GAVIN PUBLISHERS

OPEN ACCESS

Journal of Surgery

Ramström T, et al. J Surg 6: 1363.

DOI: 10.29011/2575-9760.001363

Research Article

A Treatment Algorithm for Spasticity-Correcting Surgery in Patients with Disabling Spasticity: A Feasibility Study

Therese Ramström[1,2*], Lina Bunketorp-Käll[1,3], Carina Reinholdt[1,2], Johanna Wangdell[1,2]

[1]Centre of Advanced Reconstruction of Extremities, Department of Hand Surgery, Sahlgrenska University Hospital, Mölndal, Sweden

[2]Department of Hand Surgery at Sahlgrenska Academy, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden

[3]Department of Health and Rehabilitation, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

[*]**Corresponding author**: Therese Ramström, Centre of Advanced Reconstruction of Extremities, Department of Hand Surgery, Sahlgrenska University Hospital, Mölndal, House U1, level 6, SE-431 80 Mölndal, Sweden

Citation: Ramström T, Bunketorp-Käll L, Reinholdt C, Wangdell J (2021) A Treatment Algorithm for Spasticity-Correcting Surgery in Patients with Disabling Spasticity: A Feasibility Study. J Surg 6: 1363. DOI: 10.29011/2575-9760.001363

Received Date: 08 January, 2021; **Accepted Date:** 20 January, 2021; **Published Date:** 25 January, 2021

Abstract

Background: Spasticity is a common secondary consequence of an injury to the Central Nervous System (CNS). It is a complex problem that can cause profound disability.

Aim: To evaluate the feasibility of a treatment algorithm for spasticity-correcting surgery in patients with disabling Upper Limb (UL) spasticity due to CNS injuries.

Design: Retrospective observational study.

Setting: Inpatient clinic.

Population: A cohort of 58 patients with disabling spasticity due to CNS injuries aged 18 years and older admitted to the Centre for Advanced Reconstruction of Extremities (C.A.R.E), Sahlgrenska University Hospital, Sweden, between February 2017 and June 2019.

Methods: Data were extracted from the medical records of patients who underwent spasticity-correcting surgery, predominantly tendon-lengthening procedures. Depending on residual UL function prior to surgery, patients received treatment according to a high-, low- or non-functioning regimen. Analyses were based on measurements and data acquisition applied as part of routine care. Assessments were made before surgery and six months post-surgery, including measures of body function and activities. The primary outcome differed among treatment regimens, but spasticity was measured across all three groups with the Modified Ashworth Scale (MAS).

Results: Patients received treatment according to a high- (N = 18), low- (N = 27) and non- (N = 13) functioning regimen (HFR, LFR and NFR, respectively). Six months post-surgery, patients in all three groups had improved various aspects of bodily functions and activities, including the primary outcome measures; the HFR-group improved unimanual UL functioning, the LFR-group improved bimanual daily activities and the NFR-group improved passive (ease of care) aspects of activities. The mean decrease in spasticity, as measured by MAS, was 2.16 (±1.1) in the high-, 1.88 (±1.3) in the low- and 2.14 (±1.1) in the non-functioning group ($p<0.000$ for all groups).

Conclusion: This study provides data in support of a feasible treatment algorithm for spasticity-correcting surgery in patients with disabling UL spasticity.

Clinical Rehabilitation Impact: The algorithm may be used to guide clinician and patient expectations and may facilitate the tailored selection of UL rehabilitation goals based on the individual patient's capacity for improvement.

Keywords: Central nervous system diseases; Muscle spasticity; Motor activity; Rehabilitation; Surgery

Introduction

Spasticity is a common physiological consequence of an injury to the Central Nervous System (CNS). It is a highly complex problem that, alone or in combination with the other features of an upper motor neuron syndrome can cause profound disability. Even though the pathophysiology of spasticity remains unclear, two subtypes of spasticity have been defined: those with a cerebral origin and those with a spinal origin [1]. Spasticity is reported to be present in about 30% of patients with stroke [2], 60% of patients with traumatic brain injury (TBI) [3], and 80% of patients with spinal cord injuries (SCI) [4]. Numerous definitions for spasticity have evolved over time in the medical literature [5]. In this study, disabling spasticity was defined as a velocity-dependent hypertonia [6] or sustained involuntary activations of muscles [7] having impact on body function, activities, and/or participation [8]. Spasticity affecting the hand is particularly debilitating because it prevents prehension and grasp, which are critical factors in the ability to perform the Activities of Daily Living (ADLs) independently [9].

Current challenges in spasticity management include identifying and establishing correct strategies to evaluate [10]. One of the main reasons why measuring spasticity and treatment efficacy is problematic is because it involves managing both the neurogenic and biomechanical aspects of limb stiffness [10]. The upper motor neurone syndrome include a diverse spectrum of clinical features. In patients with more severe symptoms, the spasticity may cause persistent muscle spasm, limb contractures and deformities, which in turn causes problems with for instance, hygiene and pain. By contrast, patients with residual sensorimotor function commonly have difficulties with volitional motor control, such as an inability to release flexor patterns or associated reactions which may complicate daily activities. Since sensory input is critical for neurological functioning, patients with altered or lost sensation (somatic or special senses) or a cognitive impairment would be less likely to benefit from treatment [10].

Many individuals with spasticity have learned to use key trigger strategies to apply to their spasticity beneficially in daily life. Before planning an intervention, it is therefore imperative to consider whether the spasticity helps facilitate an active grasp or is purely harmful. Moreover, there is a need to identify patients for whom active spasticity management can improve muscle control and reduce long-term disability [11]. It is therefore essential to bring together the expertise and skills of different professionals to recognize the underlying potential for motor recovery [11,12]. Further, identification of clear treatment goals and selection of outcome measures appropriate to these goals is of importance [11].

