

Utility of Ultrasound Elastography to Evaluate Poststroke Spasticity and Therapeutic Efficacy: A Narrative Review

CME Credits

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Abstract

Poststroke spasticity (PSS) is a common complication that affects function and daily self-care. Conservative PSS treatments include traditional rehabilitation, botulinum toxin injection, and extracorporeal shock wave therapy. Currently, the Modified Ashworth Scale and Modified Tardieu Scale are widely used tools to clinically evaluate spasticity, but the best tool for PSS assessment remained controversial. Ultrasound elastography (UE), including shear wave and strain image as the emerging method to evaluate soft tissue elasticity, became popular in clinical applications. Spastic biceps and gastrocnemius muscles were reported to be significantly stiffer compared to nonparetic muscles or healthy control using shear wave or strain elastography. More studies investigated the utility, reliability, and validity of UE in patients with PSS, but the contemporary consensus for the utility of UE in the measurement and therapeutic follow-up of PSS remained lacking. Therefore, this narrative review aimed to appraise the literature on the shear wave and strain elastography on PSS and summarize the roles of UE in assessing the therapeutic efficacy of different PSS interventions.

Keywords: Spasticity, stroke, ultrasound elastography

INTRODUCTION

Stroke is the leading cause of death and disability worldwide. Spasticity, defined as the velocity-dependent abnormal increased muscle tone, is a common poststroke complication.^[1] Muscle stiffness is associated with impaired voluntary control, strength, and motor coordination. In addition, subsequent joint contracture, pathological fracture, or heterotopic ossification of the affected limbs developed, thereby affecting the neurological function recovery, daily self-care, and quality of life in patients with stroke.^[2] Conservative treatments for poststroke spasticity (PSS) include oral medications, stretch exercises, and physical modalities such as therapeutic ultrasound, thermotherapy, transcutaneous electrical nerve stimulation, or neuromuscular electrical stimulation.^[3] The evidence demonstrated the efficacy and safety of botulinum toxin (BoTx) injection and extracorporeal shockwave therapy (ESWT) in managing PSS.^[4]

The Modified Ashworth Scale (MAS) and Modified Tardieu Scale (MTS) were the most widely used tools in rehabilitation

units to assess and measure spasticity.^[5] However, the best tool for evaluating spasticity remained controversial due to the complexity of the mechanism. MAS is a subjective tool based on the assessor's judgment and is unable to reflect the velocity-dependent condition. The reliability of MTS in the stroke population was reported inconclusively and could not be utilized in single muscle evaluation.^[6] Therefore, there is a need for objective, reliable, and valid methods to quantify spasticity.

Ultrasound elastography (UE) as the emerging noninvasive method to measure soft-tissue elasticity is mainly developed to evaluate liver cirrhosis, breast and thyroid lesions, and various musculoskeletal conditions.^[7-10] The mechanical properties of living tissue could be obtained for the quantitative assessment using Young's modulus.^[11] Among several UE methods, strain

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elastography (SE) and shear wave elastography (SWE) are commonly utilized in clinical applications. SE is performed to detect tissue displacement with repetitive external compression to tissue by the ultrasound probe. The SE image could be quantified via strain ratio by dividing the value of the target tissue to reference tissue (e.g., the fat as reference tissue),^[11] or color histogram analysis of the sonoelastogram.^[12] Shear waves could be launched from acoustic radiation force in the SWE image.^[13] The value of Young's modulus or wave speed could be displayed in different color elastogram for elasticity quantification.^[13]

Previous studies proved the feasibility of UE assessment in the spastic forearm and gastrocnemius muscles for PSS.^[14,15] Wu *et al.* demonstrated that SWE velocity was correlated with MAS and MTS in the biceps muscle at the stroke paretic side, suggesting SWE as the reliable method.^[16] A recent systematic review investigated the reliability and validity of UE in patients with neurological diseases, thereby revealing moderate reliability and good validity for spasticity assessment.^[17] However, another review that used the quality tool for reliability evaluation revealed a low quality of most included studies, and the UE was not mature for spasticity diagnosis due to divergent protocols among researchers.^[18] The contemporary consensus for UE utility in the measurement and therapeutic follow-up of PSS remained lacking. Therefore, this narrative review aimed to appraise the literature and summarize the role of UE in evaluating PSS and the therapeutic efficacy of different PSS interventions.

