CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Stroke Rehabilitation Evidence Tables

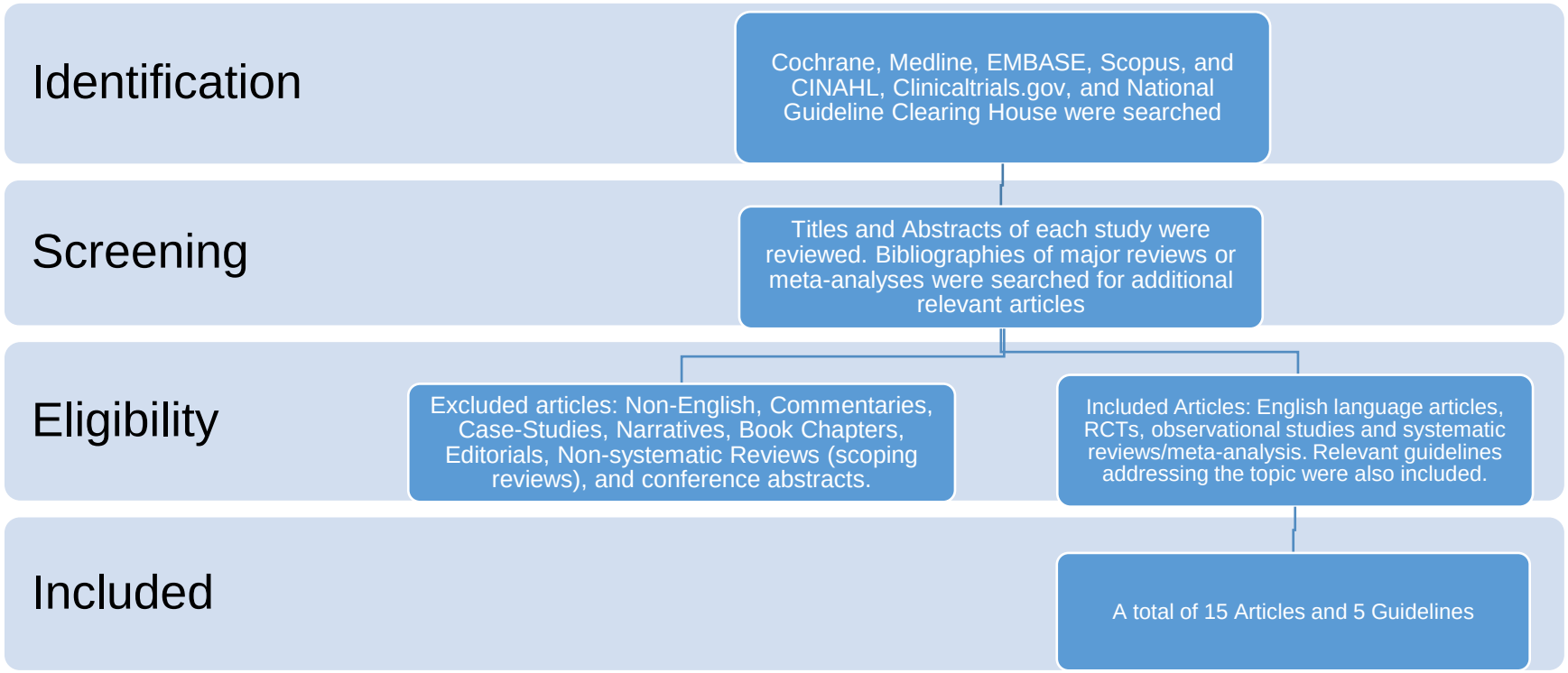
Lower Limb Spasticity following Stroke

Hebert, D, Teasell, R (Writing Group Chairs)
on Behalf of the Canadian Stroke Best Practice Recommendations
STROKE REHABILITATION Writing Group

