Extracorporeal Shock Wave Therapy on Spasticity After Upper Motor Neuron Injury

A Systematic Review and Meta-analysis

Hui-Ling Zhang, BD, Rong-Jiang Jin, PhD, Li Guan, BD, Dong-Ling Zhong, MD, Yu-Xi Li, MD, Xiao-Bo Liu, BD, Qi-Wei Xiao, MD, Xi-Li Xiao, MD, and Juan Li, PhD

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.

(Am J Phys Med Rehabil 2022;101:615–623)

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

To Claim CME Credits: Complete the self-assessment activity and evaluation online at http://www.physiatry.org/JournalCME

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.

Level: Advanced

Accreditation: The Association of Academic Physiatrists is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Association of Academic Physiatrists designates this Journal-based CME activity for a maximum of 1.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.
tone and muscle activation occurs as a result of damage to inhibitory upper motor neurons (UMNs). 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. For stroke survivors, the prevalence of spasticity ranges from 30% to 80%. In addition, spasticity is experienced in 52.5% of individuals with MS and 86.5% with chronic SCI. Spasticity is associated with pain, weakness, joint stiffness, and/or contracture, which may exacerbate spasticity. 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. Furthermore, several studies found that spasticity was associated with a worse quality of life and greater cost.

There are various interventions for managing spasticity after UMN injury, such as botulinum toxin injections, oral antispastic drugs, and chemical nerve blocks. 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, which can cause failure during secondary treatment; 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; nerve blocks often cause skin sensory loss and dysesthesia; and the procedure is time consuming and requires specialized expertise. 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. 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. Focused ESW is generated by electromagnetic, electrolydraulic, 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. It was reported that ESW therapy alleviated spasticity in stroke, MS, and CP. Some studies have reported that both types of ESW alleviate spasticity.

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. The registration number is CRD42019131059. This systematic review was conducted based on A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR 2.0) and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020) statement guidelines. 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, Cochran Library, and Web of Science systematically.
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 \( \kappa \) 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 \( \kappa \) 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 \( \kappa \) 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 calculate 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 Cochrain \( \chi^2 \) 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, \( \geq 0.1 \) mJ/mm\(^2\)); frequency of ESWT (≤5, 6–8, >8 Hz); dosage of ESWT (<2000, \( \geq 2000 \) shocks); total sessions of ESWT (1, 2–8, \( \geq 9 \) 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 \( \kappa \) 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\(^26,28–32,41,43,44,49,54,57,61,72,73,76,78\) were published in English and 26\(^26,27,33–40,42,45–48,50–53,55,56,58–60,62–65,67–71,74,75,77,79–81\) in Chinese. One study\(^28\) was about MS, one study\(^66\) was related to SCI, 11 studies\(^42,45–48,50–53,55,56,58–60,62–65,67–71,74,75,77,79–81\) focused on CP, and 29 studies\(^26,27,33–40,42,45–48,50–53,55,56,58–60,62–65,67–71,74,75,77,79–81\) 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 \( \kappa \) values for the independent assessments of each item in the RoB2.0 ranged from 0.65 to 0.81, which indicated good
consistency. The risk of bias of the included studies is presented in Table 1. Thirty-three RCTs28,42,43,45–49,51,54–58,60–64,66,68–80 reported an adequate random sequence generation process. Allocation concealment was only described in six studies46,54,55,62,68,80 thirty-seven studies28,42,43,45–52,54–60,62–66,68–81 reported that there were no statistically significant differences between groups at the baseline. Twenty-three studies28,42–48,50,51,54–56,58,62–64,66–68,70,71,74 adopted a blinding design, among which four studies42,50,51,54 performed blinding of patients only, 13 studies43–45,47,46,52,58,63,64,66,67,70,71,74 adopted blinding of outcome assessors only, and six studies28,46,48,55,62,68 performed blinding of both patients and outcome assessors. Moreover, only four studies46–48,55 provided a clinical trial registration number. In summary, 22 studies41–43,48,49,51–54,59,61,65,67,69,72,73,75–78,81 were rated as having a “high risk of bias,” and 20 studies28,44–47,50,55–58,62–64,66,68,70,71,74,79,80 were rated as having “some concerns.”

