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Systematic Review

Nonsurgical Treatment Options for Muscle Contractures in Individuals With Neurologic Disorders: A Systematic Review With Meta-Analysis

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KEYWORDS
Contracture;
Nervous System Diseases;
Range of motion, articular;
Rehabilitation

Abstract *Objective:* To investigate whether nonsurgical treatment can reduce muscle contractures in individuals with neurologic disorders. The primary outcome measure was muscle contractures measured as joint mobility or passive stiffness.
Data Sources: Embase, MEDLINE, Cumulative Index to Nursing and Allied Health, and Physiotherapy Evidence Database in June-July 2019 and again in July 2020.
Study Selection: The search resulted in 8020 records, which were screened by 2 authors based on our patient, intervention, comparison, outcome criteria. We included controlled trials of nonsurgical interventions administered to treat muscle contractures in individuals with neurologic disorders.
Data Extraction: Authors, participant characteristics, intervention details, and joint mobility/passive stiffness before and after intervention were extracted. We assessed trials for risk of bias using the Downs and Black checklist. We conducted meta-analyses investigating the short-term effect on joint mobility using a random-effects model with the pooled effect from randomized controlled trials (RCTs) as the primary outcome. The minimal clinically important effect was set at 5°.
Data Synthesis: A total of 70 trials (57 RCTs) were eligible for inclusion. Stretch had a pooled effect of 3° (95% CI, 1-4°; prediction interval (PI) = −2 to 7°; I^2 = 66%; P < .001), and robot-assisted rehabilitation had an effect of 1 (95% CI, 0-2; PI = −8 to 9; I^2 = 73%; P = .03). We found no effect of shockwave therapy (P = .56), physical activity (P = .27), electrical stimulation (P = .11), or botulinum toxin (P = .13). Although trials were generally of moderate to high quality according to the Downs and Black checklist, only 18 of the 70 trials used objective measures

List of abbreviations: BTX, botulinum toxin; CCT, controlled clinical trial; PROM, passive range of motion; PICO, patient, intervention, comparison, outcome; PI, prediction interval; RCT, randomized controlled trial.

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of muscle contractures. In 23 trials, nonobjective measures were used without use of assessor-blinding.
Conclusions: We did not find convincing evidence supporting the use of any nonsurgical treatment option. We recommend that controlled trials using objective measures of muscle contractures and a sufficiently large number of participants be performed.

Muscle contractures are a common complication of neurologic disorders such as stroke, spinal cord injury, multiple sclerosis, and cerebral palsy. The prevalence has been reported to range from 36%-60%.[1-5] Muscle contractures represent a unique muscle adaptation characterized by increased passive stiffness of the muscle and limited mobility of the joint with little or no active force production.[6] Muscle contractures lead to joints fixated in abnormal positions and limited use of the affected limbs. Furthermore, muscle contractures can cause considerable pain, strength loss, and muscle atrophy.[6,7]

To restore the mobility of affected joints, surgical procedures such as various forms of tendon lengthening and intramuscular aponeurotic recession are used.[8,9] These procedures may increase the range of motion for some time, but because they rarely have lasting effects, other effective treatment approaches should be considered also. A variety of other treatment options currently exists. A few of these have previously been reviewed (stretching and shockwave therapy[10,11]), but a systematic evaluation of the effectiveness of all the available nonsurgical treatment options in a single review has so far not been conducted. A critical and comprehensive evaluation of the effect of all treatment options in 1 single study may help clinicians to obtain a better overview of the field. It may also help to clarify where the existing knowledge needs to be strengthened by further research and point to new therapy options.

Therefore, the aim of this systematic review was to provide an overview of the evidence supporting the use of current nonsurgical treatment options for reduction of muscle contractures in individuals with neurologic disorders. We included randomized controlled trials (RCTs) and controlled clinical trials (CCTs) of nonsurgical interventions administered with the aim to treat muscle contractures in individuals with neurologic disorders. We decided to include not only RCTs but also CCTs because we wanted to review all available treatment options. The primary outcome measure was muscle contractures measured as either joint mobility or passive stiffness.

Methods

Study design

We conducted this systematic review with meta-analyses of RCTs and CCTs using a protocol based upon Cochrane Collaboration recommendations and reported it according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[12,13]

Eligibility criteria

Published trials fulfilling the following patient, intervention, comparison, outcome (PICO) criteria were included.

Participants

Individuals of all ages and sexes with muscle contractures due to a neurologic disorder.

Interventions

Nonsurgical interventions administered to treat muscle contractures.

Comparisons

Trials that compared the intervention with a control condition. Control condition included no intervention, usual care, and placebo/sham treatment.

Outcomes

The main outcome was muscle contractures measured as either passive range of motion (PROM) or passive stiffness.

Search strategy

Relevant articles were identified by searching the databases of Embase, MEDLINE, Cumulative Index to Nursing and Allied Health, and Physiotherapy Evidence Database, using a combination of subject headings and free-text terms. The search string was initially developed for MEDLINE and adapted for use in the other databases. Search strings used in all databases can be found in the supplemental table S1 (available online only at http://www.archives-pmr.org/). Publications were limited to the English language. Publications were not limited by year of publication. We performed the search in June-July 2019. We additionally searched all databases in July 2020 to detect any eligible trials published during the review process.

Data extraction

Two review authors (C.S., J.L.) screened title and abstracts of all records obtained from the searches and excluded irrelevant articles. Full texts of the remaining articles were then obtained and screened for eligibility based on our

PICO criteria by the 2 review authors (C.S., J.L.). Through subjective judgment, the reviewers doing the data extraction decided whether the intervention was administered to treat muscle contractures. Disagreements were solved by discussion and, when necessary, arbitrated by a third review author (J.B.N.) deciding whether to include or exclude the disputed.

Data synthesis

C.S. extracted short-term joint mobility data (up to 1wk after intervention). Preferably, change scores and SDs were extracted. If change scores were not available, post-intervention scores were used instead. Change scores/postintervention scores and SDs were not available for all trials. In trials where this information was not available, we contacted the corresponding author of the article in an attempt to retrieve the information. Several trials investigated the effect of the intervention on multiple joints and/or both sides. In these cases, we used data from a single joint on the right side of the body. In prioritized order, we chose to use data from the ankle joint, the elbow joint, the knee joint, or the wrist joint. This order was based on our experience of where muscle contractures are frequent and severe and is in accordance with literature on muscle contracture prevalence in different neurologic disorders.[1-3]

We identified 6 types of interventions with multiple trials: stretch, shockwave therapy, physical activity, botulinum toxin (BTX) treatment, electrical stimulation, and robot-assisted rehabilitation interventions. Based on the recommendations by Valentine et al,[14] we conducted individual meta-analyses for these 6 intervention types. Because very few trials used passive stiffness as an outcome measure, the meta-analyses were performed based on PROM results. The primary outcome measure was set as the pooled PROM from RCTs. For all intervention types, we conducted sensitivity analyses to examine the effects of randomization on joint mobility. Similarly to Harvey et al,[11] we did not consider a treatment effect of $<5^{\circ}$ PROM as clinically important. Because we considered the included trials to have varying effect sizes, all meta-analyses were performed using a random-effects model. In accordance with the Cochrane Handbook for Systematic Reviews of Intervention,[13] we reported the effects using mean differences in the meta-analysis in cases where the outcome was reported using comparable measures. In 1 case with robot-assisted rehabilitation, the outcome was not measured using comparable methods. Here, we reported the effect of the intervention using standardized mean differences in the meta-analysis.[13] In forest plots, randomized and non-randomized trials are presented separately. Subgroup analyses were used to explore possible differences between types of stretch. In studies with several relevant experimental groups (2 types of stretch protocols), we combined the experimental groups in to 1 single group.[13] Prediction intervals were calculated in accordance with the method described by Borenstein.[15] Meta-analyses were conducted using Review Manager 5.3.[a]

We assessed trials for risk of bias using the Downs and Black checklist.[16] Initially, 2 review authors (C.S., J.L.) scored the first trials together to synchronize the interpretation of the checklist. Subsequently, C.S. and J.L. scored the remaining trials independently. The maximum score attainable using the Downs and Black checklist is 33 points. The quality of included trials was ranked as high if the total score was $>75\%$ of the maximum, moderate if 60%-74% of the maximum, and low if $<60\%$ of the maximum.[17,18] In question 20 we focused on whether the primary outcome measure was objective. We defined an objective measure as a measure not easily influenced by the rater. All torque-controlled goniometric measures were defined as objective, whereas noncontrolled goniometric were not. As we were interested in whether joint mobility was measured objectively and by use of blinded assessors to not introduce bias, we focused in particular on question numbers 15 and 20.

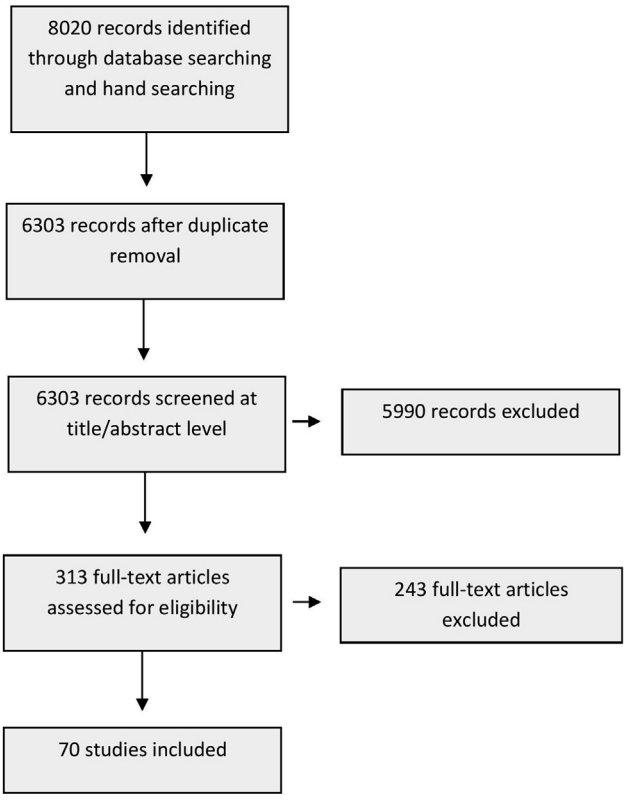

Fig 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

Ethics and registration

This study did not require ethical approval. The systematic review protocol was prospectively registered in the PROSPERO international prospective register of systematic reviews under registration number CRD42019140424.

