In this study, SWE was measured at two different ankle angles (neutral and resting positions). Boulard et al. reported that passive stiffness should be evaluated at the slack angle and within 80% of the maximum passive dorsiflexion.[23] The slack angle is the angle of ankle flexion at which tension begins. In this study, the feet were placed off the table in the prone position with the knee extended and the ankle comfortably positioned. The SWE value in the resting position was expressed as SWE-R. Furthermore, in more than 80% of the maximum passive dorsiflexion, involuntary muscle activation continued,[24] and the maximum ankle dorsiflexion angle was different for each child with CP; therefore, SWE was measured at 0 °DF, an anatomical position (SWE-N). Finally, the ratio of the two measurements (SWE-N/SWE-R) was calculated to determine the rate of increase in muscle stiffness as the muscle was stretched (SWE ratio). In this study, the median values of SWE-N and SWE-R in the GCM of all children with CP at baseline were 82.5 (kPa) and 40.9 (kPa), respectively, which were greater in the neutral position. This was consistent with previous studies, which found that stiffness increased as ankle angle increased.[1,7,23,25] The median SWE ratio in this study was 2.10, which was similar to the SWE ratio (ratio of SWE at 0° plantarflexion to SWE at 20° plantarflexion) reported as 2.2 in 13 children with CP by Brandenburg et al..[6]

Previous studies reported that age, sex, affected side, changing joint angles, body mass, and muscle mass have the potential to influence muscle properties.[1,7,25-27] In this study, the effects of sex, age, GMFCS level, history of botulinum toxin injection, BMI, and clinical assessments (MAS and MTS) on SWE were investigated.

In previous studies, gross motor function was not correlated with elastography; however, these studies were conducted only on ambulatory CP.[3,6,10,12,13] However, some studies reported a significant association between spasticity and GMFCS level.[28,29] According to Mathewson et al., single fiber stiffness in GCM of children with CP was stiffer in GMFCS III to V than in I to II.[11] The substantial number of non-ambulatory CP were recruited as

participants and ambulatory CP in our study. Thus, there could have been a significant relationship between the GMFCS level and SWE in our study. Our findings are consistent with those reported by Mathewson et al..

In this study, BMI was significantly associated with SWE-N. A previous study demonstrated a negative relationship between BMI and SWE in healthy children, although this was not statistically significant.[30] In healthy adults, another study reported that there was a significant negative relationship between BMI and SWE.[31] Fat tissue is known to have a lower shear modulus than fibrosis tissue.[32] Thus, it may be assumed that the higher fat composition in the tissue may lead to less stiffness. From this perspective, the negative relationship between BMI and SWE observed in our study can be explained.

Age was a significant factor negatively related to SWE-R in our study. However, previous studies have reported conflicting results. Liu et al. reported that passive muscle stiffness increased with age from children to middle-aged adults and older age groups.[33] In contrast, Alfuraih et al. reported that aging was associated with a decline in skeletal muscle stiffness in healthy adult volunteers, and children were stiffer than young adults.[34] one study reported that healthy children were stiffer than healthy young adults. However, in a previous study that evaluated SWE in healthy children, no correlation was observed between age and passive muscle stiffness. In further studies, the association between age and SWE should be examined in children with or without CP.

Previous studies reported a decrease in the shear modulus of GCM in children with spastic CP after 4 weeks of BoNT-A injection.[10,12-16] Some studies reported significant associations between changes after BoNT-A in SWE and clinical evaluations for spasticity.[13,16,35] However, one study reported significant changes in SWE without significant changes in joint range of motion and spasticity.[6] Similar to previous studies, this study presented the reduction of SWE-N and SWE-R after 4 weeks of treatment with BoNT-A injection with or without the serial cast.

Increases in passive stiffness can be caused by muscle shortening, altered mechanical muscle properties, or both.[23] The improvement of muscle stiffness in the resting position

seemed to reflect changes in mechanical muscle properties, SWE-R decreased after 4 weeks only in the groups receiving BoNT-A. However, in the case of SWE-N, it decreased even in children who received only physical therapy without BoNT-A treatment, which is thought to be due to improvement in muscle shortening. In addition, since R2 (maximum dorsiflexion angle) in KE increased after 4 weeks in all groups, including the group that received only physical therapy, it is thought that GCM shortening improved and SWE-N decreased after physical therapy, including stretching. In the serial cast group, the SWE-N and SWE ratios decreased at 2 weeks, and the effect reduced or disappeared at 4 weeks. Similarly, in the clinical evaluation, the group with serial casts showed a higher increase in R2 of MTS at 2 weeks than the other two groups, and there was no difference in R2 change between the three groups at 4 weeks. As mentioned above, it is thought that this result appeared as the muscle shortening showed more improvement immediately after cast treatment for 1-2 weeks. Then the effect gradually decreased after serial casting was discontinued.