Stratification of patients may be a useful way for clinicians to recognize patients' level of disability and requirement for social support, possible beneficial effect of treatment so as to customize the appropriate rehabilitation plan for each individual [13]. Further, it has been suggested that the use of a functional scoring system in terms of simple mobility categories to stratify patients and predict functional improvement at discharge is worth exploring [10,13]. There is also a need to converge research efforts to develop appropriate tools and algorithms that enable proper evaluation in spasticity management [11]. In a previous exploratory meta-analysis investigating the relationship between reduced arm spasticity and improved arm function [14], the authors highlight that access to standardised regimens of rehabilitation (usually physiotherapy and/or occupational therapy) soon after the start of treatment enables patients to take advantage of the reduced spasticity. A variety of treatment options is available for the clinical management of spasticity, including oral medication, intrathecal pumps, intramuscular injections with botulinum toxin (BTX), surgical interventions and therapeutic modalities [15-17]. There is conflicting evidence regarding the most effective physical treatment modality to reduce spasticity and in general no single treatment modality can successfully manage the entire broad spectrum of spasticity [15-17]. Surgical treatment for spasticity has been an option for many years, and surgical management of disabling spasticity varies around the world [16,18,19]. Due to limitations in outcome assessment and the variety of surgical techniques, conclusions about the effectiveness of surgical intervention cannot be drawn [9,16,20-24]. The selection of a surgical strategy and type of postoperative rehabilitation should depend on not only the patient's remaining muscle control but also the individual's cognitive capacity. The goals of a surgical treatment can therefore vary greatly, from improving function in ADLs to improving hygiene aspects or reducing pain and joint deformities, with the aim of facilitating care [23].

This article focuses on a treatment algorithm for spasticity-correcting surgery developed at the Centre for Advanced Reconstruction of Extremities (C.A.R.E), Sahlgrenska University Hospital, Sweden. The treatment algorithm is inspired by the previously developed early active rehabilitation protocol (EAR) for patients with SCI who undergoes tendon transfer [25]. The preliminary findings of the current spasticity-correcting concept demonstrate significant gains for patients with SCI [18] and patients with mixed neurological diagnoses [26]. These findings have guided the refinement of the treatment algorithm. The aim of the present paper is to describe and evaluate the feasibility of the treatment algorithm for spasticity-correcting surgery in patients with disabling UL spasticity of cerebral or spinal origin.

Methods

Study Design and Participants

This was a retrospective observational study involving 58 patients aged 18 years and older with disabling spasticity due to CNS injuries who were admitted to C.A.R.E. We used the TIDeR checklist to enable clear and comprehensive reporting of the current treatment algorithm [27]. The patients underwent spasticity-correcting surgery at CARE between February 2017 and June 2019 as part of their routine medical care. Data were retrieved from the patients' medical records between November 2019 and March 2020 and analysed retrospectively. An application was sent to the Swedish Ethical Review Authority for ethical approval to conduct the study (Dnr 2019-05162). Since, however, it was based on retrospective data and relied on measurements and data acquisition applied solely as part of routine care, the study waived ethical approval.

Initial Assessment and Preparations

Prior to surgery, patients were assessed by a team, including hand surgeons, occupational and physical therapists using a holistic, team-based approach. The assessments included active and passive range of motion (AROM/PROM) in the affected joints, muscle hypertonicity, voluntary muscle control, and active and/or passive use of the UL in ADLs. Cognitive impairments were assessed by observing the individuals' ability to follow instructions, general confusion and presence of spatial difficulties. Additional information collected prior to surgery included posture, shoulder mobility, cognitive impairment, expected compliance and amount and access to social support and home care providers. To describe the severity and consequences of the spasticity on patients' motor and activity levels, the Functional Score (FS) was used [21]. The FS is a four-point scale ranging from 1 (absence of useful active mobility and uneasy and painful passive mobilization, making it difficult to dress and wash) to 4 (good active mobility with the possibility of prehension in the hand and fingers). The team discussed the specific activity goals expressed by the patient and the likelihood of reaching these goals by means of surgery and postoperative treatment. Based on a collective decision-making, pre-defined treatment goals were formulated for each patient, followed by assignment to the most appropriate regimen irrespective of diagnosis and muscles targeted for surgery. All patients were informed about the risks and potential benefits prior to making a decision about treatment. They also received thorough information about the surgical procedure and the post-surgical treatment regimen. If the patient required assistance or extended assistance after hospital discharge, this was arranged. In the presence of volitional control of the muscle(s) targeted for surgery, patients were informed that the surgical lengthening would most likely result in weakened muscle force over a period of time [20].

Stratification Criteria and Treatment Goals

Common to all three treatment regimens were the following inclusion criteria: I. Velocity-dependent hypertonia or sustained involuntary muscle activations should be the major contributor to the motor disorder; II: The UL spasticity should cause limitations in ADLs and III: The patient must have undergone conservative spasticity treatment and/or intramuscular injection treatment (botulinum toxin). In the case that the patient had residual volitional motor control in the spastic UL but presented with more severe cognitive impairment and/or an unstable home care situation that was judged by the team from C.A.R.E to hinder compliance, he or she was allocated to a less intense regimen. The overall treatment goal was to reduce the disabling consequences of the spasticity in order to facilitate bodily function, activities and/or participation. A stratification procedure was used in order for the team to allocate appropriate resources for patients for whom gains were anticipated in terms of volitional motor control, and less resources for patients with more severe disability, for whom no or minimal active movement was anticipated as a result of surgery. The stratification criteria allocated patients into high-, low- or non-functioning regimen (HFR, LFR, NFR). The definitions of the stratification criteria for each treatment regimen and examples of rehabilitation goals are presented in Figure 1. A complete specification of the inclusion and exclusion criteria for each treatment regimen is presented in Table 1.

Criteria	HFR	LFR	NFR
Inclusion criteria			
Velocity muscle hypertonicity or sustained involuntary activations of muscles should be the primary component of spasticity	x	x	x
The UL spasticity should cause limitations in ADLs	x	x	x
The patient must have undergone none-pharmacologic and/or pharmacologic spasticity treatment, with specific recommendations for BTX injection	x	x	x
The patient must have residual volition motor function in the UL	x	x	
The patient must agree to comply fully with the treatment regimen	x	(x)	
The patient must be motivated to participate in intensive rehabilitation	x	(x)	
The patient must have stable home care/assistance	x	(x)	
Functional score* 1			x
Functional score* 2		x	x
Functional score* 3	x	x	(x)
Functional score* 4	x	(x)	(x)
The patient must have residual shoulder mobility	x		
Exclusion criteria			
Severe cognitive impairments	x	x	
Mild cognitive impairments	x		
Severe contractures that hinder surgical benefit	x	(x)	
HFR = High-Functioning Regimen; LFR = Low-Functioning Regimen; NFR = Non-Functioning Regimen; UL=Upper Limb; ADL= Activities of Daily Living; BTX=Botulinum Toxin; * = Mertens P; S.M., Surgical management of spasticity, in Upper Motor Neuron Syndrome and Spasticity: Clinical Management and Neurophysiology, J.G.E. Barnes MP, Editor. 2001, Cambridge University Press: Cambridge. pp. 239-65.			