Results

Study selection

The review process is explained in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram (fig 1). We excluded 243 full-text articles because the trials

Table 1 Characteristics of the included trials (n=71)

Study	Participants	Intervention	Intervention details	n (Experimental Group)	n (Control Group)	Primary Outcome
Stretch						
Fox et al[19]	Elderly persons with cognitive and functional impairment	Bed positioning	Bed positioning for 40 min, 4×/wk for 8 wk	12	12	PROM of knee extension measured using a goniometer
Maas et al[20]	Children with CP	Orthosis	Foot orthosis for 1 y	13	11	PROM of ankle DF measured using a single digital inclinometer attached to a torque wrench
Copley et al[21]	Adults with acquired brain injury	Splinting	Individualized, thermoplastic resting mitt splint for 3 mo	6	4	Wrist and finger PROM measured using a goniometer
DeMeyer et al[22]	Adults with stroke	Casting/orthosis	Bivalve cast group wore custom fiberglass cast PRAFO group wore off-the-shelf AFO. Wearing schedule of 8-12 h every night for ~4 wk.	PRAFO 14 Bivalve cast 13	19	Ankle DF PROM measured using a standardized torque application
Beckerman et al[23]	Adults with stroke	Orthosis	AFO for 15 wk	16	14	PROM of ankle joint measured using a goniometer
Harvey et al[24]	Adults with stroke/ SCI/TBI	Splinting	Experimental thumbs splinted into abduction. 8 h per night for 12 wk	29 thumbs	29 thumbs	PROM of palmar measured using a standardized torque measure
Kerem et al[25]	Adults with CP	Splinting	Johnstone pressure splints. 5 d/wk for 3 mo	17	17	PROM of the lower extremity measured using a goniometer
Harvey et al[26]	Adults with SCI	Passive movements	Passive ankle for 10 min in the morning and 10 min in the evening, 5 d/wk for 6 mo	20	20	PROM of ankle DF measured through application of standardized torque
Theis et al[27]	Children with CP	Passive stretch	15 min (60-s repetitions) of ankle DF stretch 4 d/wk for 6 wk	7	6	Passive stiffness of triceps surae
Harvey et al[28]	Adults with SCI	Passive stretch	Passive hamstring stretch for 30 min/d, 5 d/wk for 4 wk	14	11	Hamstring muscle extensibility measured using a torque-controlled measure
Cheng et al[29]	Children with CP	Repetitive passive movements	Knee repetitive passive movement intervention, 3/wk for 8 wk	18	18	PROM of knee joint measured using an electric goniometer
Lannin et al[30]	Adults with stroke	Splinting	Static, palmar resting mitt splint on a daily basis, for max 12 h/night for 4 wk	18	11	PROM of wrist extension measured using a torque-controlled measure
Basaran et al[31]	Adults with stroke	Splinting	Static volar or dorsal splints for 5 wk	Volar 13 Dorsal 13	12	PROM of wrist extension measured using a goniometer
Moseley[32]	Children and adults with TBI	Casting	Below-knee cast for 7 d	9	9	PROM of the ankle joint measured using a torque-controlled measure
Pradines et al[33]	Adults with chronic hemiparesis	Passive and active stretch	Guided self-rehabilitation Contract program, consisting of daily self-stretch exercises for 1 y	12	11	Maximal extensibility (XV1 of the Tardieu Scale) of several muscles (PROM) measured with a goniometer

Lee et al[34]	Adults with stroke	Posterior talar glide	DF of the ankle joint for 10 glides of 5 sets/d, 5 d/wk for 4 wk	17	17	PROM of ankle joint measured using a digital goniometer
Harvey et al[35]	Adults with tetraplegia	Splinting	One thump of each participant was splinted each night for 3 mo	20	20	Extensibility of the flexor pollicis longus muscle measured with a standardized torque application
Hill[36]	Children and adults with brain injury	Casting	Casting for 1 mo	15	15	PROM of casted joints measured using a goniometer
Lannin et al[37]	Adults with stroke	Splinting	Hand splints positioning wrist in 0-10° extension (neutral splint group) or 45° wrist extension (extension splint group) at night for 4 wk	Neutral splint 20 Extension splint 21	21	Muscle extensibility measured using a standardized torque measure
Smedes et al[38]	Adults with stroke	Manual mobilization	10-min manual mobilization of the wrist 2 d/wk for 6 wk	9	9	PROM of wrist extension measured using a goniometer
Horsley et al[39]	Adults with stroke	Passive stretch	30 min of self-assisted stretch of the wrist and finger flexors, 5 d/wk for 4 wk	20	20	PROM of wrist extension measured using a torque-controlled measure
An and Jo[40]	Adults with stroke	Talocrural mobilization	Talocrural mobilization 3 sessions/wk for 5 wk. Each session consisted of 6 sets of 10 repetitions.	13	13	DF PROM measured using a dynamometer
Electrical stimulation						
Pool et al[41]	Children with CP	FES	8-wk FES intervention, FES used at least 1 h/d 6 d/wk	12	12	PROM of ankle DF measured using a goniometer
Pool et al[42]	Children with CP	FES	FES device, which dorsiflexes the ankle during the swing phase of gait for at least 4 h/d, 6 d/wk for 8 wk	16	16	PROM of ankle DF measured using a goniometer
Sabut et al[43]	Adults with stroke	FES	FES for 20-30 minutes to the TA muscle of the paretic limb 5 d/wk for 12 wk	27	24	PROM in the ankle joint measured using a goniometer
Bakaniene et al[44]	Children with CP	Transcutaneous electrical nerve stimulation/Mollii suit	Electrical stimulation through the Mollii suit for 1 h/d, 3/wk for 3 wk	8	8	PROM of ankle and knee joint measured using a goniometer
Malhotra et al[45]	Adults with stroke	NMES	30 min sessions of NMES to the wrist and finger extensors at least 2 times/d, 5 d/wk for 6 wk	45	45	PROM at slow stretch Passive stiffness at slow stretch
Nakipoglu Yuzer et al[46]	Adults with stroke	FES	FES for 30 min/d, 5 d/wk for a total of 20 sessions per patient	15	15	PROM of wrist extension measured using a goniometer
Leung et al[47]	Adults with TBI	Electrical stimulation	The intervention group received 30-min tilt table standing with electrical stimulation to the ankle dorsiflexor muscles 5 d/wk and ankle splinting 12 h/d, at least 5 d/wk. Control group only received tilt table standing for 30 min, 3 times/wk.	17	18	PROM of ankle DF measured with a torque-controlled measure
Sabut et al[48]	Adults with stroke	FES	FES of the TA muscle for 30 min, 5 d/wk for 12 wk	16	14	PROM of the ankle joint

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Table 1 (*continued*)

Study	Participants	Intervention	Intervention details	n (Experimental Group)	n (Control Group)	Primary Outcome
Beaulieu et al[49]	Adults with stroke	Repetitive peripheral magnetic stimulation	Single session of repetitive peripheral magnetic stimulation	9	9	PROM of ankle DF
Shockwave therapy						
Manganiotti and Amelio[50]	Adults with stroke	ESWT	As single session of ESWT	20	20	PROM of the wrist measured using a digital goniometer
Lee et al[51]	Adults with stroke	ESWT	A single session of ESWT	10	10	PROM of the ankle joint measured using a goniometer
Wang et al[52]	Children with CP	ESWT	1 ESWT session per wk for 3 mo.	34	33	PROM of the ankle joint measured using a goniometer
Gonkova et al[53]	Children with CP	ESWT	A single session of ESWT	25	25	PROM of ankle joint
Moon et al[54]	Adults with stroke	ESWT	3 sessions of ESWT, 1 session/wk for 3 wk	30	30	PROM of the ankle measured using a goniometer
Vidal et al[55]	Adults with CP	ESWT	Group 1 received ESWT in the spastic muscle, group 2 received radial ESWT in the spastic muscle and in the antagonistic muscle. 3 sessions, 1-wk intervals.	Group 1 = 14 muscles Group 2 = 13 muscles	13	PROM of lower limbs measured using a goniometer
BTX						
Love et al[56]	Children with CP	Botox	1 session of Botox into gastrocsoleus and where clinically indicated also into tibialis posterior	12	12	PROM of ankle joints measured using a goniometer
Hawamdeh et al[57]	Children with CP	Botox	3 successive Botox injections at intervals of 3-4 mo	40	40	PROM of ankle DF measured using a protractor goniometer
Rameckers et al[58]	Children with congenital spastic hemiplegia	Botox	1 session of Botox injections	10	10	PROM of wrist and elbow extension measured with a Mie goniometer
Meythaler et al[59]	Adults with stroke	Botox	Botox with therapy or placebo injections with therapy. 12-wk intervention.	21	21	PROM of elbow and wrist joint measured monthly using a goniometer
Tedroff et al[60]	Children with CP	Botox	Two Botox injections at 6-mo intervals	6	9	PROM of multiple joints measured using a goniometer
Koman et al[61]	Children with CP	Botox	Botox injections at baseline and at wk 4	56	58	PROM of ankle joint measured using a goniometer
Schasfoort et al[62]	Children with CP	Botox	Control group received 12 wk of conventional rehabilitation, intervention group received 12 wk of rehabilitation plus Botox injections	41	24	PROM of multiple joints measured using a Lafayette goniometer
El-Etribi et al[63]	Children with CP	Botox	Botox administered after baseline measurements	20	20	Ankle joint PROM measured using goniometer

