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Extracorporeal Shock Wave Therapy on Spasticity After Upper Motor Neuron Injury

A Systematic Review and Meta-analysis

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Objective: The aim of the study was to evaluate the effectiveness and safety of extracorporeal shock wave therapy on spasticity after upper motor neuron injury.

Design: Eight electronic databases were searched systematically from their inception to August 3, 2021, to provide robust evidence for the efficacy of extracorporeal shock wave therapy for spasticity and range of motion after upper motor neuron injury. Study screening, data extraction, risk of bias assessment, and evaluation of the certainty of evidence were performed independently by two independent reviewers. Data analysis was conducted using RevMan 5.3.5 and R 3.6.1 software.

Results: Forty-two studies with 1973 patients who met the eligibility criteria were selected from articles published from 2010 to 2021, of which 34 were included in the meta-analysis. A comparison intervention revealed that extracorporeal shock wave therapy significantly decreased the Modified Ashworth Scale score and increased the passive range of motion of a joint. Regarding the safety of extracorporeal shock wave therapy, slightly adverse effects, such as skin injury, bone distortion, muscle numbness, pain, petechiae, and weakness, were reported in five studies.

Conclusions: Extracorporeal shock wave therapy may be an effective and safe treatment for spasticity after upper motor neuron injury. However, because of poor methodological qualities of the included studies and high heterogeneity, this conclusion warrants further investigation.

Key Words: Extracorporeal Shock Wave Therapy, Muscle Spasticity, Upper Motor Neuron Injury, Systematic Review, Meta-analysis

What Is Known

- Spasticity, a common motor impairment after upper motor neuron injury, affects patients' motor recovery and presents challenges for researchers and clinicians.
- Extracorporeal shock wave therapy is a potential therapy for ameliorating spasticity.

What Is New

- Extracorporeal shock wave therapy is relatively effective for improving the Modified Ashworth Scale score and the passive range of motion of joint of spastic patients after upper motor neuron injury.
- The effect of extracorporeal shock wave therapy is better with higher pressure, frequency, or energy flux density.

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Spasticity is a motor disorder characterized by a velocity-dependent increase in muscle tone with an exaggerated tendon jerk resulting from hyperexcitability of the stretch reflex, as first defined by Lance in 1980.[1,2] This dysregulation of motor

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CME Objectives: Upon completion of this article, the reader should be able to: (1) Determine the impact of extracorporeal shock wave therapy on spasticity after upper motor neuron injury; (2) Describe the factors that affect the efficacy of extracorporeal shock wave therapy on spasticity; and (3) Discuss the mechanism of action of extracorporeal shock wave therapy on spasticity.

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tone and muscle activation occurs as a result of damage to inhibitory upper motor neurons (UMNs).[3] The cause of UMN injury includes cerebral palsy (CP), stroke, multiple sclerosis (MS), and spinal cord injury (SCI). The estimated prevalence of spasticity in CP is 1.78 per 1000 patients, and most (69.8%) children with CP experience spasticity.[4] For stroke survivors, the prevalence of spasticity ranges from 30% to 80%.[5] In addition, spasticity is experienced in 52.5% of individuals with MS[6] and 86.5% with chronic SCI.[7] Spasticity is associated with pain, weakness, joint stiffness, and/or contracture, which may exacerbate spasticity.[8,9] In addition, spasticity can lead to gait disorders, falls, fatigue, and sleep disturbance and may prolong the time to wheelchair dependence, which may increase disability and dependence and cause social isolation and depression.[10] Furthermore, several studies found that spasticity was associated with a worse quality of life[11–13] and greater cost.[13,14]

There are various interventions for managing spasticity after UMN injury, such as botulinum toxin injections,[15] oral antispastic drugs,[16] and chemical nerve blocks.[17] However, management of spasticity remains difficult because of the considerable adverse effects of these treatments. For example, repetitive injections of the botulinum toxin may stimulate the formation of neutralizing antibodies,[18] which can cause failure during secondary treatment[19]; antispastic drugs may reduce the force of normal muscles, which can result in sedation and drowsiness; the effects of antispastic drugs may decrease with prolonged use[20]; nerve blocks often cause skin sensory loss and dysesthesia; and the procedure is time consuming and requires specialized expertise.[21] Therefore, it is urgent to find an effective and safe therapy that alleviates spasticity and promotes rehabilitation.