METHOD

We searched PubMed, EMBASE, Scopus, and Cochrane Library from the earliest records to August 2022, and the references of relevant articles were manually checked. We utilized the following keywords: "stroke," "infarction," "ischemic," "hemorrhagic," "cerebrovascular," "CVA," "brain injury," "Spasticity," "elastography," "elastogram," "elasticity," "shear wave," "strain," "shockwave," "botulinum," or "Botox," as well as Medical Subject Heading terms: "Stroke," "Brain Infarction," "Muscle Spasticity," "Elasticity imaging techniques," "Extracorporeal shockwave therapy," and "Botulinum Toxins." The search was based on English language articles and human studies. Observational, quasi-experimental, and randomized controlled trials (RCTs) were included, but case series, single-arm studies, or conference papers were excluded from this narrative review. The inclusion criteria were studies focusing on PSS and elastography, either using UE to assess the PSS or investigating the treatment effectiveness of ESWT/BoTx for patients with PSS. Two independent authors (first and secondary) reviewed all relevant articles by title and abstract during the selection process, and full-text studies were assessed for the inclusion criteria. The disputes were resolved by discussion or decision by the corresponding author.

RESULTS AND DISCUSSION

We identified 766 studies from electronic databases. After removing the duplicate studies, 569 citations were screened

by title and abstract. This narrative review for qualitative assessment included 17 full-text articles. Among them, 11 studies compared the elastography of PSS muscles on the paretic side with that on the nonparetic side and four compared the muscle elasticity between stroke and healthy control [Table 1].^[14-16,19-28] Five studies utilized SWE or SE to evaluate the therapeutic efficacy of different interventions, including BoTx, ESWT, rehabilitation, and other treatments [Table 2].^[20,27,29-31]

Shear wave elastography for spasticity

SWE is a quantitative method to evaluate tissue properties and is widely applied in gastrointestinal and genitourinary organs.^[32] The ultrasound probe generates a push pulse in SWE to deform the tissue called focused acoustic radiation force impulse. The resulting propagation speed of tissue displacement was calculated to reflect the tissue stiffness.^[11] The role of SWE in assessing muscular stiffness is emerging in recent years. Several studies had demonstrated the high reliability and reproducibility of SWE in meat specimens and human muscles.^[33-35] Reportedly, muscle stiffness is affected by various factors, including age and sex,^[36,37] as well as joint position using SWE.^[38] SWE is also used to assess PSS. Liu *et al.* demonstrated the value of SWE in evaluating upper limb muscle spasticity of patient's poststroke.^[39] A significant difference in SWE was reported between spastic biceps brachii before and after the rehabilitation ($P < 0.01$). Lehoux *et al.* investigated the role of SWE in assessing PSS and concluded its promising potential.^[40] However, numerous methodological differences were found in previous studies, including target muscles, transducer position, and SWE setting, and may therefore affect the reliability.

Strain elastography for spasticity

Quantifying muscle stiffness in poststroke subjects with SE by compression was mainly used to compare paretic and nonparetic limbs^[14,15,19,41] to determine the treatment effects or examine the correlation with clinical parameters.^[20,29,30,42] Muscle stiffness was affected by the test position, thus studies using compression elastography (CE), were measuring muscle stiffness in certain positions. The biceps brachii in the upper limb was mostly investigated in elbow extended or 90° flexion^[19,20,29] with other muscles, including brachialis, flexor digitorum superficialis, flexor digitorum profundus, flexor carpi radialis, and flexor carpi ulnaris testing in forearm measured in forearm supination.^[14] Lower limb muscle evaluation has been mainly applied to the medial or lateral gastrocnemius muscle, with subjects positioned prone and ankles neutral.^[15,41] Gao *et al.* applied external compression for axial deformation of the biceps brachii muscle, then used phase-sensitive cross-correlation methods for speckle tracking to measure the initial and altered distance of the biceps brachii muscle.^[19,20] Other studies estimate SE through applied light repetitive compression manually with the handheld transducer by providing visual feedback from the quality bar indicator.^[14,15,41] The elastography of the region of interest (ROI) was obtained according to the color-coded image of the ROI. The described CE outcomes as strain ratio, strain

Table 1: The characteristics of studies - Measurement of poststroke spasticity by ultrasound elastography