Physical activity						
Horsley et al[64]	Adults with stroke	Upper limb training	Active repetitive motor training by using the SMART Arm device for up to 1 h/d, 5 d/wk for 5 wk	25	25	PROM of multiple joints measured using a digital goniometer and a torque-controlled measure
Scholtes et al[65]	Children with CP	Resistance training	12-wk program of functional PRE training, 3 times/wk for 60 min	24	25	PROM of the multiple joints measured using a goniometer
Schmid et al[66]	Adults with stroke	Yoga	Therapeutic yoga sessions were delivered in group sessions for 1 h 2 times/wk for 8 wk	37	10	PROM of hamstrings muscles measured using a goniometer
Rydwik et al[67]	Adults with stroke	Exercise program	Exercise program including active and passive range of motion of the ankle with a portable device (Stimulo), 3 times/wk for 30 min, over a 6-wk period	9	9	PROM of ankle joint measured using a goniometer
Baik et al[68]	Children with CP	Horseback riding	Therapeutic horseback riding 60 min/d, 2 d/wk for 12 wk. Daily program consisted of 10 min of warm-up, 40 min of workout, and 10 min of cooldown.	8	8	PROM of hip joint measured using a goniometer
Lorentzen et al[69]	Adults with CP	Treadmill training	30-min daily uphill gait training for 6 wk on a treadmill	12	11	Passive stiffness of the ankle joint quantified using a stationary and hand-held dynamometer. The hand-held dynamometer also to assess the PROM of the ankle joint.
Kirk et al[70]	Adults with CP	Resistance training	Resistance training, 3 times/wk for 12 wk	12	11	Passive stiffness of ankle plantar flexors measured using a stationary dynamometer
An and Won[71]	Adults with stroke	MWM and WBE	30 min of MWM or WBE 3 times/wk for 5 wk	MWM 12 WBE 8	10	PROM of the ankle joint using a isokinetic dynamometer
Teixeira-Machado and DeSantana[72]	Children with CP	Dance	24 one-h sessions twice a wk for 3 m	13	14	PROM of multiple joint measured using a goniometer
Hemachitara et al[73]	Children with CP	Horse riding	1 session of horse riding using a horse riding simulator	12	12	PROM of hip abduction measured using a goniometer
Robot-assisted rehabilitation						
Mirbagheri et al[74]	Adults with SCI	Robotic-assisted step training	Three 1-h robotic-assisted step training sessions/wk for 4 wk	23	23	Intrinsic ankle stiffness measured as using torque/unit change in ankle position
Waldman et al[75]	Adults with stroke	Stretch and active movements	A portable rehabilitation robot with controlled passive stretching and active movement training capabilities. 18 sessions, 3 times/wk for 6 wk	12	12	Ankle DF PROM measured using the robotic device
Mirbagheri et al[76]	Adults with SCI	Robot-assisted locomotor training LOKOMAT	LOKOMAT training 3 d/wk for 4 wk	23	28	Intrinsic dynamic stiffness of the ankle joint
Franceschini et al[77]	Adults with stroke	Upper limb rehabilitation	Upper limb robot-assisted rehabilitation; 30 sessions, 5 d/wk for 6 wk	25	23	PROM of shoulder and elbow joint

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Table 1 (*continued*)

Study	Participants	Intervention	Intervention details	n (Experimental Group)	n (Control Group)	Primary Outcome
Sale et al[78]	Adults with stroke	Robot-assisted therapy	Thirty 45-min sessions, 5 d/wk for 6 wk, using the robotic system that supported arm movements	26	27	PROM of the shoulder and elbow joint
Other						
Rayegani et al[79]	Adults with SCI	Passive cycling	Motorized cycle that passively moved legs for 20 min, 3 times/wk for 2 mo	35	29	PROM of multiple joints measured using a goniometer
Xu et al[80]	Adults with stroke	MT combined with neuromuscular electrical stimulation	MT group received 30 min of MT training. Control group performed the same training but with nonreflecting side of the mirror. MT+NMES group combined MT with 30 min NMES.	MT 23 MT+NMES 23	23	PROM of ankle joint DF assessed using a goniometer
Lorentzen et al[81]	Adults with TBI	Neural tension technique	1 session of neural tension technique treatment	10	10	Passive knee stiffness measured using the Neurokinetics RA1 Rigidity Analyzer
Mathew et al[82]	Children with CP	Antispastic medication	Participants received A (placebo), B (0.5/1.0mg diazepam), or C (1.0/2.0mg diazepam) for 15-20 d	60	60	PROM of ankle joint measured using a goniometer
Velasco et al[83]	Children with CP	Physical therapy based on head movements and serious games	10 sessions of gaming using the ENLAZA interface	5	5	Cervical PROM
Wayne et al[84]	Adults with stroke	Acupuncture	Traditional Chinese acupuncture, twice a wk for 10 wk	16	17	PROM of each major upper extremity joint
Cheng et al[85]	Children with CP	Whole body vibration	8-wk whole body vibration intervention	16	16	PROM of knee joint measured using an electrogoniometer
Fosdahl et al[86]	Children with CP	Stretching and PRE	16 wk of 3 weekly sessions of stretching and resistance training	17	20	Passive popliteal angle registered as maximum passive extension of the knee measured using a goniometer
Takeuchi et al[87]	Adults with cerebrovascular disease	HI-LPNR and stretching	Participants were randomized to 1 session of HI-LPNR, stretching, a combination, or a control group	HI-LPNR 10 stretching 10 combination 10	10	PROM of ankle DF and passive resistive joint torque of ankle DF
Ghannadi et al[88]		Dry needling	1 session of dry needling	12	12	PROM of dorsiflexors measured using a goniometer

Abbreviations: AFO, ankle-foot orthosis; CP, cerebral palsy; DF, dorsiflexion; ESWT, extracorporeal shock wave therapy; FES, functional electrical stimulation; HI-LPNR, high-intensity pulse irradiation with linear polarized near-infrared rays; MT, mirror therapy; MWM, mobilization with movement; NMES, neuromuscular electrical stimulation; PRE, progressive resistance exercise; SCI, spinal cord injury; TA, tibialis anterior; TBI, traumatic brain injury; WBE, weight-bearing exercise.

Table 2 Risk of bias in the included trials assessed using the Downs and Black checklist

Study	Reporting	External Validity	Internal Validity: Bias	Internal Validity: Confounding	Power	Total	Percentage	Quality
Stretch								
Fox et al[19]	10	3	5	5	3	26	79	High
Maas et al[20]	11	3	6	6	3	29	88	High
Copley et al[21]	10	3	4	5	1	23	70	Moderate
DeMeyer et al[22]	10	3	5	5	3	26	79	High
Beckerman et al[23]	7	3	3	5	3	21	64	Moderate
Harvey et al[24]	11	3	6	6	5	31	94	High
Kerem et al[25]	10	0	4	3	3	20	61	Moderate
Harvey et al[26]	10	3	6	3	4	26	79	High
Theis et al[27]	8	1	5	3	2	19	58	Low
Harvey et al[28]	10	2	5	6	3	26	79	High
Cheng et al[29]	10	0	3	4	3	20	61	Moderate
Lannin et al[30]	9	2	5	5	3	24	73	Moderate
Basaran et al[31]	10	1	5	5	3	24	73	Moderate
Moseley[32]	9	1	4	5	2	21	64	Moderate
Pradines et al[33]	10	1	5	5	3	24	73	Moderate
Lee et al[34]	9	0	3	5	3	20	61	Moderate
Harvey et al[35]	11	2	5	4	3	25	76	High
Hill[36]	6	1	3	4	3	17	52	Low
Lannin et al[37]	9	0	6	5	3	23	70	Moderate
Smedes et al[38]	10	2	3	2	2	19	58	Low
Horsley et al[39]	11	2	6	6	3	28	85	High
An and Jo[40]	9	1	3	5	3	21	64	Moderate
Averages	10	2	5	5	3	23	71	Moderate
Electrical stimulation								
Pool et al[41]	9	0	3	3	3	18	55	Low
Pool et al[42]	9	1	4	6	3	23	70	Moderate
Sabut et al[43]	10	3	3	5	4	25	76	High
Bakaniene et al[44]	9	0	4	2	2	17	52	Low
Malhotra et al[45]	9	2	5	5	5	26	79	High
Nakipoglu Yuzer et al[46]	9	0	4	4	3	20	61	Moderate
Leung et al[47]	10	1	5	5	3	24	73	Moderate
Sabut et al[48]	9	3	5	4	3	24	73	Moderate
Beaulieu et al[49]	10	0	6	5	2	23	70	Moderate
Averages	9	1	4	4	3	22	67	Moderate
Shockwave therapy								
Manganiotti and Amelio[50]	11	2	5	3	3	24	73	Moderate
Lee et al[51]	10	3	6	6	2	27	82	High
Wang et al[52]	11	3	4	3	5	26	79	High
Gonkova et al[53]	6	1	4	1	4	16	48	Low
Moon et al[54]	10	0	4	4	4	22	67	Moderate
Vidal et al[55]	5	0	4	3	3	15	45	Low
Averages	9	2	5	3	4	22	66	Moderate
Botox								
Love et al[56]	10	3	4	5	4	26	79	High
Hawamdeh et al[57]	10	2	4	5	4	25	76	High
Rameckers et al[58]	9	0	4	5	2	20	61	Moderate
Meythaler et al[59]	8	0	6	4	4	22	67	Moderate
Tedroff et al[60]	11	1	5	4	2	23	70	Moderate
Koman et al[61]	6	0	4	3	5	18	55	Low
Schasfoort et al[62]	10	1	5	2	5	23	70	Moderate
El-Etribi et al[63]	8	0	2	3	3	16	48	Low
Averages	9	1	4	4	4	22	66	Moderate

(*continued on next page*)

Table 2 (*continued*)

Study	Reporting	External Validity	Internal Validity: Bias	Internal Validity: Confounding	Power	Total	Percentage	Quality
Physical activity								
Horsley et al[64]	10	3	6	6	4	29	88	High
Scholtes et al[65]	11	3	5	5	5	29	88	High
Schmid et al[66]	9	0	2	4	5	20	61	Moderate
Rydwik et al[67]	9	0	5	5	2	21	64	Moderate
Baik et al[68]	8	0	2	0	2	12	36	Low
Lorentzen et al[69]	10	0	6	5	3	24	73	Moderate
Kirk et al[70]	9	0	5	3	4	21	64	Moderate
An and Won[71]	8	0	3	3	2	16	48	Low
Teixeira-Machado and DeSantana[72]	10	0	3	5	3	21	64	Moderate
Hemachitara et al[73]	11	0	5	5	3	24	73	Moderate
Averages	10	1	4	4	3	22	66	Moderate
Robot-assisted rehabilitation								
Mirbagheri et al[74]	10	2	5	4	4	25	76	High
Waldman et al[75]	10	3	5	5	3	26	79	High
Mirbagheri et al[76]	5	0	3	3	4	15	45	Low
Franceschini et al[77]	11	1	4	6	4	26	79	High
Sale et al[78]	10	0	5	5	4	24	73	Moderate
Averages	9	1	4	5	4	23	70	Moderate
Other interventions								
Rayegani et al[79]	10	3	2	5	5	25	76	High
Xu et al[80]	9	3	5	6	4	27	82	High
Lorentzen et al[81]	11	1	6	5	2	25	76	High
Mathew et al[82]	7	3	6	3	5	24	73	Moderate
Velasco et al[83]	8	0	4	4	1	17	52	Low
Wayne et al[84]	9	0	5	5	3	22	67	Moderate
Cheng et al[85]	9	0	3	3	3	18	55	Low
Fosdahl et al[86]	11	1	4	6	3	25	76	High
Takeuchi et al[87]	8	0	3	4	2	17	52	Low
Ghannadi et al[88]	9	0	6	6	3	24	73	Moderate

did not fulfill our PICO criteria (211); because the full text was not available (12), not accessible (14), or was a duplicate (3); or because the primary data/summary statistics was not presented (3). The remaining 70 articles were included in this systematic review. Of the 70 articles included in the review, 57 were RCTs (see fig 1).