Primary Outcome

A total of 35 studies28,42–49,51–56,58–62,65,66,68–78,80,81 reported the MAS; however, the data of MAS from nine articles44,47,48,56,59,69–71,77 could not be synthesized. Two studies44,48 only presented the baseline of MAS scores and difference of MAS scores before and after treatment. The other two studies47,59 provided dichotomous outcomes of MAS. Five studies46,69–71,77 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 patients47,48,56–59,69–71,77 and in children with CP.44 Pooled data of the 26 RCTs42,43,45,46,48,51–55,58,60–62,65,66,68,72,73,75–78,81 showed that ESWT significantly decreased the MAS score (standardized mean difference = −0.97, 95% CI = −1.23 to −0.71, P = 0.00001; Supplementary Fig. 2, Supplemental Digital Content 6, http://links.lww.com/PHM/B338).

Results of subgroup analyses for MAS are summarized in Table 2. Different types of UMN injury or ESWT, the EF 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, tESWT was superior to iESWT 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 EF of ESWT demonstrated that the single session of ESWT and the EF of ESWT of 0.1 mJ/mm² 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 Sairong77 confirmed that ESWT was
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. Siwei et al. 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 reported that no adverse effects occurred in ESWT groups. Five studies reported slightly adverse effects, such as skin injury, bone distortion, muscle numbness, pain, petechiae, and weakness.

Certainty of Evidence

The \( \kappa \) 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/mm² 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 2. Subgroup analyses of the MAS

| Type of UMN injury | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|-------------------|---|---------------------|-----|-----|
| 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      | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|------------------|---|---------------------|-----|-----|
| 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 | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|--------------------------|---|---------------------|-----|-----|
| 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     | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|---------------------------|---|---------------------|-----|-----|
| <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/mm² | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|-------------------------------------|---|---------------------|-----|-----|
| <0.1                                | 4  | −0.41 (−0.71 to −0.10) | 0.009 | 49% |
| ≥0.1                                | 4  | −0.63 (−1.02 to 0.02) | 0.06 | 62% |

| Frequency of ESWT, Hz              | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|------------------------------------|---|---------------------|-----|-----|
| ≤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              | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|------------------------------------|---|---------------------|-----|-----|
| <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    | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|------------------------------------|---|---------------------|-----|-----|
| 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                          | n | Effect Size (95% CI) | \( P \) | \( I^2 \) |
|------------------------------------|---|---------------------|-----|-----|
| 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) | 0.068 | 88% |
| >1 mo                              | 3  | −1.18 (−2.27 to −0.08) | 0.04 | 88% |

**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.
| Quality Assessment | No. Studies | Design | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | No. Patients | Experimental | Control | Relative Effect (95% CI) | Absolute Effect | Quality | Importance |
|--------------------|-------------|--------|--------------|---------------|--------------|-------------|---------------------|--------------|--------------|----------|------------------------|----------------|----------|------------|
| MAS                | 26          | Randomized trials | Serious<sup>a</sup> | Serious<sup>b</sup> | Not serious | Not serious | None                | 602          | 586          | —        | SMD = 0.97 lower (1.23 to 0.71 lower) | ΘΘ ΘΘ ΘΘ ΘΘ ΘΘ ΘΘ | LOW      | CRITICAL  |
| H<sub>max</sub>/M<sub>max</sub> ratio | 5           | Randomized trials | Not serious | Serious<sup>b</sup> | Not serious | Not serious | None                | 115          | 115          | —        | MD = 0.14 lower (0.3 lower to 0.03 higher) | ΘΘ ΘΘ ΘΘ ΘΘ ΘΘ ΘΘ | MODERATE | IMPORTANT |
| CSS                | 4           | Randomized trials | Not serious | Serious<sup>b</sup> | Not serious | Serious<sup>c</sup> | Reporting bias<sup>d</sup> | 102          | 102          | —        | MD = 1.98 lower (3.21 to 0.74 lower) | ΘΘΘΘΘΘΘΘΘΘ | VERY LOW | IMPORTANT |
| iEMG               | 2           | Randomized trials | Not serious | Serious<sup>b</sup> | Not serious | Serious<sup>c</sup> | None                | 16           | 16           | —        | MD = 107.79 lower (410.47 lower to 194.89 higher) | ΘΘ ΘΘ ΘΘ ΘΘ ΘΘ | 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) | ΘΘ ΘΘ ΘΘ ΘΘ ΘΘ | HIGH     | IMPORTANT |
| MTS                | 4           | Randomized trials | Not serious | Serious<sup>b</sup> | Not serious | Serious<sup>c</sup> | None                | 86           | 69           | —        | MD = 2.04 higher (18.17 lower to 22.24 higher) | ΘΘ ΘΘ ΘΘ ΘΘ | LOW      | IMPORTANT |
| H-reflex latency   | 2           | Randomized trials | Not serious | Not serious | Not serious | Serious<sup>c</sup> | Reporting bias<sup>d</sup> | 60           | 60           | —        | MD = 3.24 higher (1.94 to 4.53 higher) | ΘΘ ΘΘ ΘΘ ΘΘ | LOW      | IMPORTANT |