Reference	Study group	Control group	Muscle	US equipment	UE/unit	Clinical outcomes	Results
Paretic versus nonparetic side							
Yaşar <i>et al.</i> , 2016 ^[14]	Paretic side (n=23)	Nonparetic side (n=23)	Forearm muscle	GE Logiq S7	SE/elasticity index and ratio	MAS, TS	Elasticity index and elasticity ratio on paretic side significantly increased compared with healthy side
Kesikburun <i>et al.</i> , 2015 ^[15]	Paretic side (n=26)	Nonparetic side (n=26)	Gastrocnemius	Linear probe (GE Logiq S7)	SE/elasticity index and ratio	MAS	Elasticity index/ratio of paretic side significantly increased compared with nonparetic side, but no correlation with MAS
Wu <i>et al.</i> , 2017 ^[16]	Paretic side (n=31)	Nonparetic side (n=31)	Biceps brachii	Siemens Acuson S2000	SWE/velocity (m/s)	MAS, MTS, STREAM score	SWV significantly greater on the paretic side than on the nonparetic side
Gao <i>et al.</i> , 2018 ^[19]	Paretic side (n=12)	Nonparetic side (n=12)	Biceps brachii	Siemens Acuson S3000	SWE/velocity (m/s)	MAS, MTS, passive ROM	SWV significantly differed between spastic and nonparetic side
Gao <i>et al.</i> , 2019 ^[20]	Paretic side (n=7)	Nonparetic side (n=7)	Biceps brachii	Siemens Acuson S3000	SE/strain ratio	MAS, TS, passive ROM	Significant differences of strain ratio between paretic and nonparetic biceps
Mathevon <i>et al.</i> , 2018 ^[21]	Paretic side (n=14)	Nonparetic side (n=14)	Gastrocnemius; tibialis anterior	Aixplorer SuperSonic Imagine	SWE/kPa	MAS, TS, passive ROM	The reliability of SWE was good only for gastrocnemius on the paretic side
Lee <i>et al.</i> , 2019 ^[22]	Paretic side (n=14)	Nonparetic side (n=14)	Biceps brachii	Aixplorer Supersonic Imagine	SWE/velocity (m/s)	Nil	SWV significantly greater in paretic side than in nonparetic side
Jakubowski <i>et al.</i> , 2017 ^[23]	Paretic side (n=14)	Nonparetic side (n=14)	Gastrocnemius; tibialis anterior	Aixplorer SuperSonic Imagine	SWE/velocity (m/s)	Fugl-Meyer score, active/passive ROM	Significant increased SWV between paretic and nonparetic side in gastrocnemius, but not in tibialis anterior muscle
Leng <i>et al.</i> , 2019 ^[24]	Paretic side (n=15)	Nonparetic side (n=15)	Flexor carpi radialis	Aixplorer Supersonic Imagine	SWE/kPa	MAS, Fugl-Meyer score	Young's modulus significantly higher in the paretic side than that of the nonparetic side
Lee <i>et al.</i> , 2015 ^[25]	Paretic side (n=16)	Nonparetic side (n=16)	Biceps brachii	Aixplorer Supersonic Imagine	SWE/velocity (m/s)	MAS, MTS, Fugl-Meyer, active/passive ROM	SWV and echo intensity significantly greater in paretic side than in nonparetic side
Rasool <i>et al.</i> , 2018 ^[26]	Paretic side (n=13)	Nonparetic side (n=13)	Biceps brachii	Aixplorer SuperSonic Imagine	SWE/velocity (m/s)	Nil	SWV significantly higher in paretic muscle
Liu <i>et al.</i> , 2020 ^[27]	Paretic side (n=14)	Nonparetic side (n=14)	Biceps brachii	Siemens Acuson S2000	SWE/velocity (m/s)	MAS, Fugl-Meyer score	SWV significantly faster in paretic muscle than in nonparetic muscle
Stroke versus healthy control							
Gao <i>et al.</i> , 2018 ^[19]	Stroke (n=12)	Healthy (n=16)	Biceps brachii	Siemens Acuson S3000	SWE/velocity (m/s)	MAS, TS, passive ROM	SWV significantly differed between spastic and healthy control. Strong negative correlation between SWV and passive ROM
Gao <i>et al.</i> , 2019 ^[20]	Stroke (n=7)	Healthy (n=8)	Biceps brachii	Siemens Acuson S3000	SE/strain ratio	MAS, TS, passive ROM	Significant differences of strain ratio between healthy and stroke group
Lee <i>et al.</i> , 2019 ^[22]	Stroke (n=14)	Healthy (n=8)	Biceps brachii	Aixplorer Supersonic Imagine	SWE/velocity (m/s)	Nil	SWV significantly higher in stroke patients than in control

Contd...