Of the included trials, there were 22 trials (19 RCTs) on stretch interventions, 6 trials (2 RCTs) on shockwave interventions, 8 trials (7 RCTs) on BTX interventions, 9 trials (5 RCTs) on electrical stimulation interventions, 10 trials (8 RCTs) on physical activity interventions, and 5 trials (5 RCTs) on robot-assisted interventions. We performed meta-analyses for all of these intervention types. Additionally, we found 10 trials investigating other interventions. These trials are described in the section "Other interventions."

Study characteristics

Table 1 depicts the characteristics of the included studies, including information about the intervention, the number of participants, and the measure of muscle contractures.

Evidence quality

Table 2 summarizes the quality assessments performed based on the Downs and Black checklist. Data are presented as the subtotal scores, the total score, and the quality ranking of all trials. Furthermore, the average score for the different intervention types are presented. For detailed scoring of each individual article, we refer to the supplemental table S2 (available online only at http://www.archives-pmr.org/).

For stretch interventions, 8 trials were of high quality, 11 trials of moderate quality, and 3 trials of low quality. For electrical stimulation interventions, 2 trials were of high quality, 5 trials of moderate quality, and 2 trials of low quality. For shockwave interventions, 2 trials were of high quality, 2 trials of moderate quality, and 2 trials of low quality. For BTX interventions, 2 trials were of high quality, 4 trials of moderate quality, and 2 trials of low quality. For physical activity interventions, 2 trials were of high quality, 6 trials of moderate quality, and 2 trials of low quality. For robot-assisted interventions, 3 trials were of high quality, 1 trial of moderate quality, and 1 trial of low quality (table 3).

Table 3 Assessment of outcome measures

Study	Blinded Assessor	Objective Outcome Measure
Stretch		
Fox et al[19]	Yes	No
Maas et al[20]	Yes	Yes
Copley et al[21]	Yes	No
DeMeyer et al[22]	No	Yes
Beckerman et al[23]	Unable to determine	No
Harvey et al[24]	Yes	Yes
Kerem et al[25]	No	No
Harvey et al[26]	Yes	Yes
Theis et al[27]	No	Yes
Harvey et al[28]	Yes	Yes
Cheng et al[29]	No	No
Lannin et al[30]	Yes	No
Basaran et al[31]	Yes	No
Moseley[32]	No	Yes
Pradines et al[33]	Yes	No
Lee et al[34]	No	No
Harvey et al[35]	Yes	Yes
Hill[36]	Yes	No
Lannin et al[37]	Yes	Yes
Smedes et al[38]	No	No
Horsley et al[39]	Yes	Yes
An and Jo[40]	Unable to determine	No
Electrical stimulation		
Pool et al[41]	No	No
Pool et al[42]	No	No
Sabut et al[43]	No	No
Bakaniene et al[44]	No	No
Malhotra et al[45]	Yes	Yes
Nakipoglu Yuzer et al[46]	Unable to determine	No
Leung et al[47]	Yes	No
Sabut et al[48]	Yes	No
Beaulieu et al[49]	Yes	No
Shockwave therapy		
Manganiotti and Amelio[50]	No	No
Lee et al[51]	Yes	No
Wang et al[52]	Unable to determine	No
Gonkova et al[53]	Yes	Unable to determine
Moon et al[54]	No	No
Vidal et al[55]	Yes	No
Botox		
Love et al[56]	No	No
Hawamdeh et al[57]	No	No
Rameckers et al[58]	Yes	No
Meythaler et al[59]	Yes	No
Tedroff et al[60]	Yes	No
Koman et al[61]	Yes	Unable to determine
Schasfoort et al[62]	Yes	No
El-Etribi et al[63]	No	No
Physical activity		
Horsley et al[64]	Yes	Yes
Scholtes et al[65]	Yes	No
Schmid et al[66]	No	No
Rydwik et al[67]	Yes	No
Baik et al[68]	No	No
Lorentzen et al[69]	Yes	Yes
Kirk et al[70]	No	Yes
An and Won[71]	No	No
Teixeira-Machado and DeSantana[72]	Yes	No
Hemachitara et al[73]	Yes	No
Robot-assisted rehabilitation		
Mirbagheri et al[74]	No	Yes
Waldman et al[75]	Unable to determine	Yes
Mirbagheri et al[76]	No	Yes
Franceschini et al[77]	Yes	No
Sale et al[78]	Yes	No
Other interventions		
Rayegani et al[79]	No	No
Xu et al[80]	Yes	No
Lorentzen et al[81]	Yes	Yes
Mathew et al[82]	Yes	No
Velasco et al[83]	Unable to determine	No
Wayne et al[84]	Yes	No
Cheng et al[85]	No	No
Fosdahl et al[86]	Yes	No
Takeuchi et al[87]	No	No
Ghannadi et al[88]	Yes	No

NOTE. The information in this table corresponds to the results of questions 15 and 20 in the Downs and Black checklist.

Table 3 depicts the results of question numbers 15 and 20 of the Downs and Black checklist. Question number 15 concerns assessor blinding; question number 20 concerns whether joint mobility was measured objectively. The assessor was blinded in 39 trials and not blinded in 25 trials. We were unable to determine whether the assessor was blinded in 6 trials. We rated the primary outcome measure as objective in 18 trials and not objective in 50 trials. In 2 trials, we were unable to determine if the primary outcome measure was measured objectively. In 19 trials, joint mobility was measured using neither assessor blinding nor an objective measure. In 4 of the trials where we were unable to determine the use of assessor blinding, joint mobility was measured using a nonobjective measure.

Effect of stretch on joint mobility (fig 2, fig 3)

Short-term effect is defined as effects measured up to 1 week after the end of the intervention. Of the 22 trials investigating

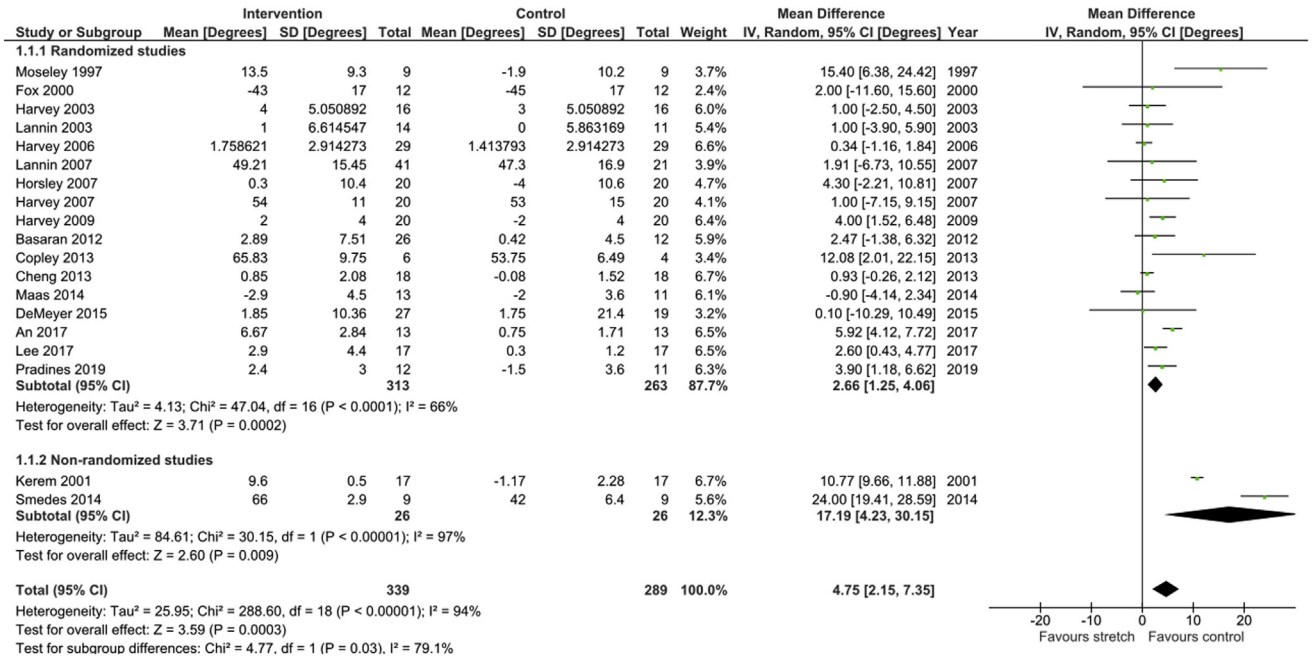

Fig 2 Forest plot showing the mean difference with 95% CI for short-term effects of stretch on joint mobility.

the short-term effect of stretch on joint mobility,[19-40] we were able to obtain pre/post (±SD) measurements of PROM from 19 studies.[19-22,24-26,28-35,37-40] Three of these trials[22,31,37] compared 2 types of stretch interventions with a control situation. For these trials, we combined the experimental groups into 1 single group. The short-term effect of stretch intervention on joint mobility was investigated by pooling data from 17 RCTs with available data. Stretch had a pooled effect of 3° (95% CI, 1-4°; prediction interval (PI) = −2 to 7°; $I^2 = 66\%$; $P < .001$). To explore differences in types of stretch, we explored the use of subgroup analysis. Here, we divided RCT studies in a casting/splinting subgroup and a stretching subgroup (including passive stretching protocols, self-stretching protocols, etc) (see fig 3). The effect of casting/splinting was 2° (95% CI, 0-5°) and the effect of stretching was 3° (95% CI, 1-5°).