Clinical assessments using MAS and MTS did not correlate with SWE in the baseline evaluation in this study. However, many studies have reported moderate to strong correlations of SWE with MAS and TS,[1,7,12,25] except a few that reported no correlation between MAS and SWE.[6,36] This study included children aged 2.5–10.6 years. It is difficult to reliably evaluate the clinical assessments of MAS and MTS in young children because of lack of cooperation. Therefore, the relationship between SWE and the clinical measure of spasticity of MAS or MTS should be re-examined in children who will cooperate during the whole procedure. Another limitation was the significant differences in clinical measures at baseline assessment between the groups. Thus, this study could not compare the effects of BoNT-A injection or combined therapy with BoNT-A and short leg cast on SWE. Comparing the effects of therapeutic interventions on SWE may be an interesting topic for further studies. Finally, there is no consensus on the ROI window for SWE. In this study, as in previous studies, an ROI with a diameter of 0.5 cm was placed in the middle of the muscle belly, but there has been no research on whether

this could reflect the stiffness of the entire muscle.

V. CONCLUSION

This study revealed that BMI, GMFCS level, and age were significantly associated with SWE in children with spastic CP. The significant changes in SWE after BoNT-A injection and combined therapy with BoNT-A injection and short leg cast suggest positive effects of the therapeutic intervention on passive muscle stiffness. Our study suggests that SWE may be a useful outcome measure for therapeutic interventions in children with spastic CP. SWE quantified the degree of muscle stiffness and showed a change in muscle stiffness after therapeutic interventions. In children with CP, SWE can be a good diagnostic tool for assessing passive muscle stiffness in the spastic muscles, determining treatment plans, and monitoring the effectiveness of treatment modalities.

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ABSTRACT(IN KOREAN)

경직성 뇌성마비 소아에서 횡파 탄성 초음파를 통한 수동적 근육 뻣뻣함에 영향을 미치는 요인 분석

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배경: 경직성 뇌성마비의 근긴장항진은 신경 요소와 비신경 요소가 모두가 기여한다. 비신경 구성 요소 중 하나인 수동적 근육 뻣뻣함은 뇌성마비 소아에서 정상 발달 소아보다 더 크다.

목표: 본 연구의 목적은 경직성 뇌성마비 소아에서 횡파 탄성 초음파 영상을 사용하여 수동적 근육 뻣뻣함에 영향을 미치는 요인을 조사하고 치료적 중재 후 횡파탄성초음파의 변화를 알아보는 것이다.

방법: 32명의 경직성 뇌성마비 소아(남 21명, 여 11명, 2.5-10.6세)가 모집되었다. 횡파탄성계수는 발목을 0도 족저굴곡(SWE-N) 및 안정 위치(SWE-R)에 두고 내측 비복근에서 횡파탄성초음파를 사용하여 측정되었다. 참가자 중 일부는 석고고정술을 포함하거나 포함하지 않은 보툴리눔 독소 주사로 치료를 받았다. 중재 전, 2주 후, 4주 후에 횡파탄성초음파, 수정된 Ashworth 척도, 수정된 Tardieu 척도를 평가하였다.

결과: 다중회귀분석 결과, 체질량 지수는 SWE-N에 유의하게 부정적인 영향을 미쳤다. SWE-R에서 대운동분류시스템 수준은 양의 요인, 연령은 음의 요인이었다. 임상적 경직 평가는 횡파탄성계수와 유의한 관계를 나타내지 않았다. SWE-N은 치료 방식에 관계없이 감소했고, SWE-R은 석고고정술 유무에 관계없이 보툴리눔 독소 주사 이후 감소했다. 그리고 SWE-N 대 SWE-R의 비율은 보툴리눔 독소와 석고고정술 병합 치료 후와 물리 치료 후에 감소했다.

결론: 본 연구는 뇌성마비 소아에서 체질량지수, 대운동분류시스템 수준 및

연령이 횡파탄성계수와 유의한 관련이 있음을 밝혔다. 치료적 중재 후 횡파탄성초음파 영상의 의미 있는 변화는 횡파탄성초음파가 뇌성마비 소아의 경직 관리에 유용한 결과 측정 도구가 될 수 있음을 시사한다.

핵심되는 말 : 뇌성마비, 근육 뻣뻣함, 탄성초음파, 횡파