Extracorporeal shock wave (ESW) is defined as a sequence of single acoustic pulses characterized by a high peak of pressure, fast pressure rise, short time of duration, and rapid propagation in three-dimensional space.[22] There are two types of ESW generators: focused ESW (fESW) and radial ESW (rESW), which differ in shock wave propagation and physical characteristics of energy.[23] Focused ESW is generated by electromagnetic, electrohydraulic, and piezoelectric sources. It can increase pressure rapidly, which means it is more invasive, with the highest energy exposure occurring in the focal area of deep zones. Radial ESW is a low- to medium-energy type of shock wave produced by pneumatic devices located inside a generator. The depth of penetration of rESW is lower than that of fESW (up to 3 vs. 12 cm), which means it is less invasive and is better tolerated.[24–26] It was reported that ESW therapy (ESWT) alleviated spasticity in stroke,[27] MS,[28] and CP.[25] Some studies have reported that both types of ESW alleviate spasticity.[26] Previous systematic reviews[29–34] also suggested that ESWT might ameliorate spasticity. However, four systematic reviews[29,30,32,33] focused on poststroke patients, and one[31] focused on children with CP. A study by Martínez et al.[34] was the only narrative review of ESWT for spasticity. Recently, several clinical trials of the effects of ESWT on spasticity after UMN injury were conducted. Thus, we conducted this systematic review and meta-analysis to comprehensively investigate the effectiveness and safety of ESWT for treating spasticity after UMN injury and to provide robust evidence for the efficacy of ESWT for spasticity after UMN injury.

METHODS

Study Registration

The protocol of this systematic review was registered in PROSPERO (http://www.crd.york.ac.uk/PROSPERO) and was published in advance.[35] The registration number is CRD42019131059. This systematic review was conducted based on A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2.0)[36] and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020) statement guidelines.[37] The completed PRISMA 2020 checklist is shown in Supplementary File 1 (Supplemental Digital Content 1, http://links.lww.com/PHM/B533).

Inclusion Criteria

Type of Studies

Randomized controlled trials (RCTs) of the effects of ESWT on spasticity after UMN injury published in Chinese or English.

Type of Participants

Participants with spasticity after UMN injury (stroke, CP, MS, etc.). There were no restrictions on age, sex, race, or nation.

Type of Interventions

The types of interventions are (1) ESWT and (2) ESWT in combination with conventional rehabilitation training (physiotherapy, occupational therapy, orthotics, etc.). There was no limitation on the parameters of ESWT.

Type of Comparators

The types of comparators are (1) sham ESWT stimulation and (2) conventional rehabilitation training, which was consistent with the intervention group.

Outcome Measurements

The primary outcome was the Modified Ashworth Scale (MAS). Secondary outcomes included the Composite Spasticity Scale (CSS), Modified Tardieu Scale, ratio of maximum H-reflex to maximum M response (H_{max}/M_{max} ratio), integrated electromyogram, H-reflex latency, surface electromyography, co-contraction ratio, passive range of motion (PROM), and mechanical properties of muscles (tone, stiffness, and elasticity). Adverse events (pain, petechiae, numbness, etc.) were assessed as a safety measurement.

Exclusion Criteria

Exclusion criteria included: (1) cross-over RCTs, cluster RCTs, *n* of 1 RCTs, factorial RCTs; (2) ESWT combined with other active treatments (botulinum toxin A injections, baclofen, acupuncture, etc.); (3) duplicate publications; and (4) full text could not be obtained.

Search Strategy

We searched the China National Knowledge Infrastructure, China Science and Technology Journal Database, Wanfang Database, China Biology Medicine, PubMed, Embase, Cochrane Library, and Web of Science systematically

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from their inception to August 3, 2021, to obtain RCTs that studied the efficacy of ESWT for spasticity after UMN injury. The following key search terms were used: "extracorporeal shock wave therapy" and "muscle spasticity." The full search strategies, which were tailored according to the characteristic of the databases mentioned previously, are listed in Supplementary File 2 (Supplemental Digital Content 2, http://links.lww.com/PHM/B534). We then manually searched the gray literature, reference lists of identified studies, Chinese Clinical Trial Registry, and ClinicalTrials.gov for eligible RCTs.