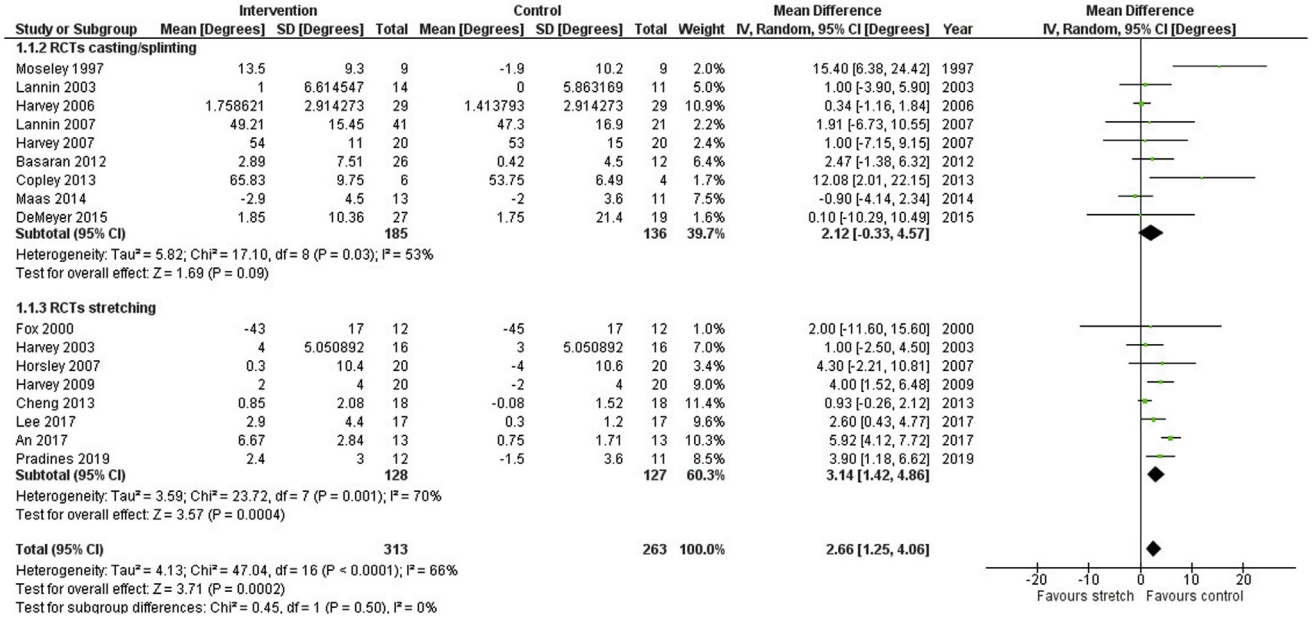

Fig 3 Forest plot with subgroups showing the mean difference with 95% CI for short-term effects of stretch on joint mobility. Stretching includes interventions such as passive stretching and self-stretch protocols.

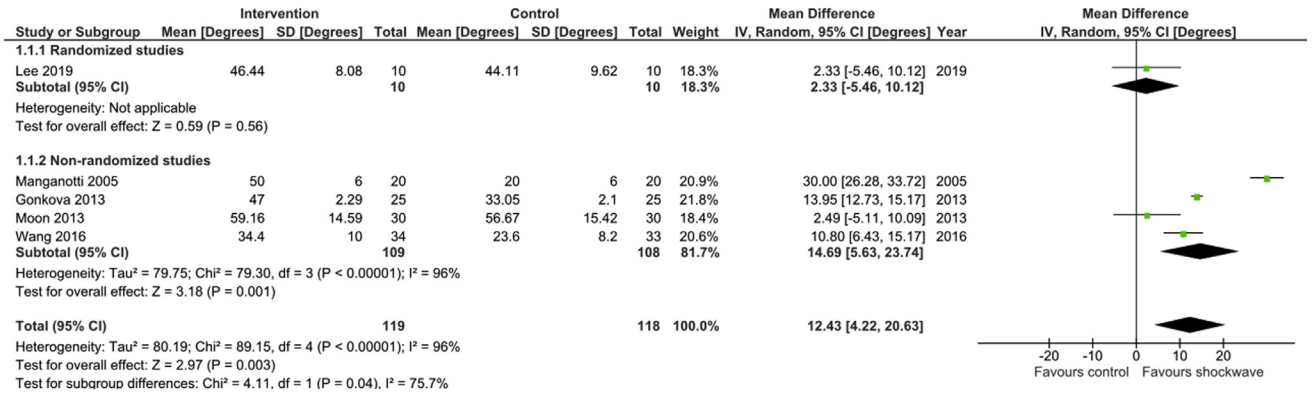

Fig 4 Forest plot showing the mean difference with 95% CI for short-term effects of shock wave therapy on joint mobility.

Effect of shockwave therapy on joint mobility (fig 4)

Of the 6 included trials investigating the effect of shockwave therapy on joint mobility,[50-55] we were able to obtain pre/post (±SD) measurements of PROM from 5 studies.[50-54,89] However, only 1 of these studies was an RCT.[51] The single RCT study had a short-term effect of 2° (95% CI, −5 to 10°; P=.56).

Effect of physical activity on joint mobility (fig 5)

Of the 10 trials investigating the effect of physical activity,[64-73] we obtained pre/post (±SD) measurements of PROM from 9 studies.[64-72] The short-term effect of physical activity on joint mobility was investigated by pooling data from 7 RCTs with available data. Physical activity had a pooled effect of 3° (95% CI, −2 to 8°; PI=−15 to 20°; I^2=87%; P=.28).

Effect of BTX on joint mobility (fig 6)

Of the 8 included trials investigating the effect of BTX on joint mobility,[58-65] we were able to obtain pre/post (±SD) measurements of PROM from 6 studies.[58-63] The short-term effect of BTX on joint mobility was investigated by pooling data from 5 RCTs with available data. BTX had a pooled effect of 4° (95% CI, −1 to 8°; PI=−13 to 20°; I^2=85%; P=.13).

Effect of electrical stimulation on joint mobility (fig 7)

Of the 9 included trials investigating the effect of electrical stimulation on joint mobility,[56-63] we were able to obtain pre/post (±SD) measurements of PROM from 8 studies.[41-47,49] The short-term effect of electrical stimulation on joint mobility was investigated by pooling data from 5 RCTs with available data. Electrical stimulation had a pooled effect of 3° (95% CI, −1 to 6°; PI=−8 to 13°; I^2=78%; P=.11).

Effect of robot-assisted rehabilitation on joint mobility (fig 8)

Of the 5 included trials investigating the effect of robot-assisted rehabilitation on joint mobility,[74-78] we were able to obtain pre/post (±SD) measurements of PROM from 3 studies.[75,77,78] The short-term effect of robot-assisted rehabilitation on joint mobility was investigated by pooling data from 5 RCTs with available data. Robot-assisted rehabilitation had a pooled effect of 1 (95% CI, −0 to 2; PI=−8 to 9; I^2=73%; P=.03).

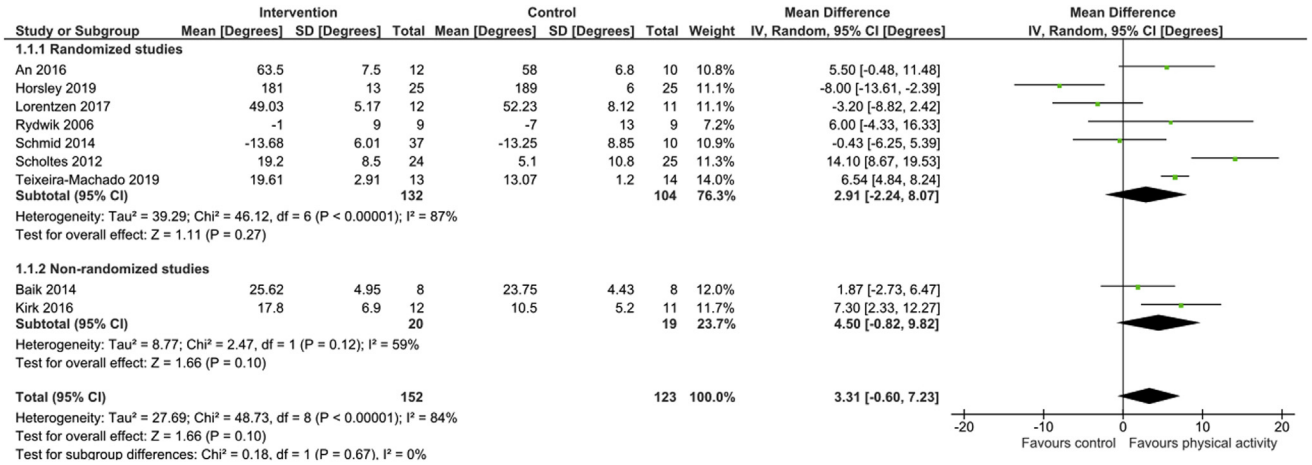

Fig 5 Forest plot showing the mean difference with 95% CI for short-term effects of physical activity on joint mobility.

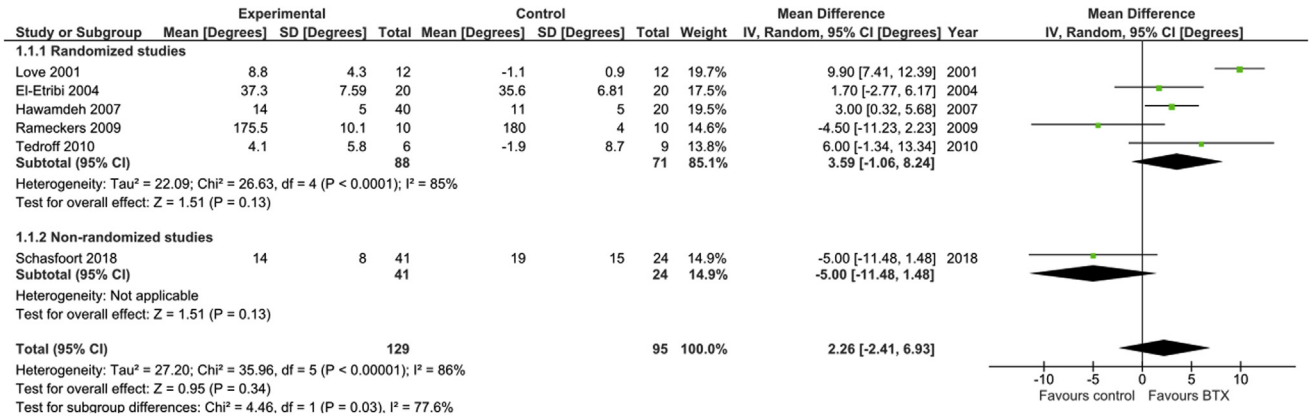

Fig 6 Forest plot showing the mean difference with 95% CI for short-term effects of BTX on joint mobility.