December 2015

Table of Contents

Search Strategy



Cochrane, clinicaltrials.gov, Medline, EMBASE, CINAHL and Scopus were searched using the keywords: Stroke AND (“spasticity” OR “contracture”) AND (“lower extremity” OR “lower limb”) AND (rehabilitation OR therapy OR intervention). Three new sections: shock wave therapy, stretching, and vibration were added for the 2014 update. Titles and abstract of each article were reviewed for relevance. The same databases were searched to identify paediatric related evidence using the keywords: (stroke OR CVD OR cerebrovascular disease) AND (rehabilitation OR intervention OR therapy) AND (paediatric OR paediatrics OR youth OR child OR children OR young) AND ("Lower Limb" OR "lower extremity" OR gait OR mobility OR falls). Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 15 and 5 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: rehabilitation, prevention and management of complications, and discharge planning. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2010 Jun. 101 p.31	(NB-recommendations not specific to the lower extremity) **4.9.1 Summary of recommendations** **Not recommended** routine resting splinting of the upper limb *Clostridium botulinum* toxin type A **Insufficient evidence** routine functional electrical stimulation robot-mediated passive therapy oral antispasticity agents intrathecal antispasticity agents alcohol neurolysis tibial nerve neurotomy
Management of Stroke Rehabilitation Working Group. VA/DoD clinical practice guideline for the management of stroke rehabilitation. Washington (DC): Veterans Health Administration, Department of Defense; 2010. p. 86-88.	(NB-recommendations not specific to the lower extremity) Use of antispastic positioning, range of motion exercises, stretching, splinting, serial casting or surgical correction for spasticity. **C** Use of tizanidine (in chronic stroke patients), dantrolene, and oral baclofen for spasticity **B** Avoid drugs with central nervous system effects that may impair recovery **D** Use of botulinum toxin improves spasticity **B** Use of intrathecal baclofen for chronic stroke patients **B** Use of certain neurosurgical procedures **I**
Clinical Guidelines for Stroke Management 2010. Melbourne (Australia): National Stroke Foundation; 2010 Sep. p. 99.	(NB-recommendations not specific to the lower extremity) Interventions to decrease spasticity other than an early comprehensive therapy program should NOT be routinely provided for people who have mild to moderate spasticity (i.e. spasticity that does not interfere with a stroke survivor's activity or personal care) **GPP** In stroke survivors who have persistent moderate to severe spasticity (i.e. spasticity that does not interfere with a stroke survivor's activity or personal care): Botulinum toxin A should be trialed in conjunction with rehabilitation therapy which includes setting clear goals. **B** Electrical stimulation and/or EMG biofeedback can be used. **C** **Contracture** Conventional therapy (i.e. early tailored interventions) should be provided for stroke survivors at risk who have developed contracture. **GPP** For stroke survivors at risk of, or who have developed contractures and are undergoing comprehensive rehabilitation, the routine use of splints or prolonged positioning of muscles in a lengthened position is NOT recommended. **C** Overhead pulley exercises should NOT be used routinely to maintain ROM of the shoulder **C** Serial casting can be used to reduce severe, persistent contracture when conventional therapy has failed. **GPP**
Duncan PW, Zorowitz R, Bates B, Choi JY, Glasberg JJ, Graham GD, Katz RC, Lamberty	(NB-recommendations not specific to the lower extremity)