Selection of Studies

Two reviewers (H-LZ, D-LZ) independently identified eligible studies according to inclusion and exclusion criteria. After removing duplicates, primary selection was performed based on titles and abstracts. Then, full texts were thoroughly reviewed according to eligible criteria. Disagreements were resolved by consensus, and the reasons for excluding studies were recorded.

Data Extraction

We piloted the data extraction form on the bases of a sample of eligible studies and calculated the κ coefficient for examination consistency. Two reviewers (LG, Y-XL) independently extracted the following data: study characteristics (first author, publication year, and country); participant characteristics (sample size, sex, and type of UMN injury); results (main conclusions, results of interested outcomes, adverse events, and duration of follow-up); key elements of risk assessment of bias; and sources of funding. A cross-check was performed to ensure no mistakes. Discrepancies were resolved through a team discussion.

Risk of Bias Assessment

To reach at least 80% consistency in the risk of bias assessments, a sample of eligible studies was preassessed, and the results and an evaluation of the κ value were discussed among reviewers. Two reviewers independently (X-BL, Q-WX) used the revised Cochrane risk of bias tool for individually randomized, parallel group trials (RoB2.0) to assess the risk of bias of each included study.[38] Disagreements were arbitrated by a third reviewer (JL).

Data Analysis

The level of agreement between reviewers was determined by Cohen κ coefficient test and was performed using Statistical Package for the Social Sciences (version 13.0) software. Data analysis was conducted using Review Manager software (RevMan, version 5.3.5) and R (version 3.6.1) software. The relative risk was estimated to analyze dichotomous outcomes. The mean difference was used to analyze continuous outcomes with the same unit; otherwise, the standardized mean difference was used. We presented results as an effect size with 95% confidence intervals (CIs). We defined $P \leq 0.05$ as showing statistical significance between studies. Statistical heterogeneity was assessed by both Cochran χ^2 test (Q test) and an I^2 test. A fixed-effect model was used with acceptable heterogeneity ($I^2 \leq 50\%$, $P \geq 0.1$), and we used a random-effect model for significant statistical heterogeneity ($I^2 > 50\%$, $P < 0.1$). We narratively described the results if outcomes could not be quantitatively analyzed.

A subgroup analysis was carried out to investigate potential heterogeneity based on types of UMN injury (stroke, CP, MS, and SCI); types of ESWT (rESWT and fESWT); application site of ESWT (upper limb and lower limb); pressure of ESWT (<2, 2–3, >3 bar); energy flux density (EFD) of ESWT (<0.1, ≥0.1 mJ/mm^2); frequency of ESWT (≤5, 6–8, >8 Hz); dosage of ESWT (<2000, ≥2000 shocks); total sessions of ESWT (1, 2–8, ≥9 sessions); and follow-up (immediately, ≤1 wk, 1 wk to 1 mo, >1 mo).

We performed sensitivity analysis by excluding the included studies one by one to verify the robustness and reliability of the pooled results. We conducted funnel plots to explore the likelihood of publication bias if the outcomes of included studies were greater than 10. Moreover, Begg's test and Egger's test were used to assess publication bias quantitatively.

Grading of Recommendations Assessment, Development, and Evaluation

To ensure satisfactory consistency in our certainty of evidence assessment, we preassessed a sample of outcomes and evaluated the κ value. Two independent reviewers (X-LX, R-JJ) used a Grading of Recommendations Assessment, Development, and Evaluation system to assess the certainty of evidence. Each outcome was evaluated from the following five aspects: limitations, inconsistency, indirectness, imprecision, and publication bias.[39] The certainty of evidence was graded as "high," "moderate," "low," or "very low."[40]

RESULT

Eligible Studies and Characteristics

The literature search yielded 1922 references, of which 790 duplicates were excluded. After screening titles and abstracts preliminarily, 1060 studies were excluded. For the remaining articles, we scrutinized the full texts, and 30 were excluded. Eventually, 42 studies satisfied the eligibility criteria,[28,41–81] and 34 studies were included in the meta-analysis.[28,41–43,45–47,49,51–55,58–66,68,70–76,78–81] A flow diagram of the selection process was presented in Supplementary Figure 1 (Supplemental Digital Content 3, http://links.lww.com/PHM/B535). The reasons for exclusion of studies are listed in Supplementary File 3 (Supplemental Digital Content 4, http://links.lww.com/PHM/B536).