Table 1: Contd...

Reference	Study group	Control group	Muscle	US equipment	UE/unit	Clinical outcomes	Results
Stroke versus healthy control							
Le Sant <i>et al.</i> , 2019 ^[28]	Stroke (n=13)	Healthy (n=13)	Lower leg muscles†	Aixplorer Supersonic Imagine	SWE/kPa	MAS	Stroke survivors with higher shear modulus than controls in gastrocnemius and soleus, but not in other muscles

†Including gastrocnemius medialis/lateralis, soleus, flexor digitorum longus, flexor hallucis longus, peroneus longus, tibialis anterior and extensor digitorum longus. MAS: Modified Ashworth Scale, TS: Tardieu Scale, MTS: Modified TS, STREAM: Stroke Rehabilitation Assessment of Movement, SWV: Shear wave velocity, UE: Ultrasound elastography, SWE: Shear wave elastography, SE: Strain elastography, ROM: Range of motion

Table 2: The ultrasound elastography to evaluate therapeutic efficacy of botulinum toxin and other interventions

Reference	Study group	Control group	Muscle	US equipment	UE/unit	Clinical outcomes	Results
Botulinum toxin							
Aşkın <i>et al.</i> , 2017 ^[29]	Stroke affected side before and after BoNT-A injection (n=48)	N/A	Biceps brachii	Linear probe (Toshiba Aplio 500)	SE/strain index	MAS, passive ROM	Strain index significantly decreased at 4-week postinjection. No correlation with MAS
Gao <i>et al.</i> , 2019 ^[20]	Stroke affected side before and after BoNT-A injection (n=7)	N/A	Biceps brachii	Linear probe (Siemens Acuson S3000)	SE/strain ratio; SWE/SWV (m/s)	MAS TS	Strain ratio significantly increased, SWV significantly decreased 17–30 days' postinjection. Both ultrasound elasticity parameters correlated significantly with MAS and TS
Other interventions							
Yoldaş <i>et al.</i> , 2021 ^[30]	rESWT + CR (n=17) sham ESWT + CR (n=17)	CR only (n=17)	Gastrocnemius	Linear probe (GE Logiq S7)	SE/strain index	MAS TS	Strain index decreased in all three groups, but no between-group differences. MAS only decreased in the rESWT + CR group
Huang <i>et al.</i> , 2020 ^[31]	WBV group (n=36)	Non-WBV group (n=36)	Gastrocnemius soleus	Linear probe (SSI Aixplorer)	SWE/shear modulus (kPa)	N/A	No significant change of the shear modulus after WBV
Liu <i>et al.</i> , 2020 ^[27]	Stroke affected side before and after CR + ES (n=60)	N/A	Biceps brachii	Linear probe (GE Logiq E9)	SWE/SWV (m/s), Young's modulus	MAS	SWV significantly decreased after treatment

MAS: Modified Ashworth Scale, TS: Tardieu Scale, ROM: Range of motion, SWV: Shear wave velocity, ESWT: Extracorporeal shock therapy, rESWT: Radial ESWT, CR: Conventional rehabilitation, WBV: Whole body vibration, ES: Electrical stimulation, BoNT-A: Botulinum toxin A, N/A: Not available, SWE: Shear wave elastography, SE: Strain elastography, UE: Ultrasound elastography

index, or elasticity index varied across studies, depending on the algorithms for capturing images and calculating stiffness values in the different UE systems. Few studies tried to correlate muscle stiffness evaluated by CE to clinical outcomes, such as the MAS or MTS have shown weak to strong negative correlations, but the results were not congruent.^[14,15,29,41]

Reliability and validity of ultrasound elastography in poststroke spasticity

UE was applied to evaluate several muscles in healthy participants and proved good reliability as well as intraclass correlation coefficients (ICC).^[43] Several studies issued the inter-rater and intra-rater reliability of performing UE to