Guideline	Recommendations
K, Reker D. Management of adult stroke rehabilitation care: a clinical practice guideline. Stroke, 2005;36:e129.	Use of antispastic positioning, range of motion exercises, stretching, splinting, serial casting, or surgical correction for spasticity. **C** Use of tizanidine (in chronic stroke patients), dantrolene, and oral baclofen for spasticity. **D** Use of central nervous system effects may deteriorate recovery. **B** Use of botulinum toxin and phenol/alcohol to treat spasticity. **B** Use of intrathecal baclofen for chronic stroke patients **C** Use of certain neurosurgical procedures. **I**
Intercollegiate Stroke Working Party. *National clinical guideline for stroke,* 4th edition. London: Royal College of Physicians, 2012.	**6.10 Impaired tone – spasticity and spasms** *6.10.1 Recommendations* A Any patient with motor weakness should be assessed for the presence of spasticity as a cause of pain, as a factor limiting activities or care, and as a risk factor for the development of contractures. B For all the interventions given below, specific goals should be set and monitored using appropriate clinical measures (eg numerical rating scales for ease of care (eg Arm Activity measure (ArmA)) or pain (eg 10-point numerical rating scale), the modified Ashworth scale, and range of movement). C In any patient where spasticity is causing concern, the extent of the problem should be monitored and simple procedures to reduce spasticity should be started. This may include positioning, active movement and monitoring range of movement for deterioration of function, passive movement and pain control. D Patients with persistent or progressing troublesome focal spasticity affecting one or two joints and in whom a therapeutic goal can be identified (usually ease of care also referred to as passive function) should be given intramuscular botulinum toxin. This should be in the context of a specialist multidisciplinary team service accompanied by rehabilitation therapy or physical maintenance strategies (eg splinting or casting) over the next 2–12 weeks following botulinum toxin injection. Functional assessment should be carried out at 3–4 months post injection and further botulinum toxin and physical treatments planned as required. E For patients experiencing troublesome general spasticity after initial treatment, antispastic drugs should be tried unless contraindicated. Either baclofen or tizanidine should be tried first. Other drugs and combinations of drugs should only be started by people with specific expertise in managing spasticity. F Intrathecal baclofen, intra-neural phenol and other rare procedures should only be used in the context of a specialist multidisciplinary spasticity service or a clinical trial.

GPP Good Practice Point

Summary of Spasticity Interventions and Associated Strength of Evidence from Selected Guideline Documents

Intervention	CBPR 2013	SIGN 118 2010*	NSF 2010*	VA/DoD 2010 *	AHA/ASA 2005*	RCP 2012*
Positioning/ROM exercises	Recommended	Not included	Not included	C	C	Recommended
Splinting	Not included	A Not recommended	B Not recommended for contracture	C	C	Not Included
BT-type A	Recommends	Not recommended	B	B	B	Recommended
Phenol/alcohol	Not included	I	Not included	Not included	B	Not Included
Oral agents	Recommends (Tizanidine)	I	Not included	B (Tizanidine for chronic), oral baclofen)	B (Tizanidine, dantrolene, oral baclofen)	Recommneded (baclofen, Tizanidine)
Benzodazepines	Not recommended	Not included	Not included	D Not recommended	Not included	Not Included
Electrical stimulation	Not included	I	C	Not included	Not included	Not Included
Robotic devices	Not included	I	Not included	Not included		Not Included
Intrathecal agents	Not included	I	Not included	No recommendation for UE	C	Not Included
Surgery	Not included	I	Not included	I (spasticity) C (contracture)	I	Not Included

I: Insufficient evidence to recommend for/against providing intervention
* General recommendations regarding spasticity, not specific to LE