The sample size of included studies ranged from 12 to 96. The population of total studies included 1973 spastic patients. Of the 42 studies published from 2010 to 2021, 16[28,41–55] were published in English and 26[56–81] in Chinese. One study[28] was about MS, one study[66] was related to SCI, 11 studies[41,43,44,49,54,57,61,72,73,76,78] focused on CP, and 29 studies[42,45–48,50–53,55,56,58–60,62–65,67–71,74,75,77,79–81] involved stroke. In addition, one article[68] reported two trials; one of the trials focused on upper limb, whereas the other focused on the lower limb. The two trials had different outcomes; thus, we extracted the data separately. The basic characteristics of the included studies are listed in Supplementary Table 1 (Supplemental Digital Content 5, http://links.lww.com/PHM/B537).

Risk of Bias Assessment

The κ values for the independent assessments of each item in the RoB2.0 ranged from 0.65 to 0.81, which indicated good

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consistency. The risk of bias of the included studies is presented in Table 1. Thirty-three RCTs[28,42,43,45–49,51,54–58,60–64,66,68–80] reported an adequate random sequence generation process. Allocation concealment was only described in six studies.[46,54,55,62,68,80] Thirty-seven studies[28,42,43,45–52,54–60,62–66,68–81] reported that there were no statistically significant differences between groups at the baseline. Twenty-three studies[28,42–48,50,51,54–56,58,62–64,66–68,70,71,74] adopted a blinding design, among which four studies[42,50,51,54] performed blinding of patients only, 13 studies[43–45,47,56,58,63,64,66,67,70,71,74] adopted blinding of outcome assessors only, and six studies[28,46,48,55,62,68] performed blinding of both patients and outcome assessors. Moreover, only four studies[46–48,55] provided a clinical trial registration number. In summary, 22 studies[41–43,48,49,51–54,59–61,65,67,69,72,73,75–78,81] were rated as having a "high risk of bias," and 20 studies[28,44–47,50,55–58,62–64,66,68,70,71,74,79,80] were rated as having "some concerns."

TABLE 1. ROB 2.0 assessment results of the included studies

Study	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall
S1[28]	Some	Low	Low	Low	Some	Some
S2[41]	Some	High	High	Low	Some	High
S3[42]	Some	Some	Low	High	Some	High
S4[43]	Some	High	High	Low	Some	High
S5[44]	Some	Some	Low	Low	Some	Some
S6[45]	Some	Some	Low	Low	Some	Some
S7[46]	Low	Some	Low	Low	Some	Some
S8[47]	Some	Some	Low	Low	Some	Some
S9[48]	Some	Low	Low	Low	High	High
S10[49]	Some	Some	Low	High	Some	High
S11[50]	Some	Some	Low	Low	Some	Some
S12[51]	Some	High	High	High	Some	High
S13[52]	Some	High	High	High	Some	High
S14[53]	Some	High	High	High	Some	High
S15[54]	Low	High	High	High	Some	High
S16[55]	Low	Some	Low	Low	Some	Some
S17[56]	Some	Some	Low	Low	Some	Some
S18[57]	Some	Some	Low	Low	Some	Some
S19[58]	Some	Some	Low	Low	Some	Some
S20[59]	Some	Some	Low	High	Some	High
S21[60]	Some	Some	Low	High	Some	High
S22[61]	Some	Some	Low	High	Some	High
S23[62]	Low	Some	Low	Low	Some	Some
S24[63]	Some	Some	Low	Low	Some	Some
S25[64]	Some	Some	Low	Low	Some	Some
S26[65]	Some	Some	Low	High	Some	High
S27[66]	Some	Some	Low	Low	Some	Some
S28[67]	Some	High	High	Low	Some	High
S29[68]	Low	Some	Low	Low	Some	Some
S30[69]	Some	Some	Low	High	Some	High
S31[70]	Some	Low	Low	Low	Some	Some
S32[71]	Some	Some	Low	Low	Some	Some
S33[72]	Some	Some	Low	High	Some	High
S34[73]	Some	Some	Low	High	Some	High
S35[74]	Some	Some	Low	Low	Some	Some
S36[75]	Some	Some	Low	High	Some	High
S37[76]	Some	Some	Low	High	Some	High
S38[77]	Some	Some	Low	High	Some	High
S39[78]	Some	Some	Low	High	Some	High
S40[79]	Some	Some	Low	Some	Some	Some
S41[80]	Low	Some	Low	Some	Some	Some
S42[81]	Some	Some	Low	High	Some	High