Table 1. Inclusion and exclusion criteria applied preoperatively for each treatment regimen in the current study.

Regime	Stratification criteria	Rehabilitation goals	Transfer of gains into daily life
HFR	The patient is expected to significantly improve the daily use of the affected upper limb in activities of daily living.	Increased volitional motor control and active range of motion in the affected upper limb and minimized compensation with the other hand.	Increased ability to use the spastic upper limb in unimanual and bimanual activities of daily living.
LFR	The patient has potential to regain some active movement in the affected limb but the hand is likely to be used primarily in bimanual activities.	Increased passive range of motion and possibly increased volitional motor control in the affected upper limb, though reduced compensation with the other hand is unlikely.	Increased capacity to use the affected upper limb in bimanual activities of daily living.
NFR	The patient is expected to have no or minimal active movement after surgery.	Increased passive range of motion.	Facilitation of hygiene, caregiving, rest positioning and amelioration of spasticity-induced upper limb pain.

Figure 1: Stratification criteria and overview of rehabilitation goals in the present study.

Outcome Measures

The data extracted from patients' records included demographic and clinical characteristics at baseline. To evaluate the effectiveness of the current treatment concept on spasticity, all treatment groups were collapsed to analyse the change in spasticity in the targeted muscles from baseline to the six-month follow-up using the Modified Ashworth Scale (MAS) [28]. Even though its psychometric properties have been questioned [29,30], the MAS was used in the present study to enable comparisons with previous findings. For analysis purposes, the MAS scores were summed to provide a 'composite spasticity score' of treated muscles in the whole study population.

Based on the fact that the treatment goals in the present study differed (Figure 1) and that the outcome measures of primary interest should be appropriate to the goal, the selections of primary and secondary outcome measures was made for each regimen separately (Appendix I). In order to meet the pre-defined goals for the HFR, the ability to use the arm in unilateral activities as measured by the Grasp and Release Test (GRT) [31], served as primary outcome measure. In the GRT, the patient is to pick up, move and release six objects of varying sizes, weights and textures using a palmar or lateral grasp. In the LFR, the ability to actively use the arm in bilateral activities as measured by the section B of the Arm Activity Measure (ArmA) served as primary outcome measure. In the NFR, the section A of ArmA (facilitation of basic aspects of care) served as primary outcome. Here follows a collective description of primary and secondary outcome measures used in the present study. A detailed description of all measures used to capture treatment-induced changes for the separate regimens listed according to the International Classification of Functioning, Disability and Health (ICF) is presented in Appendix I. Evaluation of bodily functions: Active and passive ROM in the target joints was measured with a hand-held goniometer with patient in a sitting position following standard procedures [32]. Since goniometric measurements of finger ROM are of questionable accuracy, the capacity to achieve a passive and active opening of the hand was rated using a 5-point scale ranging from 0-4 (0 = closed hand; 1 = ¼-opened hand; 2 = ½-opened hand; 3 = ¾-opened hand; 4 = fully-opened hand), as described in a previous study [33] and hereafter referred to as the hand-opening scale. This 5-point scale was also used to grade resting position in the hand. Maximum handgrip strength was measured with a hydraulic hand dynamometer (JAMAR® 5030J1, Sammons Preston Rolyan, USA) [34]. Maximum pinch grip strength was measured with Preston Pinch Gauge (European Bissel Healthcare Ltd, Winchester, England) [34]. Both grip- and pinch strength were measured in standard position with the maximum value of three attempts being used for analysis. Self-rated pain intensity and UL spasticity were measured using a Visual Analog Scale (VAS) [35].

Evaluation of activities (basic and complex): Basic activities: The ability to grasp, move and release objects was measured using the GRT [31]. The ability to actively and/or passively open the hand and actively grasp and release a cylinder object was measured using a specially designed measure called the cylinder test, which was developed by the authors of this study to capture meaningful changes in patients' palmar grasp ability. The test is divided into four subtests, which are administered in the following order: normal one-handed cylinder grip, adapted one-handed cylinder grip, two-handed cylinder grip and adapted two-handed cylinder grip. The test consists of 15 hard plastic stackable cylinders ranging in diameter from 10 mm to 150 mm.

Complex activities: Passive and active uses of the UL were measured using the ArmA self-report questionnaire [36]. The ArmA is a measure for recording the pattern of change in passive and active function after focal therapy intervention, particularly for spasticity interventions. The ArmA version available for download comprises an eight-item passive function subscale (A) and a 13-item active function subscale (B). Using a Likert scoring system ranging between 0 (no difficulty) and 4 (unable to do the task), the score of the passive function subscale ranges from 0 to 32, and the score of the active function subscale ranges from 0 to 52. Problems in the prioritised daily activities were measured using the Canadian Occupational Performance Measure (COPM) [37]. In the COPM, patients are asked to identify activity limitations in daily life due to UL spasticity. On a 10-point scale, they rate their performance (from 'not able to do it at all' to 'able to do it extremely well') and satisfaction (from 'not satisfied at all' to 'extremely satisfied') with regard to each of the prioritized problems. For analysis purposes, a mean COPM score was calculated for each individual (scores were added, then divided by the number of activities, with a maximum of 5 per person), after which a mean score for each regimen was calculated. Self-rated arm and hand function (usefulness) and appearance (cosmesis) were measured with a VAS.

Surgery

Spasticity-correcting procedures were performed by five surgeons and primarily comprised tendon-lengthening but also releases (tenotomy) and fractional muscle lengthening (rarely, on the brachialis muscle). Lengthening a tendon or releasing a muscle from its insertion results in the relaxation of the whole muscle-tendon unit. Hence, the spasticity is not eliminated but reduced in strength. The tendon-lengthening procedure was performed by a step-cut incision technique, followed by reattachment in the lengthened position using a side-to-side, cross-stich technique [38,39]. The load to failure of the sutured tendon gives a sufficient safety margin for the early active mobilization of the tendons involved [40]. This suture technique thus enables active training directly after surgery [25]. The degree of lengthening of the tendon was decided by aiming for normal resting length, which was

estimated at full relaxation during general anaesthesia; 2-3 cm was usually sufficient. Fractional lengthening was performed in the biceps and brachialis muscles since there is no tendon available. Muscle release was performed when there was hypertonus of the pectoralis, pronator teres and/or the adductor pollicis muscles. In all other muscles, tendon lengthening were performed.