Effect of other interventions on joint mobility

Of the 70 included trials, 10 were not of the abovementioned intervention types. Rayegani et al[79] found significant improvements in hip and ankle PROM after a 2-month passive cycling intervention in individuals with spinal cord injury. Xu et al[80] investigated the effect of 4 weeks of mirror therapy or mirror therapy plus neuromuscular electrical stimulation. Compared with a control group, they found a significant effect of both interventions on ankle dorsiflexion PROM. Mathew et al[82] investigated the effect of the antispasticity drug diazepam in children with cerebral palsy. After 15-20 days of intervention, they found a significant increase in PROM in the group receiving a large dose of diazepam but not in groups receiving placebo treatment or low-dose treatment. Wayne et al[84] investigated the effect of up to 20 sessions of traditional Chinese acupuncture in adults with chronic hemiparesis after stroke. After treatment, they found significant increases in some but not all PROM measures in the acupuncture group compared with the control group. Ghannadi et al[88] investigated the effect of dry needling in adults with stroke and found significant improvements of dorsiflexion PROM after treatment compared with the control group. Trials investigating the effect of neural tension technique,[81] serious games,[83] whole body vibration,[85] stretch combined with resistance training,[86] and high-intensity pulse irradiation with near-infrared rays[87] found no significant effects on joint mobility.

Sensitivity analysis

Table 4 depicts the results of the sensitivity analyses. In the sensitivity analyses, we examined the effect of randomization.

Discussion

In this systematic review, we aimed to determine whether the existing literature supports that nonsurgical treatment options can reduce muscle contractures in individuals with neurologic disorders. Through our systematic search, we found 70 trials (57 RCTs) eligible for inclusion; 22 trials (19 RCTs) on stretch interventions, 6 trials (2 RCTs) on shockwave interventions, 8 trials (7 RCTs) on BTX interventions, 9 trials (5 RCTs) on electrical stimulation interventions, 10 trials (8 RCTs) on physical activity interventions and 5 trials (5 RCTs) on robot-assisted interventions. Additionally, there were 10 single trials on other intervention types. Through meta-analysis and quality assessment, we did not find

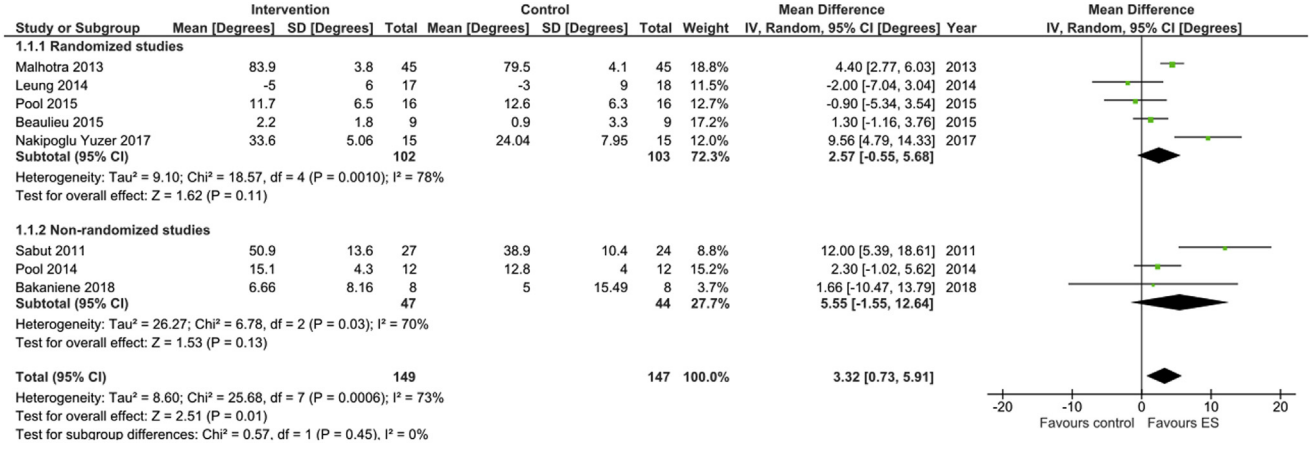

Fig 7 Forest plot showing the mean difference with 95% CI for short-term effects of electrical stimulation on joint mobility.

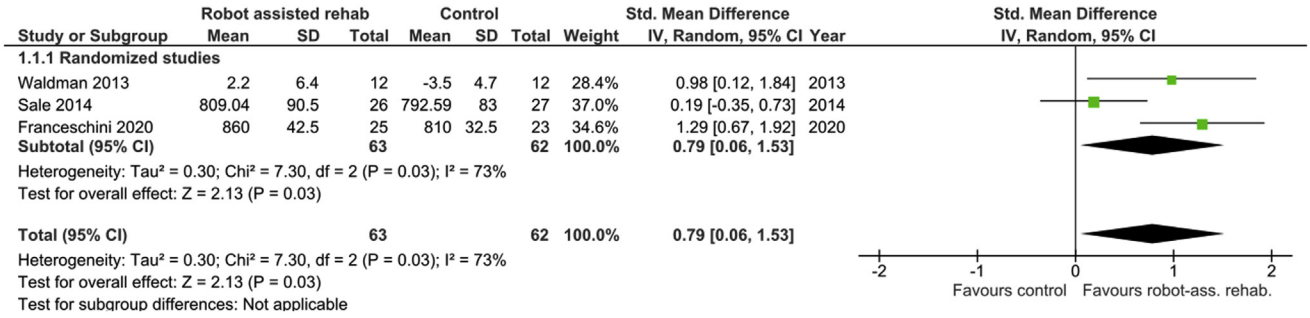

Fig 8 Forest plot showing the mean difference with 95% CI for short-term effects of robot-assisted rehabilitation on joint mobility.

convincing evidence supporting the use of any nonsurgical treatment option.

Similarly to Harvey et al,[11] we do not consider a treatment effect of <5° PROM as clinically important. From the only available RCT on shockwave therapy, we found a nonsignificant effect of 2°. By including the 4 available nonrandomized studies, there was a significant effect of 12° (CI, 4-21°) (see fig 4 and table 4). Based on the Downs and Black checklist, 1 trial was of low quality, 2 were of medium quality, and 2 were of high quality. Perhaps more importantly, 2 of the 5 trials used neither assessor blinding nor an objective measure of joint mobility, thus introducing a large possibility of bias. The trial reporting the largest short-term effect (30°)[50] did not use assessor blinding, an objective measure of joint mobility, or randomization. Four of the 5 trials measured PROM of the ankle joint, 1 measured PROM of the wrist. Four studies used a single session of shockwave therapy, and 1 study used 3 sessions of shockwave therapy. Because of limited data, we were not able to investigate the long-term effect of shockwave treatment through meta-analysis. However, 4 trials did in fact investigate possible sustained effects at follow-up intervals.[50,51,53,54] Gonkova et al[53] found an immediate significant effect of 14° after shockwave treatment; after 4 weeks the effect was 11° and still significant compared with before treatment. Moon et al[54] found a significant 30° effect of the shockwave intervention; at the 4-week follow-up the effect was 20°, and at the 12-week follow-up the effect was 10°. They found significant differences between baseline and measurements immediately after and 4 weeks after intervention. They did not find a statistical difference between baseline and 12-week follow-up measurements. Manganotti et al[50] found an immediate nonsignificant effect of 3°; at the 4-week follow-up this difference was 4° and still nonsignificant compared with baseline. Lee et al[51] found an immediate nonsignificant difference in joint mobility of 2.33° between the control group and the shockwave group; at the 4-week follow-up this difference was 3.55° and still nonsignificant. Because all indications concerning the effect of shockwave therapy are based on only a few trials of limited quality, we encourage cautious interpretations of the results.

From RCTs on stretch and robot-assisted rehabilitation interventions, we found small, clinically nonimportant effects on joint mobility. The estimated effect of stretch interventions was 3° PROM (CI, 1-4°). This finding is roughly consistent with that of the most recent systematic Cochrane review on the effect of stretch interventions on joint mobility in individuals with neurologic disorders by Harvey et al.[14] Harvey[14] found no short-term effect of stretch (mean difference=2° (95% CI, 0-3°). The estimated effect of robot-assisted rehabilitation interventions was 1° PROM (95% CI, 0-2°). We did not find significant effects from RCTs on physical activity (P=.27), electrical stimulation (P=.11), or BTX interventions (P=.13) on joint mobility.

An important finding of this review was the lack of objective measures of muscle contractures found in many trials. Only 18 of the 70 included trials used objective measures of muscle contractures such as passive stiffness or torque-controlled goniometric measurements; most of these were trials investigating the effect of stretch. The remaining 52 trials measured PROM using primarily standard, non—torque-controlled goniometric measurements. Furthermore, these nonobjective measures were used in 23 trials without convincing use of assessor blinding, thus introducing a large possibility of bias. In future research in this field, we strongly advocate the use of objective, instrumented measures such as passive stiffness (eg, measured using the portable stiffness assessment device[90]) or torque-controlled goniometric measurements.

Study limitations

As with all systematic review studies, there is a possibility of retrieval bias—the fact that potentially eligible trials might have been missed. To minimize retrieval bias we chose to use a broad search string, which we tested by its ability to identify already known eligible trials. This strategy resulted in a large amount of identified trials, but we hope that it minimized the amount of missed trials. We are aware of the fact that the inclusion of nonrandomized studies introduces a possibility for bias. To address this issue we based conclusions primarily on meta-analyses performed on RCTs only and performed sensitivity analyses investigating the effect of randomization. In the data extraction process, the reviewers doing the data extraction used subjective judgment to determine if the intervention was administered to treat muscle contractures. We acknowledge that doing this without objective and clear criteria is problematic but believe that this was the best

Table 4 Sensitivity analyses

Variables	Intervention Type						
	Stretch	Shockwave Therapy	Physical Activity	Botox	Electrical Stimulation	Robot-Assisted Rehabilitation
Pooled effect	5° (2 to 7°) n=19	12° (4 to 21°) n=4	3° (−1 to 7°) n=9	2° (−2 to 7°) n=6	3° (1 to 6°) n=8	1° (0 to 2°) n=3
Randomization (studies with adequate sequence allocation)	3° (1 to 4°) n=17	2° (−5 to 10°) n=1	3° (−2 to 8°) n=7	4° (−1 to 8°) n=5	3° (−1 to 6°) n=5	1° (0 to 2°) n=3

NOTE. Pooled effect with all studies included in the analysis and with only randomized trials included. Results are presented as mean difference/standardized mean difference (95% CI). n=no. of studies included in analysis.

possible solution. In the meta-analyses, we combined data from studies on different joints using absolute PROM measures. Although range of motion does differ between joints, we decided to maintain the use of an absolute outcome measure to ensure easy transferability and interpretation in a clinical setting. In all included trials, the severity of contractures at baseline may affect the effect of the intervention. Unfortunately, we were not able to quantify the severity of contractures at baseline because the included trials used different measurement tools, investigated different joints, etc. Similarly, past treatment history is likely to influence the effect of the intervention. Because only a very limited number of studies included information on treatment history, we were not able to include this information. This is therefore a limitation to the study. A possibility of bias is also introduced because 2 of the authors (J.L., J.B.N.) of this review were also authors of included trials. We addressed this possibility of bias by not letting authors extract data from trials in which they had been involved. Despite the fact that all trials were screened by 2 authors and arbitrated by a third review author in case of unsolvable disagreement, we acknowledge the possibility of selection bias in systematic reviews such as this.