Domain 1, risk of bias arising from the randomization process; domain 2, risk of bias due to deviations from the intended interventions (effect of assignment to intervention); domain 3, risk of bias due to missing outcome data; domain 4, risk of bias in measurement of the outcome; domain 5, risk of bias in selection of the reported result; high, high risk of basis; low, low risk of basis; ROB 2.0, version 2 of the Cochrane risk-of-bias tool; S, study; some, some concerns.

Primary Outcome

A total of 35 studies[28,42–49,51–56,58–62,65,66,68–78,80,81] reported the MAS; however, the data of MAS from nine articles[44,47,48,56,59,69–71,77] could not be synthesized. Two studies[44,48] only presented the baseline of MAS scores and difference of MAS scores before and after treatment. The other two studies[47,59] provided dichotomous outcomes of MAS. Five studies[56,69–71,77] solely provided the number of patients of each level of the MAS before and after treatment. The results of these studies showed that the ESWT could decrease the MAS when compared with the control group ($P < 0.05$), in stroke patients[47,48,56,59,69–71,77] and in children with CP.[44] Pooled data of the 26 RCTs[28,42,43,45,46,49,51–55,58,60–62,65,66,68,72–76,78,80,81] showed that ESWT significantly decreased the MAS score (standardized mean difference = −0.97, 95% CI = −1.23 to −0.71, $I^2 = 77\%$, $P < 0.00001$; Supplementary Fig. 2, Supplemental Digital Content 6, http://links.lww.com/PHM/B538).

Results of subgroup analyses for MAS are summarized in Table 2. Different types of UMN injury or ESWT, the EFD of ESWT, frequency of ESWT, and total sessions of ESWT seemed to be potential sources of heterogeneity. Extracorporeal shock wave therapy lowered the MAS score more in children with CP than in survivors of stroke. In addition, rESWT was superior to fESWT in relieving spasticity. Furthermore, higher pressure or frequency of ESWT showed a better antispasmodic effect, and the effect of ESWT was sustained for a month after treatment, according to the subgroup analyses of the follow-up period. However, the results of the subgroup analyses based on the total sessions of ESWT or EFD of ESWT demonstrated that the single session of ESWT and the EFD of ESWT of 0.1 mJ/mm^2 or greater showed no significant difference in the MAS score compared with the control group. No significant differences were found in application sites, or dosages of ESWT. We performed sensitivity analysis by excluding the included studies one by one, and there was no substantial modification of the MAS score or heterogeneity.

Secondary Outcomes

The pooled data of secondary outcomes are shown in Table 3. There were statistically significant differences in the CSS, PROM, and H-reflex latency between ESWT and the control group. Except for PROM, the results of CSS and H-reflex latency were altered during sensitivity analysis, which might be caused by a small number of included studies and high heterogeneity.

We narratively described these results, which could not be synthesized. Dymarek et al.[42] concluded that ESWT could decrease the activity of surface electromyography in spastic muscles. Park et al.[50] and Sairong[77] confirmed that ESWT was

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TABLE 2. Subgroup analyses of the MAS