Postoperative Treatment

The day after surgery, wrapping and custom-made splints were fashioned, with the aim of facilitating prolonged soft-tissue stretch and prevent postoperative oedema. The splints were worn at all times to provide additional stretch during the first three weeks, except during training sessions. When possible, dynamic activation of the antagonist muscles of the lengthened muscles was performed the first day after surgery, as was passive or dynamic activation of the lengthened muscles. Training was allowed to the maximum ROM without any restrictions in lengthened muscles or their antagonists. As a result of the surgical lengthening, the treated muscles were commonly weakened, which increases a patient's likelihood of being able to recruit the antagonists to the spastic muscles voluntarily. Therefore, even though the closing of the hand was weakened, training the finger extensors was prioritized at this point. Early active mobilization was applied in order to reduce the risks of adhesions, joint stiffness and muscle weakness. Before discharge, patients in the HFR and LFR were taught a personalised home-training program, which was to be performed 2-4 times daily, independently or with assistance from their carers or relatives. Patients were also trained and encouraged to use the hand frequently (while wearing the splint) in daily activities in order to maintain muscle fitness and prevent oedema by using the muscle pump. The postoperative treatment and length of stay varied by regimen.

Three weeks postoperative

All patients returned to the ward three weeks after surgery for a follow-up and inpatient rehabilitation of varying length. From this point on, splints were worn only at night until at least three months after surgery. The splints were re-adjusted if needed until an optimal fit was obtained and in order to achieve further stretch. The continued training was individually tailored to meet the goals of each patient. A detailed description of the therapy content for each regimen is presented in Table 2.

Regimen	Therapy content
HFR	The training in the HFR included functional tasks, such as grasp and release exercises using objects varying in size and form, object-manipulation tasks and positioning of objects in various positions in space. Motor re-education was used to relearn appropriate movement patterns in bimanual and single-handed tasks, as well as ROM exercises and strength and endurance training. In the case that the patient had difficulty steering goal-directed movements, coordinative exercises were performed. The training was meant to facilitate the transfer of regained active UL function into common daily activities and minimize compensation with the other hand. The activity training was geared towards the individual patient's needs and goals. The training was characterized by intense practice in task- and context-specific environments in which patients were guided to correctly apply their regained motor function in movements as smooth and isolated as possible. The exercises were gradually progressed with the aim of achieving the highest possible level of independence. Before discharge, the patient was commonly taught appropriate exercises to be carried out at home four times daily. Training after discharge was usually done independently, without the further guidance of professionals. The patient was encouraged to minimize compensation with the other hand and involve the operated UL in daily activities, such as eating, dressing and hygiene, depending on the individualized goals and prioritized activities.
LFR	The training in the LFR was focused on relearning appropriate movement patterns rather than isolated muscle training. The activity training was focused on the adaptive and compensatory skills needed to perform certain activities despite limited AROM, often with the operated arm acting as a supportive limb in bimanual tasks. Both the functional and activity-based training are often restricted by spasticity or stiffness in the shoulder or elbow or lack of strength and/or endurance, which hampers the ability to reach out in space. In the case of such limitations, if the patient could make use of the opposite arm, the training focused on improving and increasing the supportive use of the operated arm, such as by placing objects in the low- or non-functioning hand. For patients with cognitive impairment (e.g. brain fatigue or poor working memory) the tasks were adjusted to suit the cognitive capacity of each patient. Before discharge, the patient was taught a training program, including stretching exercises, recommended use of the UL in daily activities, and functional resting positions to prevent the development of stiffness and contractures or deformities. After discharge, the training was usually done independently or with help from relatives and/or assistants 1-2 times daily.

NFR	The therapy in the NFR focused on PROM exercises and functional resting positions for the UL to prevent deterioration with increasing stiffness and contractures or deformities. The splint was checked to ensure a continued optimal fit and possible further stretch. After discharge, it was recommended that PROM exercises be carried out with help from relatives and/or assistants as a complement to splinting.
HFR = High-Functioning Regimen; LFR = Low-Functioning Regimen; NFR = Non-Functioning Regimen; UL= Upper Limb.	

Table 2: Therapy content in each treatment regimen beginning three weeks after surgery.

Clinical Follow-Up

Data were routinely recorded during outpatient clinic visits according to standardised protocols. Three months after surgery, follow-up assessments were made (data not reported), and information about therapy compliance and complication rates was recorded. The continued training, frequency and duration of splint use were individually adjusted from that point on. Some patients with weak or no active antagonistic function at this point were recommended to continue use of the night splint in order to achieve continued long-term stretch of the tendon-muscle units. Depending on residual function, patients were recommended to continue active use, stretching and functional resting positions of the UL to maintain the results from surgery. The primary time point for feasibility assessment and outcome evaluation was data-retrieved from the assessment at six months post-surgery. Patients who completed clinical assessments twelve months after surgery were included in a subgroup analysis.

Data Collection and Statistical Analyses

Patients´ records were reviewed to compile the incidence of postoperative complications (e.g. infection, bleeding) and information about treatment compliance, as well as relevant demographic information and data from the clinical assessments. As a complementary analysis, the outcomes of the patients who had conducted a clinical twelve-month follow-up were examined. Demographics and baseline clinical characteristics were summarized with descriptive statistics. The changes from baseline to the six-month follow-up are reported as mean ± SD and median IQR for all outcome measures. Depending on the level and distribution of the data, a T-test or Wilcoxon signed-rank test was used to determine significant improvements after surgery. All statistical analyses were performed using SPSS 20.0 (IBM, Armonk, New York). All tests of significance were two-sided; $P<0.05$ was considered statistically significant. For outcome measures with no previously published minimal clinically important difference (MCID) available, the MCID was defined prior to data analysis in this study based on an international consensus discussion.

Results

A total of 60 patients underwent spasticity-correcting surgery during the set time period. Of these, two did not fulfil the inclusion criteria regarding age and were excluded. Thus, the study comprises data retrieved from 58 patient records. The mean age was 57 (range 19-79), 52% were men and most patients were diagnosed with SCI (52%). After surgery patients received treatment according to HFR (N = 18;31%), LFR (N = 27;47%) or NFR (N = 13;22%). Figure 2 presents the flow of the study. Detailed demographic data and the clinical characteristics of the study population are presented in Table 3, with no differences among groups apart from type of injury, showing that a higher number of patients with SCI were assigned to the HFR compared to the other two regimens. The presence of pre-operative UL pain was more frequently reported in the LFR and NFR groups (35% and 40%, respectively) than in the HFR group (20%). In total, surgical procedures were carried out on 273 muscles. The most frequent procedures were lengthening of the finger flexors and wrist flexors and the release of the m. pronator teres. A detailed summary of all surgical procedures is presented in Figures 3 a-c.