Evidence Tables

Botulinum Toxin-Type A (BT-A)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Picelli et al. 2014 **Italy** **RCT**	CA: ☑ Blinding: Assessor ☒ Patient ☑ ITT: ☒	30 patients with chronic stroke and spastic equinus (MAS >1), at least 6 months post stroke.	Subjects were randomized to one of three groups: 1) therapeutic ultrasound (US) to the affected leg calf muscles, 2) transcutaneous electrical nerve stimulation (TENS) to the tibial nerve of the affected leg, 3) onabotulinum toxin A (BoNT-A) in the spastic gastrocnemius.	**Primary Outcomes:** MAS Outcomes were assessed immediately before treatment and 15, 30, and 90 days after treatment.	MAS was significantly different between groups at 30 days (p=.002) and 90 days (p=0.005), whereby patients in the BoNT-A group had greater improvement on the MAS than those receiving US and TENS at 30 days (p=0.002 and p=0.003, respectively) and 90 days (p=0.006 and p=0.006, respectively). No significant difference in outcome was noted between those receiving US and TENS groups (p>0.05).
Sanamato et al. 2013a **Italy** **Pre-Post**	N/A	71 patients with post-stroke spasticity (MAS=2, ankle flexors); mean time since stroke 28.8±12.9 months.	Subjects received intramuscular injections of onabotulinum toxin A (BoNT-A) NT 201 in the soleus, and medial and lateral gastrocnemius with a maximum dose of 180 U (range 25-100 U per muscle).	**Primary Outcomes:** MAS, Spasm Frequency Scale (SFS) Outcomes were assessed at baseline, 30 days and 90 days after treatment.	A reduction was noted at 30 days and 90 days in MAS (p<0.001 for both) and SFS (p<0.001 for both).
Sanamato et al. 2013b **Italy** **Pre-Post**	N/A	25 subjects with upper and lower limb spasticity (AS≥2, Disability Assessment Scale [DAS] ≥2, ankle flexors) with mean time since stroke 32.4±8.3 months.	Subjects received one set of injections of onabotulinum toxin A (BoNT-A) NT 201, in the lower limbs. A dosage of maximum 340 U (range 250-340 U per muscle) was administered.	**Primary Outcomes:** MAS, Disability Assessment Scale Outcomes were assessed at baseline, 30 days and 90 days after treatment.	A significant reduction in spasticity was noted for both MAS and DAS at 30 days (p<0.001 for both) and 90 days (p<0.001 for both) after treatment.
Foley et al. 2010 **Canada** **Systematic review and meta-analysis**	N/A	8 trials (5 RCTs, 3 uncontrolled trials)(228 subjects) that examined the use of BT-A for the treatment of spastic equinovarus deformity. Subjects in all trials could ambulate with/without a	Comparisons of a single injection of BT-A vs. placebo or before and after single injection. Doses varied from 190 to 400 U of Botox and 500 to 2,000 U of Dysport	**Primary Outcomes:** Gait speed Outcome was assessed at baseline and from 4 weeks to 5 months	Gait speed: SMD= 0.193±0.081, 95% CI 0.033 to 0.353, p<0.018

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		device and with/without assistance for at least 5 metres Mean of median interval from stroke to entry into study was > 6 months if all trials.			
Kaji et al. 2010 **Japan** **RCT**	CA: ☑ Blinding: Assessor ☑ Patient ☑ ITT: ☑	120 patients from 19 medical institutions with lower limb spasticity (MAS>3 ankle flexors) following stroke > 6 months previously	Subjects were randomized to receive a single treatment of 300 U Botox or placebo. 75 U was injected per muscle group Sites included: gastrocnemius, soleus and tibialis posterior	**Primary Outcomes:** MAS **Secondary Outcomes:** Gait pattern scale assessed using a -1 to 9 point scale, based on 3 parameters over 10m (initial foot contact, foot contact at midstance and gait assisting devices), gait speed. Clinical Global Impression scale (CGI) scored from -5 to 5. Outcomes were assessed at baseline, weeks 1,4,6,8 and 12.	Mean ±sd Δ from baseline at 12 weeks for subjects in experimental and control groups MAS: -0.56±0.69 vs. -0.40±0.58, p=0.240 (p<0.05 at weeks 4 and 8) Gait pattern scale: 0.55±1.26 vs. 0.58±1.57, p=0.775 Gait speed (sec over 10 m): -10.14±26.93 vs. -8.53±24.71, p=0.585 CGI (investigator): 0.81±1.30 vs. 0.52±1.27, p=0.166 CGI (patient): 0.49±1.53 vs. 0.49±2.18, p=0.409 Drop outs: experimental group n=6, control group n=1 Adverse events (serious): experimental group n=9%, control group n=2%
Dunne et al. 2012 **Australia** **RCT with open-label extension**	CA: ☑ Blinding: Assessor ☑ Patient☑ ITT: ☑	85 stroke patients (≥ 6 weeks post stroke), with lower extremity hypertonia (AS≥2)	Subjects received a single injection of 200 U Botox (n=28), 300 U Botox (n=28) or saline injections to the tibialis posterior, soleus and flexor digitorum longus or medial gastrocnemius.	**Primary Outcomes:** Adverse event incidence, MAS (ankle plantarflexors) **Secondary Outcomes:** Self-reported spasm frequency, physician rated hypertonia (7- point likert scale). Assessments were conducted at baseline (on 2	Data from the 2 Botox groups were not different and combined. Adverse events (serious): experimental group n=6, placebo group n=3. Improvement in AS≥1 at 12 weeks BT-A group vs. placebo: 16/54 vs. 5/29, p=0.22 Reduction in leg spasms at 12 weeks: BT-A group vs. placebo: 22/26 vs. 4/19, p=0.01 Improvement in Physician rating of hypertonia of