	MAS			
	n	Effect Size (95% CI)	*P*	I^2
Type of UMN injury				
Stroke	16	−0.79 (−1.15 to −0.44)	<0.0001	78%
CP	8	−1.26 (−1.53 to −0.99)	<0.00001	29%
MS	1	−0.54 (−1.02 to −0.06)	0.03	—
SCI	1	−0.44 (−0.55 to −0.33)	<0.00001	—
Type of ESWT				
rESWT	15	−1.07 (−1.40 to −0.75)	<0.00001	74%
fESWT	6	−0.39 (−0.70 to −0.08)	0.01	30%
Application site of ESWT				
Upper limb	10	−0.71 (−1.12 to −0.29)	0.0008	75%
Lower limb	16	−0.98 (−1.29 to −0.67)	<0.00001	73%
Pressure of ESWT, bar				
<2	8	−0.79 (−1.15 to −0.43)	<0.0001	63%
2–3	11	−1.39 (−1.68 to −1.09)	<0.00001	53%
>3	1	−2.10 (−2.25 to −1.95)	<0.00001	—
Energy flux density of ESWT, mJ/mm^2				
<0.1	4	−0.41 (−0.71 to −0.10)	0.009	49%
≥0.1	4	−0.63 (−1.28 to 0.02)	0.06	62%
Frequency of ESWT, Hz				
≤5	9	−0.55 (−0.94 to −0.16)	0.005	65%
6–8	9	−1.07 (−1.53 to −0.60)	<0.00001	78%
>8	6	−1.25 (−1.57 to −0.92)	<0.00001	42%
Dosage of ESWT, shock				
<2000	11	−1.15 (−1.78 to −0.53)	0.0003	87%
≥2000	17	−1.20 (−1.57 to −0.83)	<0.00001	83%
Total sessions of ESWT, session				
1	4	−0.03 (−0.33 to 0.27)	0.82	0%
2–8	15	−1.09 (−1.47 to −0.71)	<0.00001	79%
≥9	8	−1.05 (−1.42 to −0.67)	<0.00001	64%
Follow-up				
Immediately	18	−1.05 (−1.33 to −0.77)	<0.00001	68%
≤1 wk	7	−0.85 (−1.64 to −0.06)	0.04	89%
1 wk to 1 mo	8	−0.83 (−1.43 to −0.24)	0.006	88%
>1 mo	3	−1.18 (−2.27 to −0.08)	0.04	88%

effective in improving the mechanical properties of muscles in spastic patients after stroke. Furthermore, ESWT could immediately improve the foot dorsiflexion angle of spastic children with CP.[57] Xiyu[67] reported that ESWT decreased the integrated electromyogram and co-contraction ratio of pectoralis major in stroke patients. Siwei et al.[70] also revealed that ESWT could inhibit the co-contraction of biceps brachii and improve the motor function of the upper limb.

Publication Bias

The results of the funnel plot analysis of MAS scores is shown in Supplementary Figure 3 (Supplemental Digital Content 7, http://links.lww.com/PHM/B539). Egger's test ($P = 0.4789$) and Begg's test ($P = 0.3777$) did not detect publication bias.

Safety

Among 42 included RCTs, 15 studies[28,42,45,48,54,56,58–60,62,71,73,74,79,80] reported that no adverse effects occurred in ESWT groups. Five studies[55,61,63,64,68] reported slightly adverse effects, such as skin injury, bone distortion, muscle numbness, pain, petechiae, and weakness.

Certainty of Evidence

The κ values for independent assessments of each item in the Grading of Recommendations Assessment, Development, and Evaluation ranged from 0.63 to 0.85. Certainty of evidence was high in PROM, moderate in the H_{max}/M_{max} ratio, and low or very low in other outcomes. Of the five downgrading factors, inconsistency was the most common downgrading factor, followed by imprecision, publication bias, and risk of bias (Table 4).

DISCUSSION

Summary of Findings

Our systematic review included 42 RCTs of the effects of ESWT on spasticity, with a total of 1973 participants; the results demonstrated that ESWT could significantly relieve spasticity after UMN injury. Subgroup analyses of MAS suggested that children with CP benefited more from ESWT. The efficacy of rESWT was superior to fESWT. Higher pressure or frequency of ESWT had a better antispasmodic effect. The effect of ESWT was sustained for a month after treatment. However, the results of subgroup analyses based on total sessions of ESWT or EFD of ESWT demonstrated that a single session of ESWT and the EFD of ESWT of 0.1 mJ/mm^2 or greater had no significant difference in the MAS score compared with the control group. For secondary outcomes, ESWT could increase the PROM of the joint and H-reflex latency as well as decrease the CSS score. Furthermore, ESWT could decrease the activity of the surface electromyography, integrated electromyogram,