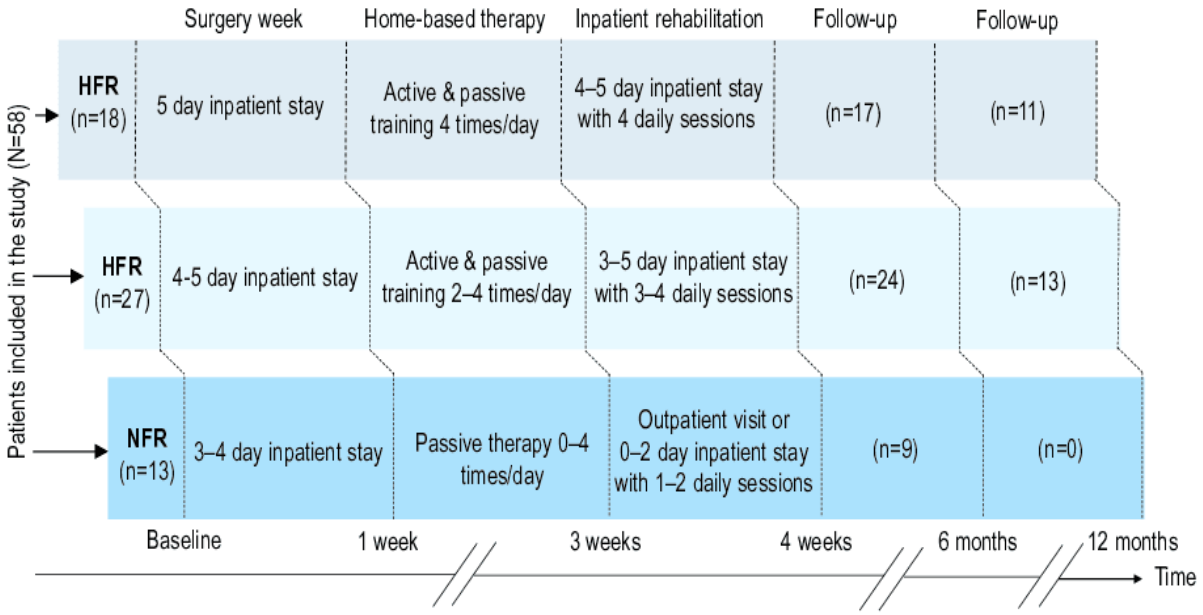


Figure 2: Flow of the study in which 58 patients received the current treatment algorithm for upper limb spasticity-correcting surgery according to three different treatment regimens.

	Total	HFR	LFR	NFR
Patients	58(100)	18(31)	27(46)	13(22)
Functional score (FS) *				
FS1	18(31)	0(0)	0(0)	12(92)
FS2	9(15)	0(0)	13(48)	1(8)
FS3	20(34)	13(72)	9(33)	1(8)
FS4	6(10)	5(28)	1(4)	0(0)
Missing FS data	4(7)	0(0)	4(15)	0(0)
Age mean (min-max)	57(19-79)	59(40-79)	56(24-76)	55(19-76)
Gender				
Women	21(36)	4(22)	10(37)	7(54)
Men	37(64)	14(78)	17(63)	6(46)
Diagnosis				
SCI	30(52)	16(89)	10(37)	4(31)
Stroke	17(29)	2 (11)	11(41)	4(31)
TBI	4(7)	0(0)	4(15)	0(0)
Other**	7(12)	0(0)	2(7)	5(38)

Time (years) between injury and surgery mean (min-max)	8.6(0-31)	7 (0-30)	8.9(1-31)	10.1(2-26)
Operated arm right/left	29(50)/29(50)	12(67)/6(33)	10(37)/17(63)	7(54)/6(46)
Transfers				
Wheelchair	28(48)	6(33)	10(37)	12(92)
Wheelchair partial	6(10)	5 (28)	1(4)	0(0)
Walking	24(41)	7(39)	16(59)	1(8)

HFR = High-Functioning Regimen; LFR = Low-Functioning Regimen; NFR = Non-Functioning Regimen; Max = Maximum; Min = Minimum; SCI = Spinal Cord Injuries; TBI = Traumatic Brain Injuries, **other diagnosis: multiple sclerosis, cerebral paralysis, spina bifida, Wilson disease. Data is reported as number (%) unless reported otherwise. * = Mertens P, S.M., Surgical management of spasticity, in Upper motor neuron syndrome and spasticity: clinical management and neurophysiology, J.G.E. Barnes MP, Editor. 2001, Cambridge University Press: Cambridge. pp. 239-65.

Table 3: Demographic and clinical characteristics of the study cohort, stratified by treatment regimens.

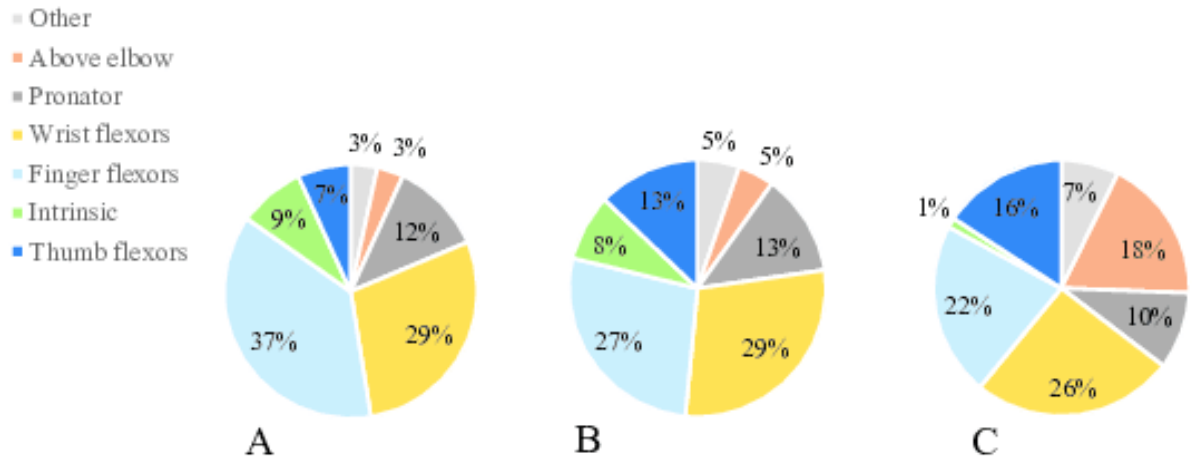


Figure 3: a-c: Spasticity-corrected muscles presented as a percentage of all surgical procedures performed in each group (A = High Functioning Regimen, B = Low Functioning Regimen, C = Non Functioning Regimen). The muscles are grouped as follows: Above elbow: pectoralis, triceps, biceps, brachioradialis, brachialis; pronator teres; Wrist flexors; flexor carpi ulnaris, flexor carpi radialis, palmaris longus; Finger flexors: flexor digitorum superficialis, flexor digitorum profundus; Thumb flexors: flexor pollicis brevis, flexor pollicis longus and Others: adductor pollicis, abductor pollicis, extensor pollicis longus and brevis, extensor carpi radialis/brevis/ulnaris and extensor digitorum.