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				occasions) and at 4, 8, and 12 weeks post injection	≥1 at 12 weeks BT-A group vs. placebo: 29/54 vs. 8/29, p=0.04 Improvement in pain (≥20%) at 12 weeks BT-A group vs. placebo: 8/14 vs. 1/8, p=0.02 Increase in ankle dorsiflexion (≥15%) at 12 weeks BT-A group vs. placebo: 8/54 vs. 1/29, p=0.03 Drop outs: n=5 (all experimental group)

Intrathecal Baclofen (ITB)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Meythaler et al. 2001 **USA** **Randomized crossover screening period followed by open-label follow-up**	Screening period: assessor ☑ patient ☑ Open-label portion: assessor ☒ patient ☒ ITT: ☒	21 subjects with disabling and painful intractable hypertonia (AS score of at least 3 in one affected extremity or an average spasm score of at least 2 in the affected extremities on the day of screening) following stroke of at least 6 months duration, and failure to respond to oral antispasticity medications.	Subjects were randomized to receive a screening bolus trial of either 50 µg baclofen or saline placebo. 17 subjects responded to the active drug and were then implanted with a continuous-infusion pump and continued to receive treatment for up to a year. Subjects were initiated to continued treatment at 100 µg/day with dose increases up to an average of 268 ± 175 µg/day.	**Primary Outcome:** AS (average of hip abduction, knee flexion, knee extension, ankle dorsiflexion) **Secondary Outcomes:** 5-point Penn Spasm Frequency Scale, 6-point reflex scale (patella, Achilles) At 1 year, data from 13 subjects were available.	Mean (± sd) scores at baseline and 12 months AS: 3.7 ± 1.0 to 1.8 ±1.1, p<0.0001. Spasm score: 1.2±1.3 to 0.6±1.0, p=ns Reflex Score: 2.4 ±1.3 to 1.0±1.3, <0.0001 3 subjects who were wheelchair dependent at the start of treatment progressed to independent ambulation with assistive devices. Adverse events: Several mild and transient adverse events were reported.

Physical Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kluding et al. 2008 **RCT** **USA**	CA: ☑ Blinding: Assessor ☒ ITT: ☒	16 subjects with hemiparesis persisting from 6 months to 5 years following stroke with less than 8° of passive ankle dorsiflexion ROM on the hemiparetic side.	Subjects were randomized to receive 8 sessions lasting 30 minutes each over 4 weeks of either functional task practice (FP) combined with ankle joint mobilizations or functional task practice only.	**Primary Outcomes:** Ankle ROM, ankle kinematics during sit-to-stand (STS) and gait, and lower-extremity weight-bearing symmetry during STS and static standing, Rivermead Mobility Index (RMI) Outcome measures were assessed before and after treatment.	Mean ±sd change scores for subjects in the mobilization + FP and FP groups Dorsiflexion passive ROM (deg): 5.7 ±3.1 vs. 0.2±2.6, p<0.01 Total active ROM (deg): 17.3±6.5 vs. 2.3±7.6, p<0.05 Peak dorsiflexion: STS (deg):-1.88±4.72 vs. 1.42±3.93, p=ns Peak dorsiflexion: gait (deg): 0.38±3.44 vs. 2.58±8.14, p=ns Peak weight bearing difference during STS (deg): -0.79±4.9 vs. -14.9±15.0, p<0.05 STS time (sec); -0.82±0.91 vs. 0.17±0.77, p<0.05 RMI: 0.75±0.71 vs. 0.63±1.1, p<0.05 Drop outs: n=1 (control group) Adverse events: None related to intervention