TABLE 3. Meta-analysis of other outcomes

Outcomes	No. Studies	I^2	*P*	MD	95% CI	*P*
H_{max}/M_{max} ratio	5	89%	<0.00001	−0.14	−0.30 to 0.03	0.11
CSS	4	73%	0.01	−1.98	−3.21 to −0.74	0.002
iEMG	2	80%	0.03	−107.79	−410.47 to 194.89	0.49
PROM	7	0%	0.87	1.96	1.28 to 2.63	<0.00001
MTS	4	94%	<0.00001	2.04	−18.17 to 22.24	0.84
H-reflex latency	2	0%	0.77	3.24	1.94 to 4.53	<0.00001

iEMG, integrated electromyogram; MD, mean difference; MTS, Modified Tardieu Scale.

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TABLE 4. Results of the GRADE

Quality Assessment							No. Patients		Effect			
No. Studies	Design	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Experimental	Control	Relative (95% CI)	Absolute	Quality	Importance
MAS												
26	Randomized trials	Serious[a]	Serious[b]	Not serious	Not serious	None	602	586	—	SMD = 0.97 lower (1.23 to 0.71 lower)	⊕⊕OO LOW	CRITICAL
H_{max}/M_{max} ratio												
5	Randomized trials	Not serious	Serious[b]	Not serious	Not serious	None	115	115	—	MD = 0.14 lower (0.3 lower to 0.03 higher)	⊕⊕⊕O MODERATE	IMPORTANT
CSS												
4	Randomized trials	Not serious	Serious[b]	Not serious	Serious[c]	Reporting bias[d]	102	102	—	MD = 1.98 lower (3.21 to 0.74 lower)	⊕OOO VERY LOW	IMPORTANT
iEMS												
2	Randomized trials	Not serious	Serious[b]	Not serious	Serious[c]	None	16	16	—	MD = 107.79 lower (410.47 lower to 194.89 higher)	⊕⊕OO LOW	IMPORTANT
PROM												
7	Randomized trials	Not serious	Not serious	Not serious	Not serious	None	163	163	—	MD = 1.96 higher (1.28 to 2.63 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
MTS												
4	Randomized trials	Not serious	Serious[b]	Not serious	Serious[c]	None	86	69	—	MD = 2.04 higher (18.17 lower to 22.24 higher)	⊕⊕OO LOW	IMPORTANT
H-reflex latency												
2	Randomized trials	Not serious	Not serious	Not serious	Serious[c]	Reporting bias[d]	60	60	—	MD = 3.24 higher (1.94 to 4.53 higher)	⊕⊕OO LOW	IMPORTANT

[a] The evidence came from studies with a high risk of bias.

[b] I^2 value of the combined results was large, and high heterogeneity.

[c] The confidence intervals were wide or not match the optimal information size.

[d] There was a suspicion of publishing bias.

GRADE, Grading of recommendations assessment, development, and evaluation; iEMG, integrated electromyogram; MTS, Modified Tardieu Scale; SMD, standardized mean difference.

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and co-contraction ratio in spastic muscles, as well as improve the mechanical properties of muscle in stroke patients and the foot dorsiflexion angle of spastic children with CP. Several studies reported a few slightly adverse effects.

IMPLICATIONS FOR FUTURE STUDY

Assessment Methods for Spasticity

The MAS is the most widely used clinical scale for assessing the degree of spasticity.[82] However, the MAS relies on the interpretation of the assessor, which may induce measurement bias,[83] especially when outcome assessors are not blinded. Recently, objective indicators have been applied to assess spasticity in clinical practice, such as the H_{max}/M_{max} ratio, integrated electromyogram, H-reflex latency, surface electromyography, and co-contraction ratio. These indicators can be used to quantify spasticity more accurately, which will thus obtain more objective data.[83] Therefore, it is crucial to assess spasticity with objective indicators.