Feasibility Of the patients studied, 54 (93%) completed the assigned regimen. Based on clinical judgement post-surgery, four patients (7%) switched over to a less-intense treatment regimen due to cognitive impairment that made adherence to the assigned regimen difficult (N = 2) or less volitional motor control than anticipated after surgery (N = 2). At the three-month follow-up, 51 patients (88%) reported that they had adhered to the assigned treatment regimen. The complication rate was 0 in the HFR, 3 in the LFR (superficial wound infections) and 2 in the NFR (major oedema and bleeding, respectively).

Treatment outcome at six months Data from the six-month follow-up was available for 17 patients in the HFR group (94 %), 24 patients in the LFR group (89%) and 9 patients (69%) in the NFR group. The change in the MAS composite scores in the treated muscles for the whole study group and stratified by regimen are presented in Table 4. The mean change in the composite MAS score across all three groups collapsed revealed significantly reduced spasticity -2.0 [±1.2]; p = 0.00). Separate analyses for the three regimens showed

a reduction in target muscle spasticity of 2.2 (±1.1) in the HFR group (p = 0.00), 1.9 (±1.3) in the LFR group (p = 0.00) and 2.1 (±1.1) in the NFR group (p = 0.00; Table 4). Patients in all three regimens achieved significant and clinically meaningful gains as defined by the primary outcome measure and MCID for each regimen (Table 4). For the HFR group, this implied a significant increase (mean [SD]) in the ability to grasp, move and release objects as measured by the GRT (19.6 [±19]; p = 0.001). For the LFR group, this implied a significant decrease (median [IQR]) in activity limitations in the hand, as measured by ArmA B (-5 [-1 to-12.5]; p = 0.000). For the NFR group, this implied a significant decrease (median [IQR]) in ArmA A, i.e. in limitation in the passive use of the hand (-12 [-10 to-14]; p = 0.018).

Outcome measure	Regimen	n	Baseline	Six months	Change	MCID	P
			Mean (SD)	Mean (SD)	Mean (SD)		
			Median (IQR)	Median (IQR)	Median (IQR)		
MAS	**ALL**	109	3.16(.9)	1.1(1.1)	-2.0(1.2)	-1	**0**
Composite score			3.0(3.0-4.0)	1.0(.0-2.0)	-2.0(-1.0-(-3.0))		**0**
MAS	**HRF**	31	3.4(.8)	1.2(1.2)	-2.2(1.1)	-1	**0**
			3.0(3.0-4.0)	1.0(.0-2.0)	-2.0(-1.0-(-3.0))		**0**
MAS	**LFR**	57	2.9(1.0)	1.0(1,1)	-1.9(1.3)	-1	**0**
			3.0(2.0-4.0)	1.0(.0-2.0)	-2.0(-1.0-(-3.0))		**0**
MAS	**NFR**	21	3.6(.6)	1.4(.9)	-2.1(1.1)	-1	**0**
			4.0(3.0-4.0)	2.0(1.0-2.0)	-2.0(-2.0-(-3.0))		**0**
Primary outcome							
GRT	**HFR**	16	101.4(39.3)	121.0(49.0)	+19.6(19.0)	12	**0.001**
			103.0(73.5-133.2)	125.0(82.5-160.2)	+15(7.7-30.2)		**0.001**
ArmA B (Active)	**LFR**	21	41.5(10.4)	34.3(13.3)	-7.2(7.8)	-2	**0**
			45.0(39.0-48.5)	38.0(26.5-45.5)	-5.0(-1.0-(-12.5))		**0**
ArmA A (Passive)	**NFR**	7	15.6(4.4)	4.7(2.8)	-10.9(4.7)	-3	**0.001**
			17.0(12.0-18.0)	5.0(2.0-8.0)	-12.0(-10.0-(-14.0))		**0.018**

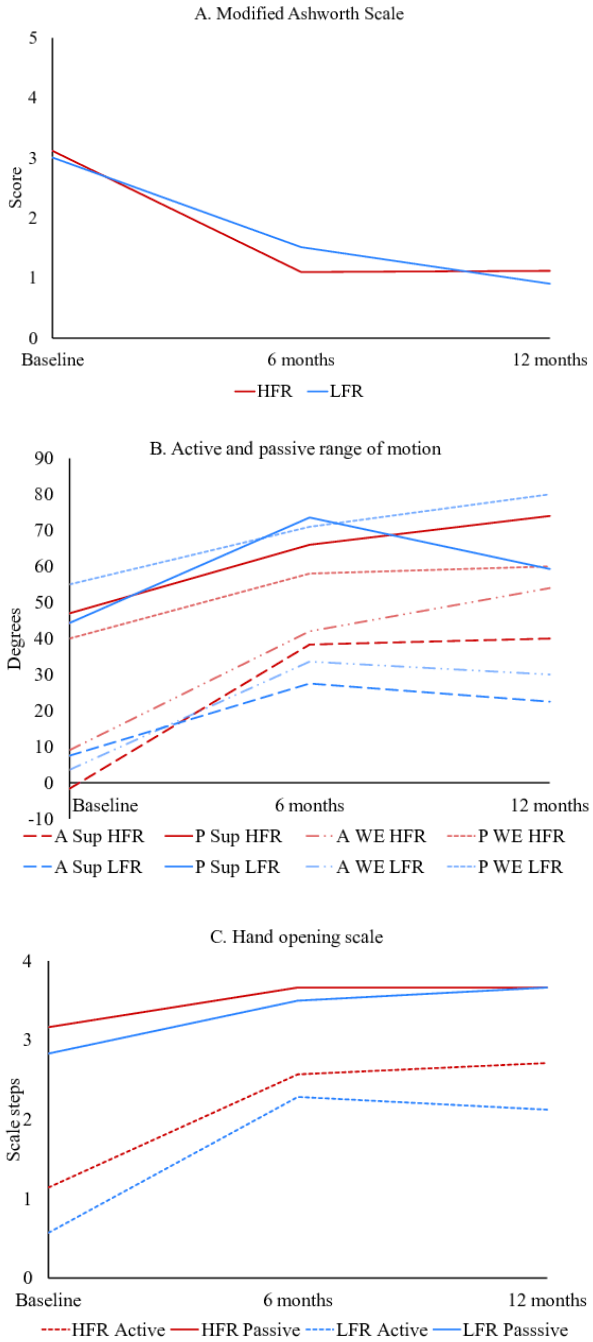
HFR = High-Functioning Regimen; LFR = Low-Functioning Regimen; NFR = Non-Functioning Regimen; SD = Standard Deviation; IQR = Interquartile Range; MCID = Minimal Clinically Important Difference; MAS = Modified Ashworth Scale; GRT = Grasp And Release Test; ArmA = Arm Activity Measure; ArmA A = Passive Subscale, ArmA B = Active Subscale. Statistical analyses of changes in mean scores were made with a paired-sample T-test, and analyses of changes in median scores were made with a Wilcoxon signed-rank test; p-values<0.05 were considered significant and are presented in bold numbers.