Shock Wave Therapy

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Santamato et al. 2014 **Italy** **Pre-Post**	N/A	23 subjects with unilateral spastic equinus foot (MAS range 1-4) 24.9±11.9 months post stroke.	Subjects received one extracorporeal shock wave therapy session applied with the EvoTron RFL0300; 1,500 pulses were applied at an intensity of 0.10 mJ/mm^2. Targeted muscles	**Primary Outcomes:** MAS stratified by Heckmatt grade (muscle echo intensity) Patients were evaluated immediately after treatment and at 30 days post treatment.	For those with Heckmatt grades I, II, and III, MAS scores were significantly reduced immediately after treatment (p<0.001) and at 30 days post treatment (p<0.001). For those with a Heckmatt grade of IV, MAS scores did not improve (p>0.05).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			included gastrocnemius and soleus.		
Moon et al. 2013 **Korea** **Pre-Post**	N/A	30 patients with ankle plantar flexor spasticity (MAS >1), on average 80.5±46.5 months post stroke.	Subjects received one session per week for 3 weeks of extracorporeal shock wave therapy. Targeted muscles included the musculo-tendinous junction of the medial and lateral gastrocnemius muscles.	**Primary Outcomes:** MAS, clonus score Patients were evaluated immediately, at 1 week and 4 weeks after treatment.	MAS scores showed significant decreases immediately after treatment (p=0.002), one week (p=0.02); however, effects were not maintained at four weeks post treatment. Improvements in clonus score were non-significant at both follow-up time points (p>0.05 for both).

Stretching

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Waldman et al. 2013 **USA** **RCT**	CA: ☒ Blinding: Assessor ☒ Patient ☒ ITT: ☒	24 stroke patients, 41.3±20.3 months post stroke with impaired ankle motor function.	Patients were randomized to 1) a 6 week training program using the portable robot in a research laboratory (controlled ROM stretching exercises), or 2) an instructed exercise program at home (control group – manual stretching of plantar flexors and active movement exercises).	**Primary Outcome:** MAS Patients were evaluated at baseline, immediately post treatment and at 6-weeks post treatment.	Compared to the control group, MAS scores for individuals in the robot group significantly improved immediately post treatment (p=0.01) and at the 6-week follow-up (p=0.020).

Vibration

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Pang et al. 2013 **Hong Kong**	CA: ☑ Blinding:	82 chronic stroke patients (treatment= 4.6±3.5 years, control=	Patients were randomized into two groups: 1) exercise	**Primary Outcome:** MAS Participants were evaluated	Knee spasticity decreased in the treatment group (p=0.005) but not the control group (p=0.465); however, ankle MAS scores did not change

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
RCT	Assessor ☒ Patient ☑ ITT: ☒	5.3±4.2 years post stroke).	training with whole body vibration (WBV) stimulation for a maximum of 15 minutes, 3 days per week for 8 weeks, 2) control group received the same exercises without WBV.	at baseline, immediately after the 8 week training period and 1 month follow-up.	significantly over time in either group (p>0.05).
Tankisheva et al. 2014 **Belgium** **RCT**	CA: ☑ Blinding: Assessor ☒ Patient ☑ ITT: ☒	15 chronic stroke patients (treatment= 7.71±8.6 years, control= 5.28±3.6 years post stroke).	Patients were randomized into two groups: 1) exercise training (static and dynamic squats) with whole body vibration (WBV) stimulation at frequencies of 35Hz and 40Hz, lasting 30-60 sec, with 5 to 17 repetitions per exercise 3 times weekly for 6 weeks, 2) control group continued usual activities and did not receive a training program.	**Primary Outcome:** MAS Patients were evaluated at baseline, upon completion of the 6-week protocol and at a 6 week follow-up.	No significant differences were noted between the two groups on MAS upon completion of the protocol or at 6-week follow-up (p>0.05 for both).