<sup>a</sup> The evidence came from studies with a high risk of bias.  
<sup>b</sup> I<sup>2</sup> value of the combined results was large, and high heterogeneity.  
<sup>c</sup> The confidence intervals were wide or not match the optimal information size.  
<sup>d</sup> 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.
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. However, the MAS relies on the interpretation of the assessor, which may induce measurement bias, especially when outcome assessors are not blinded. Recently, objective indicators have been applied to assess spasticity in clinical practice, such as the $H_{\text{max}}/M_{\text{max}}$ 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. 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.

**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. 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. 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. Moon et al. 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. 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, and reported that the $H_{\text{max}}/M_{\text{max}}$ 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, whereas others revealed a reduction of the $H_{\text{max}}/M_{\text{max}}$ ratio after ESWT, thus indicating a change in $\alpha$ motor neuron excitability. We found that ESWT lengthened H-reflex latency, although there was no significant difference in the $H_{\text{max}}/M_{\text{max}}$ 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 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. 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.
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.

ACKNOWLEDGMENTS
The authors acknowledge the editorial suggestions of Smart Study Education and Technology Group.

REFERENCES
1. Luo Z, Lo WLA, Bian R, et al: Advanced quantitative estimation methods for spasticity: a literature review. J Int Med Res 2020;48:380066519888425
2. Bijn, Park HD, Han SH, et al: Duration of treatment effect of extracorporeal shock wave on spasticity and subgroup-analysis according to number of shocks and application site: a meta-analysis. Ann Rehabil Med 2019;43:163–77
3. Patel R, Rhee PC: Assessment of 30-day adverse events in single-event, multilevel upper extremity surgery in adult patients with upper motor neuron syndrome. Hand (N Y) 2020;9:60–9
4. Pulgar S, Bains S, Gooch J, et al: Prevalence, patterns, and cost of care for children with cerebral palsy enrolled in Medicare managed care. J Manag Care Spec Pharm 2019;25:817–22
5. Kuo C-L, Hu G-C: Post-stroke spasticity: a review of epidemiology, pathophysiology, and treatments. Int J Gerontol Pract 2018;12:280–4
6. Skierlo S, Rommer PS, Zettl UK: Symptomatic treatment in multiple sclerosis—inferior analysis of a nationwide registry. Acta Neurol Scand 2017;135:394–9
7. DiPiro ND, Li C, Krause JS: A longitudinal study of self-reported spasticity among individuals with chronic spinal cord injury. Spinal Cord 2018;56:218–25
8. Brainin M, Norrving B, Sunnerhagen KS, et al: Post-stroke chronic disease management: towards improved identification and interventions for post-stroke spasticity-related complications. Int J Stroke 2015;10:42–6
9. Malhotra S, Pandyan AD, Rosewilliam S, et al: Spasticity and contractions at the wrist after stroke: time course of development and their association with functional recovery of the upper limb. Clin Rehabil 2011;25:184–91
10. Eeg-Olofsson K, Svanberg K, Edstrom LE, et al: The duration of treatment in children with cerebral palsy: a prospective cohort study. Developmental Medicine & Children’s Neurology 2009;51:276–81
11. Gillard PJ, Sucharew H, Kleindorfer D, et al: The negative impact of spasticity on the health-related quality of life of stroke survivors: a longitudinal cohort study. Health Qual Life Outcomes 2015;13:159
12. Vural M, Yalcinkaya EY, Celik EC, et al: Assessment of quality of life in relation to spasticity severity and socio-demographic and clinical factors among patients with spinal cord injury. J Spinal Cord Med 2020;43:193–200
13. Zettl UK, Herze T, Issner U, et al: Burden of disease in multiple sclerosis patients with spasticity in Germany: mobility improvement study (move I). Eur J Health Econ 2014;15:953–66
14. Lundström E, Smits A, Borg J, et al: Four-fold increase in direct costs of stroke survivors with spasticity compared with stroke survivors without spasticity: the first year after the event. Stroke 2010;41:319–24