Conclusions

The central findings of this systematic review are that effective, nonsurgical treatment of muscle contractures is yet to be convincingly achieved and that there is a need for the use of objective measures of muscle contractures. Future research in this field should focus on the use of an objective measure of muscle contractures, thereby increasing the validity of the trials. We believe that the implementation of such objective measures would advance the continued search for effective, nonsurgical treatment of muscle contractures in individuals with neurologic disorders.

Supplier

a. Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

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References

1. Diong J, Harvey LA, Kwah LK, et al. Incidence and predictors of contracture after spinal cord injurya prospective cohort study. Spinal Cord 2012;50:579-84.
2. Hoang PD, Gandevia SC, Herbert RD. Prevalence of joint contractures and muscle weakness in people with multiple sclerosis. Disabil Rehabil 2014;36:1588-93.
3. Kwah LK, Harvey LA, Diong JHL, Herbert RD. Half of the adults who present to hospital with stroke develop at least one contracture within six months: an observational study. J Physiother 2012;58:41-7.
4. Makki D, Duodu J, Nixon M. Prevalence and pattern of upper limb involvement in cerebral palsy. J Child Orthop 2014;8:215-9.
5. Sackley C, Brittle N, Patel S, et al. The prevalence of joint contractures, pressure sores, painful shoulder, other pain, falls, and depression in the year after a severely disabling stroke. Stroke 2008;39:3329-34.
6. Smith LR, Lee KS, Ward SR, Chambers HG, Lieber RL. Hamstring contractures in children with spastic cerebral palsy result from a stiffer extracellular matrix and increased in vivo sarcomere length. J Physiol 2011;589:2625-39.
7. Lindsay S. Child and youth experiences and perspectives of cerebral palsy: a qualitative systematic review. Child Care Health Dev 2016;42:153-75.
8. Li Z, Zhang N, Wang Y, Cao S, Huang Z, Hu Y. Stair-shaped Achilles tendon lengthening in continuity - a new method to treat equinus deformity in patients with spastic cerebral palsy. Foot Ankle Surg 2019;25:165-8.
9. Dreher T, Buccoliero T, Wolf SI, et al. Long-term results after gastrocnemius-soleus intramuscular aponeurotic recession as a part of multilevel surgery in spastic diplegic cerebral palsy. J Bone Joint Surg Am 2012;94:627-37.
10. Mori L, Marinelli L, Pelosin E, et al. Shock waves in the treatment of muscle hypertonia and dystonia. Biomed Res Int 2014;2014:1-9.
11. Harvey LA, Katalinic OM, Herbert RD, Moseley A, Lannin N, Schurr K. Stretch for the treatment and prevention of contractures. Cochrane Database Syst Rev 2017;1:CD007455.
12. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6:e1000100.
13. Higgins JPT, Thomas J, Chandler J, et al., editors. Cochrane handbook for systematic reviews of interventions version 6.0. London: Cochrane; 2019.
14. Valentine JC, Pigott TD, Rothstein HR. How many studies do you need? A primer on statistical power for meta-analysis. J Educ Behav Stat 2010;35:215-47.
15. Borenstein M. Research note: in a meta-analysis, the I^2 index does not tell us how much the effect size varies across studies. J Physiother 2020;66:135-9.
16. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;52:377-84.
17. Munn J, Sullivan SJ, Schneiders AG. Evidence of sensorimotor deficits in functional ankle instability: a systematic review with meta-analysis. J Sci Med Sport 2010;13:2-12.
18. Cabral EEA, Fregonezi GAF, Melo L, Basoudan N, Mathur S, Reid WD. Surface electromyography (sEMG) of extradiaphragm respiratory muscles in healthy subjects: a systematic review. J Electromyogr Kinesiol 2018;42:123-35.
19. Fox P, Mcinnes B, Bedard M. Effectiveness of a bed positioning program for treating older adults with knee contractures who are institutionalized. Phys Ther 2000;80:363-72.
20. Maas JC, Dallmeijer AJ, Huijing PA, et al. A randomized controlled trial studying efficacy and tolerance of a knee-ankle-foot orthosis used to prevent equinus in children with spastic cerebral palsy. Clin Rehabil 2014;28:1025-38.
21. Copley J, Kuipers K, Fleming J, Rassafiani M. Individualised resting hand splints for adults with acquired brain injury: a randomized, single blinded, single case design. Neuro-Rehabilitation 2013;32:885-98.
22. DeMeyer L, Brown M, Adams A. Effectiveness of a night positioning programme on ankle range of motion in patients after hemiparesis: a prospective randomized controlled pilot study. J Rehabil Med 2015;47:873-7.
23. Beckerman H, Becher J, Lankhorst GJ, Verbeek ALM, Vogelaar TW. The efficacy of thermocoagulation of the tibial nerve and a polypropylene ankle-foot orthosis on spasticity of the leg in stroke patients: results of a randomized clinical trial. Clin Rehabil 1996;10:112-20.
24. Harvey L, De Jong I, Goehl G, Marwedel S. Twelve weeks of nightly stretch does not reduce thumb web-space contractures in people with a neurological condition: a randomised controlled trial. Aust J Physiother 2006;52:251-8.
25. Kerem M, Livanelioglu A, Topcu M. Effects of Johnstone pressure splints combined with neurodevelopmental therapy on spasticity and cutaneous sensory inputs in spastic cerebral palsy. Dev Med Child Neurol 2001;43:307-13.
26. Harvey LA, Herbert RD, Glinsky J, Moseley AM, Bowden J. Effects of 6 months of regular passive movements on ankle joint mobility in people with spinal cord injury: a randomized controlled trial. Spinal Cord 2009;47:62-6.
27. Theis N, Korff T, Mohagheghi AA. Does long-term passive stretching alter muscle-tendon unit mechanics in children with spastic cerebral palsy? Clin Biomech 2015;30:1071-6.
28. Harvey LA, Byak AJ, Ostrovskaya M, Glinsky J, Katte L, Herbert R. Randomised trial of the effects of four weeks of daily stretch on extensibility of hamstring muscles in people with spinal cord injuries. Aust J Physiother 2003;49:176-81.
29. Cheng HYK, Ju YY, Chen CL, Chang YJ, Wong AMK. Managing lower extremity muscle tone and function in children with cerebral palsy via eight-week repetitive passive knee movement intervention. Res Dev Disabil 2013;34:554-61.
30. Lannin NA, Horsley SA, Herbert R, McCluskey A, Cusick A. Splinting the hand in the functional position after brain impairment: a randomized, controlled trial. Arch Phys Med Rehabil 2003;84:297-302.
31. Basaran A, Emre U, Karadavut K, Balbaloglu O, Bulmus N. Hand splinting for poststroke spasticity: a randomized controlled trial. Top Stroke Rehabil 2012;19:329-37.
32. Moseley AM. The effect of casting combined with stretching on passive ankle dorsiflexion in adults with traumatic head injuries. Phys Ther 1997;77:240-7.
33. Pradines M, Ghedira M, Portero R, et al. Ultrasound structural changes in triceps surae after a 1-year daily self-stretch program: a prospective randomized controlled trial in chronic hemiparesis. Neurorehabil Neural Repair 2019;33:245-59.
34. Lee J, Kim JO, Lee BH. The effects of posterior talar glide with dorsiflexion of the ankle on mobility, muscle strength and balance in stroke patients: a randomised controlled trial. J Phys Ther Sci 2017;29:452-6.
35. Harvey L, Simpson D. Does three months of nightly splinting reduce the extensibility of the flexor pollicis longus muscle in people with tetraplegia? Physiother Res Int 2007;12:5-13.
36. Hill J. The effects of casting on upper extremity motor disorders after brain injury. Am J Occup Ther 1994;48:219-24.
37. Lannin NA, Cusick A, McCluskey A, Herbert RD. Effects of splinting on wrist contracture after stroke: a randomized controlled trial. Stroke 2007;38:111-6.
38. Smedes F, Van Der Salm A, Koel G, Oosterveld F. Manual mobilization of the wrist: a pilot study in rehabilitation of patients with a chronic hemiplegic hand post-stroke. J Hand Ther 2014;27:209-16.