Table 4: Changes from baseline to six months in spasticity according to the MAS for the whole study cohort (n = 58) and stratified by regimen and changes in primary outcomes for the HFR (n = 18), LFR (n = 27) and NFR groups (n = 13).

The analyses of secondary outcome measures revealed significant improvements in various measures of bodily function and passive use of the hand in daily activities among patients across all regimens (Appendices II-IV). In the HFR group, all 21 secondary outcome measures improved significantly except for forearm PROM (supination), pinch strength and the VAS-rated measures (self-rated appearance, spasticity, pain intensity). Grip strength, however, deteriorated significantly. Patients in the LFR group achieved significant improvements in 21 secondary outcome measures, but not grip and pinch strength or the one- or two-handed cylinder tests. Among the secondary outcomes in the NFR group, improvement was shown in the ability to open the hand passively (hand-opening scale) and PROM measures, although it was not significant.

Treatment Outcome at Twelve Months

Data from the twelve-month follow-up was available for 11 patients in the HFR group (61%) and 13 patients in the LFR group (48%). The results presented in Figures 4 a-f show that most of the gains in active and passive ROM, spasticity, grip function, passive and active use of the hand and performance and satisfaction in prioritized activity limitations were maintained in this subgroup at twelve months.



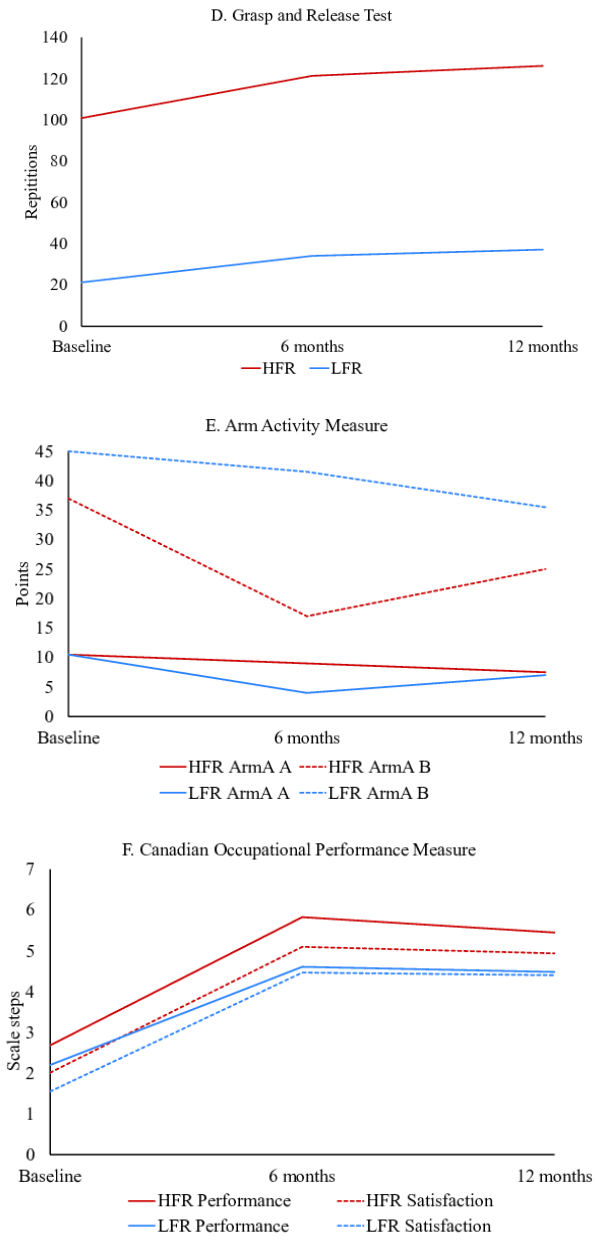


Figure 4: A-F: Changes in mean **(Figure A-D and F)** and median outcome scores **(Figure E)** from baseline to twelve months after surgery, according to the specifications below, in the High-Functioning Regimen (HFR) and Low-Functioning Regimen (LFR)

4A. Modified Ashworth Scale composite score (HFR; n = 11, LFR; n = 8).

4B. Joint range of motion; A Sup = active supination/P Sup = passive supination (HFR; n = 5/5, LFR; n = 6/7), A WE = active wrist extension/P WE = passive wrist extension (HFR; n = 5/5, LFR; n = 7/5).

4C. Hand opening scale, active/passive (HFR; n = 7/6, LFR; n = 8/6).

4D. Grasp and Release Test (HFR; n = 10, LFR; n = 11).

4E. ArmA A (passive) (HFR; n = 8, LFR; n = 8) and ArmA B (active) (HFR; n = 7, LFR; n = 8).

4F. Canadian Occupational Performance Measure, Performance (HFR; n = 10, LFR: n = 11) Satisfaction (HFR; n = 10, LFR; n = 11).