15. Blumetti FC, Belloti J, Tamaoki MJ, et al: Botulinum toxin type A in the treatment of lower limb spasticity in children with cerebral palsy. Cochrane Database Syst Rev 2019;10:CD001408
16. Navarrete-Opazo AA, González W, Servidio L: Management of spasticity in children with cerebral palsy by means of extracorporeal shockwave therapy: a systematic review of the literature. Dev Neurorehabil 2021;24:1–7
17. Xiang J, Wang W, Jiang W, et al: Effect of extracorporeal shock wave therapy on spasticity in post-stroke patients: a systematic review and meta-analysis of randomized controlled trials. J Rehabil Med 2018;50:852–9
18. Milhae EE, Dumitra L, Milhai IV, et al: Long-term efficacy of extracorporeal shock wave therapy on lower limb post-stroke spasticity: a systematic review and meta-analysis of randomized controlled trials. J Clin Med 2020;10:808
19. Martinez IM, Sempero-Rubio N, Navarro O, et al: Effectiveness of shock wave therapy as a treatment for spasticity: a systematic review. Brain Sci 2021;11:15
20. Liu DW, Zhong DL, Li J, et al: The effectiveness and safety of extracorporeal shock wave therapy (ESWT) on spasticity after upper motor neuron injury: a protocol of systematic review and meta-analysis. Medicine (Baltimore) 2020;99:e18932
21. Shua BI, Reeves BC, Wells G, et al: AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008
22. Page MJ, Moher D, Bossuyt PM, et al: PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ 2021;372:n160
23. Yang ZR, Sun F, Zhan SY: Risk on bias assessment: (2) revised Cochrane risk of bias tool for individually randomized, parallel group trials (RoB2.0). Zhonghua Liu Xing Bing Xue Za Zhi 2017;38:1285–91
24. Atkins D, Best D, Briss PA, et al: Grading quality of evidence and strength of recommendations. Br Med J 2004;328:1490
25. Zeng X-T, Wei-Dong L, Sheng L, et al: How to understand and use grade system correctly? A briefly outline. Chin J Evid Based Med 2011;11:985–90
26. Abdel Gawad HA, Abdel Karim AE, Mohammed AH: Shock wave therapy for spastic plantar flexor muscles in hemiplegic cerebral palsy children. Journal: article. Egypt J Med Hum Genet 2015;16:269–75
27. Dymarek R, Taradaj J, Rosińczuk J: The effect of radial extracorporeal shock wave stimulation on upper limb spasticity in chronic stroke patients: a single-blind, randomized, placebo-controlled study. Ultrasound Med Biol 2016;42:1862–75
28. El-Shamy SM, Eid MA, El-Banna MF: Effect of extracorporeal shock wave therapy on gait pattern in hemiplegic cerebral palsy: a randomized controlled trial. Am J Phys Med Rehabil 2019;98:1065–72
29. Farhan SN, Abdullah SS, Abdulagari MF: Impact of extracorporeal shock wave therapy on spastic handfunction with assistive devices in children with cerebral palsy. Ann Trad Med Public Health 2019;22:60–9
30. Guo Q, Qian S, Wang Y, et al: Clinical study of combined mirror and extracorporeal shock wave therapy on upper limb spasticity in poststroke patients. Int J Rehabil Res 2019;42:31–5
31. Lee CH, Lee SH, Yoo JI, et al: Ultrasonographic evaluation for the effect of extracorporeal shock wave therapy on gastrocnemius muscle spasticity in patients with chronic stroke. PM R 2019;11:363–71
32. Li G, Yuan W, Liu G, et al: Effects of radial extracorporeal shockwave therapy on spasticity of upper-limb agonist/antagonist muscles in patients affected by stroke: a randomized, single-blind clinical trial. Age Ageing 2020;49:246–52
33. Li TY, Chang CY, Chou YC, et al: Effect of radial shock wave therapy on spasticity of the upper limb in patients with chronic stroke: a prospective, randomized, single-blind, controlled trial. Medicine (Baltimore) 2016;95:e5544
34. Lin Y, Wang G, Wang B: Rehabilitation treatment of spastic cerebral palsy with radial extracorporeal shock wave therapy and rehabilitation therapy. Medicine (Baltimore) 2018;97:13828
35. Park SK, Yang DJ, Uhm YH, et al: Effects of extracorporeal shock wave therapy on upper extremity muscle tone in chronic stroke patients. J Phys Ther Sci 2018;30:361–4
36. Yoon SH, Shin MK, Choi ES, et al: Effective site for the application of extracorporeal shockwave therapy on spasticity in chronic stroke: muscle belly or myotendinous junction. Clin Rehabil 2017;31:547–55

622 | www.ajpmr.com © 2022 The Author(s). Published by Wolters Kluwer Health, Inc.
Effects of extracorporeal shock wave therapy on relieving pectoralis major spasticity

Linfei H, Aisong G, Leilei S: Effects of extracorporeal shock wave treatment on triceps surae muscle function in children with spastic cerebral palsy. Chin J Phys Med Rehabil 2015;34:565–70.