PSS. Only the reliability of gastrocnemius medialis on the paretic side revealed good with ICC of 0.86 and a coefficient of variation of 9.86% in measuring shear elastic modulus of gastrocnemius medialis and tibialis anterior on both paretic and nonparetic legs.^[21] Wu *et al.* showed good to excellent ICC of both intra- and inter-rater reliability for shear wave velocity (SWV) measurement in longitudinal and transverse axes parallel to the muscle fibers in the biceps muscle.^[16] Similarly, intra-observer reliability on the biceps SWE was reported to be excellent on the nonspastic side and good on the spastic side.^[29] Regarding validity, spastic SWV of the biceps revealed a positive correlation with MAS and/or

MTS.^[16,22] SWV of medial gastrocnemius was significantly correlated with ankle angle and joint torque.^[23] Systematic review documented UE as a reliable and valid tool to assess spasticity in patients with stroke, cerebral palsy, Duchenne muscular dystrophy, and Parkinson's disease.^[17] We believe UE has the potential to become a standard diagnostic tool for assessing PSS.

Ultrasound elastography for spasticity: Paretic versus nonparetic side

In this review, most of the included studies regarding the use of UE for PSS compared the stiffness of the paretic and nonparetic muscles. In general, the results suggested significantly increased muscle stiffness of the paretic side compared with the nonparetic side.^[14-16,19,22-26,39] However, Wu *et al.* reported slower SWV on the paretic muscle at 90° elbow flexion in patients with MAS of 0, which might be attributed to shorter stroke duration (<2 months) in this subgroup; therefore, more prominent flaccidity of the paretic side.^[16] The hardness of biceps brachii was assessed in one study utilizing SE^[19] and in six studies using SWE.^[16,19,22,25,26,39] Wu *et al.* found significantly greater SWV with increased elbow extension.^[12] Gao *et al.*^[19] demonstrated decreased strain ratio from 90° to 0° elbow flexion. Therefore, muscle stiffness may be influenced by different joint angles, and stretching the muscle may make the muscle stiffer. Leng *et al.* investigated the stiffness of flexor carpi radialis in stroke survivors and revealed significantly higher shear elastic modulus on the paretic side than that on the nonparetic side.^[24] In addition, increased wrist flexor stiffness was observed when the wrist was passively stretched from 0° palmar flexion to 50° extension. Yaşar *et al.* used SE to study forearm muscles and revealed that both elasticity index and elasticity ratio increased in the flexor carpi radialis, flexor carpi ulnaris, flexor digitorum superficialis, and flexor digitorum profundus on the affected side compared to the nonaffected side.^[14]

The stiffness of the gastrocnemius of the lower limb muscles was assessed in one study utilizing SE,^[15] while another two studies used SWE to evaluate the stiffness of gastrocnemius and tibialis anterior after stroke.^[21,23] All three studies showed increased muscle stiffness in the gastrocnemius on the impaired side compared to the healthy side. However, a different change was observed in the tibialis anterior,^[21,23] possibly implying that increased spasticity occurred more likely in gastrocnemius after stroke. Jakubowski *et al.* reported that SWV of the medial head of gastrocnemius became faster when the ankle was passively moved from plantar flexion to dorsiflexion, regarding the impact of different joint angles on muscle stiffness.^[23]

Ultrasound elastography for spasticity: Stroke versus healthy control

This review included four studies regarding the comparison of stiffness of spastic biceps brachii in patients with stroke and healthy control,^[16,19] while another study by Le Sant *et al.* investigated the stiffness of lower leg muscles.^[28] All five studies demonstrated increased muscle stiffness in stroke

survivors compared with the control subjects. Notably, the higher shear modulus was only observed in the gastrocnemius and soleus but not in other muscles (flexor digitorum longus, flexor hallucis longus, peroneus longus, tibialis anterior, and extensor digitorum longus),^[28] possibly suggesting that spasticity was more likely to develop in plantar flexors following stroke.