Glossary
RCT= Randomized Controlled Trial
N/A = Not Applicable
CA = Concealed Allocation
ITT = Intention to Treat
AS = Ashworth Scale
MAS = Modified Ashworth Scale
ROM = Range of Motion

Reference List

Burbaud P, Wiart L, Dubos JL, Gaujard E, Debelleix S, Joseph PA, Mazaux JM, Bioulac B, Marat M, Lagueny A. A randomised, double blind placebo controlled trial of botulin toxin in the treatment of spastic foot in hemiparetic patients. J Neurol Neurosurg and Psych 1996;61:265-269.

Dunne JW, Gracies JM, Hayes M, et al. A prospective, multicentre, randomized, double-blind, placebo-controlled trial of onabotulinumtoxinA to treat plantarflexor/invertor overactivity after stroke. Clin Rehabil 2012;26:787-97.

Foley N, Murie-Fernandez M, Speechley M, et al. Does the treatment of spastic equinovarus deformity following stroke with botulinum toxin increase gait velocity? A systematic review and meta-analysis. Eur J Neurol 2010;17:1419-27.

Kaji R, Osako Y, Suyama K, et al. Botulinum toxin type A in post-stroke lower limb spasticity: a multicenter, double-blind, placebo-controlled trial. J Neurol 2010;257:1330-37.

Kluding PM, Santos M. Effects of ankle joint mobilizations in adults poststroke: a pilot study. Arch Phys Med Rehabil 2008;89:449-56.

Meythaler JM, Guin-Renfroe S, Brunner RC, et al. Intrathecal baclofen for spastic hypertonia from stroke. Stroke 2001;32:2099-109.

Moon SW, Kim JH, Jung MJ, Son S, Lee JH, Shin H, et al. The effect of extracorporeal shock wave therapy on lower limb spasticity in subacute stroke patients. Annals of Rehabilitation Medicine. 2013;37:461-470.

Pang MYC, Lau RWK, Yip SP. The effects of whole-body vibration therapy on bone turnover, muscle strength, motor function, and spasticity in chronic stroke: A randomized controlled trial. European Journal of Physical & Rehabilitation Medicine. 2013;49:439-450.

Picelli A, Dambruoso F, Bronzato M, Barausse M, Gandolfi M, Smania N. Efficacy of therapeutic ultrasound and transcutaneous electrical nerve stimulation compared with botulinum toxin type a in the treatment of spastic equinus in adults with chronic stroke: A pilot randomized controlled trial. Top Stroke Rehabil. 2014;21 Suppl 1:S8-16.

Pittock SJ, Moore AP, Hardiman O, Ehler E, Kovac M, Bojakowski J, al Khawaja I, Brozman M, Kanovsky P, Skorometz A, Slawek J, Reichel G, Stenner A, timberbaeva S, Stelmasiak Z, Zifko UA, Bhakta B, Coxon E. A double-blind randomised placebocontrolled evaluation of three doses of botulinum toxin type A (Dysport®) in the treatment of spastic equinovarus deformity after stroke. Cerebrovasc Dis 2003;15:289-30.

Santamato A, Micello MF, Panza F, Fortunato F, Logroscino G, Picelli A, 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.

Santamato A, Micello MF, Panza F, Fortunato F, Pilotto A, Giustini A, et al. Safety and efficacy of incobotulinum toxin type a (nt 201-xeomin) for the treatment of post-stroke lower limb spasticity: A prospective open-label study. Eur J Phys Rehabil Med. 2013;49:483-489.

Santamato A, Panza F, Ranieri M, Frisardi V, Micello MF, Filoni S, et al. Efficacy and safety of higher doses of botulinum toxin type a nt 201 free from complexing proteins in the upper and lower limb spasticity after stroke. Journal of neural transmission (Vienna, Austria : 1996). 2013;120:469-476.

Tankisheva E, Bogaerts A, Boonen S, Feys H, Verschueren S. Effects of intensive whole-body vibration training on muscle strength and balance in adults with chronic stroke: A randomized controlled pilot study. Archives of physical medicine and rehabilitation. 2014;95:439-446.

Waldman G, Yang CY, Ren Y, Liu L, Guo X, Harvey RL, et al. Effects of robot-guided passive stretching and active movement training of ankle and mobility impairments in stroke. NeuroRehabilitation. 2013;32:625-634.