Allam HH, Almalki AJ, Elsayyad LK: Effect of shockwave therapy on kinematic gait parameters in children with spastic diplegic cerebral palsy. J Int Ther Rehabil 2021;28. doi:10.12968/jitr.2020.0029

Yoldas Aslan S, Kutlay S, Dinsinceli Atran E, et al: Does extracorporeal shock wave therapy decrease spasticity of ankle plantar flexor muscles in patients with stroke: a randomized controlled trial. Clin Rehabil 2021;35:1442–53

Sairong B, Di L, Qiming Z, et al: The effects of radial extracorporeal shock wave therapy on gait parameters and spasticity in the patients of stroke with hemiplegia. Chin J Rehabil Med 2019;34:1423–30

Lin D, Bing W, Gang W, et al: A preliminary application of extracorporeal shock wave therapy in children with spastic cerebral palsy. Chin J Clin 2014;8:3598–601

Haoyang D, Zhenlan L, Guoxing X, et al: Efficacy of extracorporeal shock wave treatment in spasticity of biceps brachii in stroke patients. J Ji Lin Univ (Medical Edition) 2017;43:151–4

Qiong D, Li L: Effects of extracorporeal shock wave therapy with exercise therapy on hemiplegic limb spasticity after stroke. Chin J Consalsentric Med 2015;24:1126–8

Linichi H, Aisong G, Leilie S: Effects of extracorporeal shock wave treatment on triceps surae muscle function in children with spastic cerebral palsy. Chin J Phys Med Rehabil 2018;40:272–7

Gushui K, Kaas L. Efficacy and safety of extracorporeal shock wave on calf triceps tendon in children with spastic cerebral palsy. China Foreign Med Treat 2018;37:99–101

Wenyu L, Jinning W, Tao L: Effects of extracorporeal shock wave therapy on wrist and finger spasticity in patients with chronic stroke. Chin J Integr Med Cardio-Cerebrovasc Dis 2017;15:3228–30

Yamei L, Rongqian F, Lin H, et al: Effects of extracorporeal shock wave therapy in different output pressures on triceps surae spasticity after stroke. Chin J Rehabil Therapy Pract 2009;25:518–23

Yamei L, Jing Z, Lin H, et al: Extracorporeal shock wave therapy alleviates spasticity in the triceps surae after stroke. Chin J Phys Med Rehabil 2018;40:272–7

Yifan L, Tianlong W, Jie S: The application of extracorporeal shock wave in the treatment of lower limb spasm after stroke. Chin Manipulation Rehabil Med 2020;11:28–30

Na L, Yanqing C, Xin C: Effect of extracorporeal shock wave therapy on gastrocnemius spasticity after spinal cord injury. Chin J Phys Med Rehabil 2020;11:28–30

Xiaohai S: Effects of Radial Extracorporeal Shock Wave Therapy on Spasticity and Motor Function in Post-stroke Subjects. M.A. Thesis. Shanghai, Shanghai Jiao Tong University, 2015

Ruijing W, Zhao C, Xiaodong F: Effects of radial extracorporeal shock wave combined with routine rehabilitation training on lower limb spasticity and walking function in elderly patients with stroke. Pract Geriatr 2019;23:1111–6

Siwei X, Yun M, Yanyan Y, et al: Effects of extracorporeal shock wave on spasticity of biceps brachii after stroke. Chin J Rehabil Therapy Pract 2014;20:1140–3

Zhiyue Y: Radial Extracorporeal Shockwave Therapy in the Treatment of Lower Limb Spasticity in Patients With Stroke. M.A. Thesis. Qingdao, Qingdao University, 2013

Guojun Y, Shoutong W, Jianguo C, et al: A clinical study of extracorporeal shock wave therapy on crouch gait in children with spastic cerebral palsy. Chin J Rehabil Med 2018;33:63–7