Ultrasound elastography to assess effectiveness of botulinum toxin injection

BoTx Type-A (BoNT-A) injection has been one of the most commonly used anti-spasticity therapy with well-established efficacy for patients with chronic stroke. The review included three studies regarding UE utilization to evaluate changes in muscle stiffness following BoNT-A injections. Aşkın *et al.* conducted a prospective study assessing the sonoelastographic changes of the biceps brachii using SE before and after BoNT-A injections in 48 chronic stroke survivors.^[29] The results showed a significantly decreased strain ratio at 4 weeks after ultrasound-guided BoNT-A injections. Another research by Gao *et al.* included seven patients with stroke who underwent electromyography-guided injections of BoNT-A to affected biceps brachii muscles and used both SE and SWE to investigate changes in muscle hardness between 17 and 30 days after BoNT-A administration.^[20] They revealed a significantly increased axial strain ratio and markedly reduced SWV, which implied softening of spastic biceps brachii after BoNT-A injections. Notably, the ultrasound elasticity parameters in this study were significantly correlated with the clinical assessment scales (MAS and MTS).

In summary, UE can be regarded as a useful tool to objectively monitor the treatment response of BoTx injection and determine further treatment dosages or targeted muscles because significant differences in ultrasound elasticity parameters were observed before and after BoTx injection.

Ultrasound elastography to assess efficacy of other interventions

ESWT has been described as a potentially effective intervention for reducing PSS in recent years. A 2020 systematic review and meta-analysis demonstrated promising effects of ESWT in improving upper limb spasticity in stroke survivors for >12 weeks.^[44] ESWT seemed to be effective in decreasing poststroke lower limb spasticity based on another meta-analysis.^[45] The RCT by Yoldaş Aslan *et al.* allocated 51 patients with stroke having ankle flexor spasticity into three groups, where the activity therapy group received two sessions of radial ESWT plus a conventional rehabilitation program, while the sham group received sham ESWT twice a week for 2 weeks plus conventional rehabilitation, and the control group received only conventional rehabilitation.^[30] The stiffness of the gastrocnemius muscle was measured using UE (strain index) immediately before, after the 2-week therapy, and 4 weeks later. The results revealed a significantly decreased MAS score only in the active therapy group after the 2-week therapy. However, all three groups had a significant

decrease in strain index immediately after treatment and in 4 weeks, without differences between groups. Therefore, the authors attributed the decreased strain index to the conventional rehabilitation program received by all groups.

Huang *et al.* recruited a total of 36 patients with chronic stroke to investigate the effect of whole-body vibration on the shear modulus in the medial gastrocnemius muscle.^[31] The results showed no significant changes in shear modulus after the whole-body vibration.

As for conventional rehabilitation plus electrical stimulation, Liu *et al.* recruited 60 stroke survivors with upper limb spasms receiving routine rehabilitation treatment of 45 min a day (including functional electrical stimulation to triceps brachii, deltoid, and deltoid muscles for 30 min/session).^[27] After the total treatment duration of 6 weeks, both SWV and Young's modulus significantly decreased in the affected biceps brachii. In comparison, no significant differences were found in both parameters in the unaffected biceps brachii before and after rehabilitation treatment.

Limitations of ultrasound elastography for poststroke spasticity

This review had several limitations. First, the number of patients enrolled in the evaluated studies is small. Second, there are markedly different study designs and research protocols, such as body position, joint angle, ultrasound machine, probe, and active contraction or passive state targeted muscle. Third, the ultrasound technique is highly operator dependent; the unequally applied transducer pressure would result in altered ultrasound elasticity parameters for both SE and SWE. Therefore, the operator's level of experience in performing elastography can influence the result. Lack of replicability due to difficulty controlling the transducer pressure remains a major limitation in UE. Furthermore, the examiners cannot be blinded to the paretic and nonparetic sides because of the visually apparent appearance.^[12] Taken together, UE is a promising tool for assessing muscle stiffness in patients poststroke. However, further studies with more robust study designs and larger sample sizes are needed to determine the optimal protocol.

CONCLUSION

This narrative review revealed the good to excellent reliability of UE which was validated with correlation to clinical assessment tools for PSS evaluation. The utility of UE is to detect the difference between the paretic and nonparetic sides of PSS, as well as patients with versus healthy controls. UE serves as a good measurement to monitor the treatment response and efficacy of targeted muscles. However, limitations, including diverse study designs, operator dependence, and lack of replicability, remained. Therefore, future high-quality studies are warranted to better explore the role of UE in the spasticity assessment.

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Conflicts of interest

There are no conflicts of interest.

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