Extracorporeal Shock Wave Therapy for Spasticity in Different Types of UMN Injury and Application Sites

In our study, the results indicated that ESWT could lower the MAS score more in children with CP than in survivors of stroke. Stroke is more common in elderly populations, whereas CP is more common in children; therefore, age may be a factor contributing to the different therapeutic effects of ESWT. This study did not find a significant difference in the MAS score regarding the application site of ESWT (upper limb or lower limb). On the bases of these findings, ESWT has similar efficacy on muscles of limbs with spasticity, which is consistent with the conclusion of a previous study.[2]

Optimal Parameters of ESWT for Spasticity

Currently, the optimal parameters for ESWT for treating spasticity remain unclear. We performed a subgroup analysis on different protocols of ESWT. We noticed that rESWT had a better effect on spasticity reduction than fESWT, which was in accordance with the results of a previous study.[84] A possible explanation is that rESWT is characterized by a broader therapeutic area and higher energy in superficial tissue in contrast to fESWT. Hence, rESWT might affect the mechanical properties of the whole muscle belly rather than a small spot in the muscle.[85] In clinical practice, therapists prefer to use rESWT, because it is less invasive, much cheaper, and more convenient to operate than fESWT. Furthermore, we found that ESWT was more effective when applied with higher pressure or greater frequency. One possible explanation might be that higher pressure or higher frequency creates more energy, which enhances the effect of ESWT. Regarding the EFD of ESWT, there was a tendency that a higher EFD had a better effect on relieving spasticity. No dramatic difference in improving spasticity was found in the dosage of ESWT among subgroups in this study. Compared with the control group, a single session of ESWT showed no significant difference in the MAS score, although it was more effective in multiple ESWTs. However, the effect of ESWT was not enhanced with increased sessions, which may be because more treatments are often associated with the development of ESWT tolerance. Despite this, the dose-response relationship of different stimulation parameters of ESWT remains uncertain because of high heterogeneity and limited studies; therefore, further studies are needed to address the dose-response relationship of different parameters of ESWT for spasticity after UMN injury.

Our result showed that the effect of ESWT was sustained for a month after treatment, which was consistent with other meta-analyses.[30,86] Moon et al.[87] revealed that increasing the intensity of stimulation energy or conducting ESWT again within 4 wks after treatment might be helpful for maintaining the effect of ESWT on spasticity. Furthermore, the mechanisms of shock wave generation, energy per unit area, sessions of ESWT treatment, applied site, and course of disease have been shown to affect the duration of efficacy of ESWT.[87] Thus, further research is needed to determine how to maximize the duration of efficacy of ESWT.

The Mechanism of Action of ESWT on Spasticity

Many studies demonstrated that increasing spinal excitability was associated with spasticity[88] and reported that the H_{max}/M_{max} ratio and latency of the H-reflex were indicators of spinal cord excitability. However, whether ESWT relieves spasticity by reducing spinal cord excitability is still in dispute. Some studies found that ESWT did not affect spinal cord excitability with decreased MAS grades,[28,89,90] whereas others[91,92] revealed a reduction of the H_{max}/M_{max} ratio after ESWT, thus indicating a change in α motor neuron excitability. We found that ESWT lengthened H-reflex latency, although there was no significant difference in the H_{max}/M_{max} ratio after ESWT. A hypothesis on spinal cord excitability needs to be studied in the future.

With this systematic review, we found that ESWT could improve PROM and the mechanical properties of muscles (stiffness, tone, and elasticity), which might be related to the direct effect of shock waves on the rheological properties of hypertonic muscles. Previous researches[89,93,94] drew the same conclusion as ours. Hence, the mechanism of ESWT for spasticity may be associated with the rheological properties of the spastic muscle.

Strengths and Limitations

As far as we know, this is the latest systematic review of ESWT for spasticity after UMN injury. We registered our review on the PROSPERO register of systematic reviews and published the protocol in advance.[36] In addition, this systematic review was conducted and reported strictly following the AMSTAR 2.0 and PRISMA 2020 statement guidelines. Furthermore, we comprehensively evaluated the effectiveness and safety of ESWT for treating spasticity on the basis of different subgroups, which may help establish the optimal parameters of ESWT for treating spasticity after UMN injury. However, we acknowledged some limitations of this study. First, the risk of bias of included trials was either high, or there were some concerns. Second, we only included studies published in Chinese and English; therefore, language bias may exist. Furthermore, because of the particularity of treatment, intervention providers could not be blinded.

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CONCLUSIONS

Extracorporeal shock wave therapy is recommended as an effective and safe treatment for spasticity after UMN injury. However, because of the poor methodological qualities of the included RCTs and high heterogeneity, this conclusion warrants further investigation.

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