Zhi Z, Junhua B, Gang L, et al: Effects and safety of extracorporeal shock wave therapy combined with routine rehabilitation training on triceps surae in children with cerebral palsy. Hebei Med 2016;32:1142–4

Jinyu W, Bingxian W, Guocheng L, et al: Effect of shockwave acupuncture therapy combined with upper limb strengthening training on upper limb with spasticity after stroke. Lishizhen Med Mater Med Res 2020;31:627–9

Wenfeng F, Chaoyun X, Jia Y, et al: Clinical study on the treatment of gastrocnemius spasm after stroke by electroacupuncture combined with radial extracorporeal shock wave. Henan Tradit Chin Med 2020;40:1281–4

Yuxia W, Fei G, Qiuying Y, et al: Clinical effect of extracorporeal shockwave therapy in treatment of spasticity of triceps surae muscle in children with cerebral palsy. J Qiqingdu Univ (Medical Sciences) 2021;57:559–62

Hezeng L, Yong Z, Bingxu J, et al: Effect of extracorporeal shock wave combined with occupational therapy on forearm pronation disorder in children with spastic cerebral palsy. Rehabil Med 2020;30:202111974

Yujian S, Dianqian Z, Shiwei X, et al: Effect of extracorporeal shock wave combined with acupuncture on spastic lower extremity in patients with stroke. Neurul Injury Funct Reconstruction 2021;16:414–51422

Hongyan S: Effect of focused extracorporeal shock wave on lower limb spasticity in patients after stroke [D]. Guangdong Med Univ 2020

Mingjie Z: Investigate the clinical effect of extracorporeal shock wave in the treatment of spastic paralysis after stroke. World Latest Med Inform 2020;20:357–8

van Wijck FM, Panday AD, Johnson GR, et al: Assessing motor deficits in neurological rehabilitation: patterns of instrument usage. Neurorehabil Neural Repair 2001;15:23–30

Aloraini SM, Gîverth J, Yeung E, et al: Assessment of spasticity after stroke using clinical measures: a systematic review. Desabil Rehabil 2015;37:2313–23

Dymarek R, Ptaszkowski K, Przaszalkowska L, et al: Shock waves as a treatment modality for spasticity reduction and recovery improvement in post-stroke adults—current evidence and qualitative systematic review. Int J Aging 2020;15:9–28

Wu YT, Chang CN, Chen YM, et al: Comparison of the effect of focused and radial extracorporeal shock waves on spastic equinus in patients with stroke: a randomized controlled trial. J Phys Ther Sci 2018;54:518–25

Lee J-Y, Kim N-S, Lee I-S, et al: Effects of extracorporeal shock wave therapy on spasticity in patients after brain injury: a meta-analysis. J Phys Ther Sci 2014;26:1641–7

Moon SW, Kim JH, Jung MJ, et al: The effect of extracorporeal shock wave therapy on lower limb spasticity in subacute stroke patients. Ann Rehabil Med 2013;37:461–70

Shehgal N, McGuire JR: Beyond Ashworth. Electrophysiologic quantification of spasticity. Phys Med Rehabil Clin N Am 1998;9:949–79, ix

Manganotti P, Amelio E: Long-term effect of shock wave therapy on upper limb hypertonia in patients affected by stroke. Stroke 2005;36:1967–71

Soheil MK, Cho KH, Kim YJ, et al: Spasticity and electrophysiologic changes after extracorporeal shock wave therapy on gastrocnemius. Ann Rehabil Med 2011;35:599–604

Dalin SS, Fororg B, Emanzi Razavi SZ, et al: A single blind, clinical trial to investigate the effects of a single session extracorporeal shock wave therapy on wrist flexor spasticity after stroke. Neurorehabilitation 2015;36:67–72

Sawas S, Abd-Allah F, Hegazy MM, et al: Effect of shock wave therapy on ankle plantar flexors spasticity in stroke patients. Neurorehabilitation 2017;40:115–8

Santamato A, Micello MF, Panza F, et al: Extracorporeal shock wave therapy for the treatment of poststroke plantar-flexor muscles spasticity: a prospective open-label study. Top Stroke Rehabil 2014;21(suppl 1):S17–24

Amelio E, Manganotti P: Effect of shock wave stimulation on hypertonic plantar flexor muscles in patients with cerebral palsy: a placebo-controlled study. J Rehabil Med 2010;42:339–43

© 2022 The Author(s). Published by Wolters Kluwer Health, Inc. www.ajpmr.com | 623