39. Horsley SA, Herbert RD, Ada L. Four weeks of daily stretch has little or no effect on wrist contracture after stroke: a randomised controlled trial. Aust J Physiother 2007;53:239-45.
40. An CM, Jo SO. Effects of talocrural mobilization with movement on ankle strength, mobility, and weight-bearing ability in hemiplegic patients with chronic stroke: a randomized controlled trial. J Stroke Cerebrovasc Dis 2017;26:169-76.
41. Pool D, Blackmore AM, Bear N, Valentine J. Effects of short-term daily community walk aide use on children with unilateral spastic cerebral palsy. Pediatr Phys Ther 2014;26:308-17.
42. Pool D, Valentine J, Bear N, Donnelly CJ, Elliott C, Stannage K. The orthotic and therapeutic effects following daily community applied functional electrical stimulation in children with unilateral spastic cerebral palsy: a randomised controlled trial. BMC Pediatr 2015;15:1-10.
43. Sabut SK, Sikdar C, Kumar R, Mahadevappa M. Functional electrical stimulation of dorsiflexor muscle: effects on dorsiflexor strength, plantarflexor spasticity, and motor recovery in stroke patients. NeuroRehabilitation 2011;29:393-400.
44. Bakaniene I, Urbonaviciene G, Janaviciute K, Prasauskiene A. Effects of the inerventions method on gross motor function in children with spastic cerebral palsy. Neurol Neurochir Pol 2018;52:581-6.
45. Malhotra S, Rosewilliam S, Hermens H, Roffe C, Jones P, Pandyan AD. A randomized controlled trial of surface neuromuscular electrical stimulation applied early after acute stroke: effects on wrist pain, spasticity and contractures. Clin Rehabil 2013;27:579-90.
46. Nakipoğlu Yuzer GF, Köse Dönmez B, Özgirgin N. A randomized controlled study: effectiveness of functional electrical stimulation on wrist and finger flexor spasticity in hemiplegia. J Stroke Cerebrovasc Dis 2017;26:1467-71.
47. Leung J, Harvey LA, Moseley AM, Whiteside B, Simpson M, Stroud K. Standing with electrical stimulation and splinting is no better than standing alone for management of ankle plantarflexion contractures in people with traumatic brain injury: a randomised trial. J Physiother 2014;60:201-8.
48. Sabut SK, Sikdar C, Mondal R, Kumar R, Mahadevappa M. Restoration of gait and motor recovery by functional electrical stimulation therapy in persons with stroke. Disabil Rehabil 2010;32:1594-603.
49. Beaulieu LD, Massé-Alarie H, Brouwer B, Schneider C. Noninvasive neurostimulation in chronic stroke: a double-blind randomized sham-controlled testing of clinical and corticomotor effects. Top Stroke Rehabil 2015;22:8-17.
50. 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.
51. Lee CH, Lee SH, Yoo J Il, Lee SU. 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.
52. Wang T, Du L, Shan L, et al. A prospective case-control study of radial extracorporeal shock wave therapy for spastic plantar flexor muscles in very young children with cerebral palsy. Medicine (Baltimore) 2016;95:1-13.
53. Gonkova MI, Ilieva EM, Ferriero G, Chavdarov I. Effect of radial shock wave therapy on muscle spasticity in children with cerebral palsy. Int J Rehabil Res 2013;36:284-90.
54. 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.
55. Vidal X, Morral A, Costa L, Tur M. Radial extracorporeal shock wave therapy (rESWT) in the treatment of spasticity in cerebral palsy: a randomized, placebo-controlled clinical trial. NeuroRehabilitation 2011;29:413-9.
56. Love SC, Valentine JP, Blair EM, Price CJ, Cole JH, Chauvel PJ. The effect of botulinum toxin type A on the functional ability of the child with spastic hemiplegia a randomized controlled trial. Eur J Neurol 2001;8:50-8.
57. Hawamdeh ZM, Ibrahim AI, Al-Qudah AA. Long-term effect of botulinum toxin (A) in the management of calf spasticity in children with diplegic cerebral palsy. Eura Medicophys 2007;43:311-8.
58. Rameckers EAA, Speth LAWM, Duysens J, Vles JSH, Smits-Engelsman BCM. Botulinum toxin-A in children with congenital spastic hemiplegia does not improve upper extremity motor-related function over rehabilitation alone: a randomized controlled trial. Neurorehabil Neural Repair 2009;23:218-25.
59. Meythaler JM, Vogtle L, Brunner RC. A preliminary assessment of the benefits of the addition of botulinum toxin A to a conventional therapy program on the function of people with longstanding stroke. Arch Phys Med Rehabil 2009;90:1453-61.
60. Tedroff K, Löwing K, Haglund-ÅKerlind Y, Gutierrez-Farewik EM, Forssberg H. Botulinumtoxin A treatment in toddlers with cerebral palsy. Acta Paediatr Int J Paediatr 2010;99:1156-62.
61. Koman LA, Mooney JF, Smith BP, Walker F, Leon JM. Botulinum toxin type A improved ankle function in children with cerebral palsy and dynamic equinus foot deformity. J Bone Joint Surg Am 2000;20:108-15.
62. Schasfoort F, Pangalila R, Sneekes E, et al. Intramuscular botulinum toxin prior to comprehensive rehabilitation has no added value for improving motor impairments, gait kinematics and goal attainment in walking children with spastic cerebral palsy. J Rehabil Med 2018;50:732-42.
63. El-Etribi MA, Salem ME, El-Shakankiry HM, El-Kahky AM, El-Mahboub SM. The effect of botulinum toxin type-A injection on spasticity, range of motion and gait patterns in children with spastic diplegic cerebral palsy: an Egyptian study. Int J Rehabil Res 2004;27:275-81.
64. Horsley S, Lannin NA, Hayward KS, Herbert RD. Additional early active repetitive motor training did not prevent contracture in adults receiving task-specific upper limb training after stroke: a randomised trial. J Physiother 2019;65:88-94.
65. Scholtes VA, Becher JG, Janssen-Potten YJ, Dekkers H, Smallenbroek L, Dallmeijer AJ. Effectiveness of functional progressive resistance exercise training on walking ability in children with cerebral palsy: a randomized controlled trial. Res Dev Disabil 2012;33:181-8.
66. Schmid AA, Miller KK, Van Puymbroeck M, DeBaun-Sprague E. Yoga leads to multiple physical improvements after stroke, a pilot study. Complement Ther Med 2014;22:994-1000.
67. Rydwik E, Eliasson S, Akner G. The effect of exercise of the affected foot in stroke patients - a randomized controlled pilot trial. Clin Rehabil 2006;20:645-55.
68. Baik K, Byeun JK, Baek JK. The effects of horseback riding participation on the muscle tone and range of motion for children with spastic cerebral palsy. J Exerc Rehabil 2014;10:265-70.
69. Lorentzen J, Kirk H, Fernandez-Lago H, et al. Treadmill training with an incline reduces ankle joint stiffness and improves active range of movement during gait in adults with cerebral palsy. Disabil Rehabil 2017;39:987-93.
70. Kirk H, Geertsen SS, Lorentzen J, Krarup KB, Bandholm T, Nielsen JB. Explosive resistance training increases rate of force development in ankle dorsiflexors and gait function in adults with cerebral palsy. J Strength Cond Res 2016;30:2749-60.
71. An CM, Won JI. Effects of ankle joint mobilization with movement and weight-bearing exercise on knee strength, ankle range of motion, and gait velocity in patients with stroke: a pilot study. J Phys Ther Sci 2016;28:689-94.
72. Teixeira-Machado L, DeSantana J. Effect of dance on lower-limb range of motion in young people with cerebral palsy: a blinded randomized controlled clinical trial. Adolesc Health Med Ther 2019;10:21-8.

73. Hemachithra C, Meena N, Ramanathan R, Felix AJW. Immediate effect of horse riding simulator on adductor spasticity in children with cerebral palsy: a randomized controlled trial. Physiother Res Int 2020;25:1-6.
74. Mirbagheri MM, Kindig MW, Niu X. Effects of robotic-locomotor training on stretch reflex function and muscular properties in individuals with spinal cord injury. Physiol Behav 2015;126:997-1006.
75. Waldman G, Yang CY, Ren Y, et al. Effects of robot-guided passive stretching and active movement training of ankle and mobility impairments in stroke. NeuroRehabilitation 2013;32:625-34.
76. Mirbagheri MM. Comparison between the therapeutic effects of robotic-assisted locomotor training and an anti-spastic medication on spasticity. Proc Annu Int Conf IEEE Eng Med Biol Soc 2015;2015:4675-8.
77. Franceschini M, Mazzoleni S, Goffredo M, et al. Upper limb robot-assisted rehabilitation versus physical therapy on subacute stroke patients: a follow-up study. J Bodyw Mov Ther 2020;24:194-8.
78. Sale P, Franceschini M, Mazzoleni S, Palma E, Agosti M, Posteraro F. Effects of upper limb robot-assisted therapy on motor recovery in subacute stroke patients. J Neuroeng Rehabil 2014;11:1-8.
79. Rayegani SM, Shojaee H, Sedighipour L, Soroush MR, Baghbani M, Amirani OB. The effect of electrical passive cycling on spasticity in war veterans with spinal cord injury. Front Neurol 2011;2:39.
80. Xu Q, Guo F, Salem HMA, Chen H, Huang X. Effects of mirror therapy combined with neuromuscular electrical stimulation on motor recovery of lower limbs and walking ability of patients with stroke: a randomized controlled study. Clin Rehabil 2017;31:1583-91.
81. Lorentzen J, Nielsen D, Holm K, Baagøe S, Grey MJ, Nielsen JB. Neural tension technique is no different from random passive movements in reducing spasticity in patients with traumatic brain injury. Disabil Rehabil 2012;34:1978-85.
82. Mathew A, Mathew MC, Thomas M, Antonisamy B. The efficacy of diazepam in enhancing motor function in children with spastic cerebral palsy. J Trop Pediatr 2005;51:109-13.
83. Velasco MA, Raya R, Muzzioli L, et al. Evaluation of cervical posture improvement of children with cerebral palsy after physical therapy based on head movements and serious games. Biomed Eng Online 2017;16(Suppl 1):157-69.
84. Wayne PM, Krebs DE, Macklin EA, et al. Acupuncture for upper-extremity rehabilitation in chronic stroke: a randomized sham-controlled study. Arch Phys Med Rehabil 2005;86:2248-55.
85. Cheng HYK, Yu YC, Wong AMK, Tsai YS, Ju YY. Effects of an eight-week whole body vibration on lower extremity muscle tone and function in children with cerebral palsy. Res Dev Disabil 2015;38:256-61.
86. Fosdahl MA, Jahnsen R, Kvalheim K, Holm I. Stretching and progressive resistance exercise in children with cerebral palsy: a randomized controlled trial. Pediatr Phys Ther 2019;31:264-71.
87. Takeuchi N, Takezako N, Shimonishi Y, Usuda S. Effects of high-intensity pulse irradiation with linear polarized near-infrared rays and stretching on muscle tone in patients with cerebrovascular disease: a randomized controlled trial. J Phys Ther Sci 2017;29:1449-53.
88. Ghannadi S, Shariat A, Ansari NN, et al. The effect of dry needling on lower limb dysfunction in poststroke survivors. J Stroke Cerebrovasc Dis 2020;29:104814.
89. 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.
90. Yamaguchi T, Hvass Petersen T, Kirk H, et al. Spasticity in adults with cerebral palsy and multiple sclerosis measured by objective clinically applicable technique. Clin Neurophysiol 2018;129:2010-21.