Discussion

This study shows that a treatment algorithm for spasticity-correcting surgery that considers the degree of functional impairment is feasible for patients with disabling spasticity resulting from CNS injuries. All patients-high-, low- and non-functioning-achieved significant gains in the pre-defined primary and secondary outcomes. The improvements were sustained at six months and, when coupled with our previous findings [18,26], the sub-analyses at twelve months indicate that the gains were maintained even longer. The degree of spasticity was significantly reduced at six months as measured by the MAS, both when analysing all regimens collapsed and when performing a separate analysis for each regimen. The lack of similar studies renders comparisons with previous findings unfeasible. As a comparison, however, patients with hemiparesis after stroke who received BTX treatment in spastic UL muscles were after four weeks shown to have decreases in MAS of 1.2 or 1.4, depending on the BTX dose. After additional eight weeks, the improvements in MAS scores had diminished to 0.6 and 0.7, respectively [41]. For patients in the present study, retention of improvement over a follow-up period of six months may have given them enough time to transfer the regained function into ADLs.

The composition of diagnostic groups and the wide range of disability presented among the participants in the present study made the selection of one single primary outcome measure a challenge. To the knowledge of the authors to the present study, there is no measure capable of detecting changes in the areas being targeted in the heterogenous group of patients. Commonly used measures whose items or tasks are too difficult to accomplish (even when encounter anticipated improvements after surgery) would result in a large proportion of participants obtaining lowest possible score, thus skewing the distribution of scores and making it impossible to differentiate among the many individuals at that low level, as well as significantly reduce the ability to detect improvements [42]. As formulated by professor Coster "Important knowledge about the impact of the intervention may be lost because the selected measure was unable to capture it or, even worse, distorted the true results" [42]. As Coster further points out "A scale might be excellent at discriminating differences in performance among people experiencing moderate degrees of functional limitation but not be able to detect differences among people with more significant limitations. A requirement of the primary outcome measure to be used in the present study was that the measure should be sensitive to the degree of change expected from the treatment, irrespective of diagnoses and muscles targeted for treatment. By using function as a subgrouping measure instead of diagnoses or affected muscles we consider the goals and aims of the treatment to be easier to set and to evaluate. Based on these foundations and the empirically-based practice at C.A.R.E. as well as the pre-defined treatment goals for each regimen we choose to let regimen-specific measures serve as primary outcomes in the study.

The algorithm to stratify patients into different regimens proved successful, with 54 patients (93%) completing the preoperatively chosen regimen. The complication rate was low, supporting the algorithm further. The present findings clearly agree with the statement by Francis et al. [14] that, to enable patients to take advantage of lessened spasticity, they should be given access to standardised regimens of rehabilitation soon after the start of treatment.

The primary treatment goals as defined by the primary outcome measures were reached for all regimens; the HFR did result in significant improved active grasp and release ability of the hand in ADLs, whereas the LFR did produce significant gains in active use of the hand in ADLs, as measured by ArmA B, and NFR did significantly improve the passive (taking care of) aspects of activities, evaluated by ArmA A. These results contrasts to the compiled research on BTX, confirming the lack of effects of BTX treatment on arm-hand capacity [43]. One possible explanation of the sustained arm-hand capacity in this study could be that the surgical procedures did not totally disrupt existing volitional motor function but rather weakened the muscles instead of paralysing them. Among patients in the HFR group, active rather than passive use of the UL was shown to improve after surgery. This is most likely explained by passive measures having ceiling effects due to presence of residual motor control among high-functioning patients.

Since patients with SCI were overrepresented in the HFR group (89%), the results are best compared to other studies on patients with SCI. One such study was conducted by Palazón-García et al. [44] and reported improvements in spasticity, ROM and pain intensity one month after BTX treatment for study participants with SCIs. The mean reduction in muscle hypertonicity, as measured by MAS, was 1.3, which is somewhat inferior to the results of the current study. Moreover, the treatment gains were sustained at six months in this study, versus one month in the Palazón-García et al. study [44]. The group receiving the LFR primarily included patients with acquired brain injury (stroke 40.7%, TBI 14.8%). At six months, the mean reduction in spasticity for the LFR group, as measured by the MAS, was 1.9. In populations with stroke and TBI, the reduction in spasticity, as measured by MAS after BTX treatment, is reported to reach a maximum of 1.6 and 1.7, respectively, at six weeks [45,46]. Both passive and active uses of the hand were shown to improve among patients in the present study who received the LFR, as measured by ArmA. This could be compared to a previous study by Demitrios et al. [45] that examined the effectiveness of BTX treatment for post-stroke spasticity complemented by either high-intensity

ambulatory rehabilitation or usual care. The result at six weeks in the Demitrios et al. study showed non-significant reductions in passive and active ArmA median scores of 4 and 2, respectively, for the high-intensity group, and 2 and 1, respectively, for the usual-care group. The decreases were markedly lessened in both groups at 12 and 24 weeks [45], compared to the results at six months in present study (4 and 5, respectively). Even though there is growing evidence for the effectiveness of BTX on routine aspects of care, the results of previous studies are highly heterogeneous [43].

Patients in the NFR group in the present study were expected to achieve gains from surgery primarily with respect to routine aspects of care (e.g. hygiene, dressing, resting position). The present results show that these goals were reached. The improvements in spasticity (MAS) and passive activities (ArmA A) are in line with previous studies on patients with non-functioning ULs in which surgical interventions vastly increased the ease of care [16,23].

In individuals suffering from severe and disabling spasticity, comorbidity is often high, which may hinder traveling in connection with follow-up appointments. This was why three patients in the NFR did not complete the six-month follow-up. Moreover, one patient in the NFR group died shortly after the surgery, with no connection between surgery and death. Cognitive impairment often limits the use of questionnaires, which is why outcomes measures are fewer and drop-outs were higher in the NFR group than in the other two groups. Therefore, the results must be interpreted cautiously. Patients in all three regimens reported less intense pain at six months, as compared to baseline. Two patients in the HFR who reported no pain prior to surgery, however, reported having pain at six months. Amelioration of pain has been reported as a result of BTX treatment in patients with post-stroke spasticity [47]. Repeated BTX injections were, however, required for long-lasting effects on pain intensity. Indications of pain relief have also been reported after surgical tendon-lengthening [26]. Thus, interventions to treat spasticity may have welcome side effects, but worth mentioning is that pain may be multifactorial, and mechanisms behind the pain in the present study are not defined, and the results after surgery cannot be predicted.

After spasticity-correcting surgery, the muscles operated upon are weakened. By the conclusion of the present study, the mean grip strength across groups had not reached the preoperative level, most likely due to the new length-tension properties of the muscles. A previous study on the same treatment concept showed that patients not only reached the preoperative level in grip strength but were significantly stronger at twelve months, as compared to baseline [26].

Limitations and further studies: Even though the current study presents promising results, it has limitations that must be considered. The primary one is the lack of a comparison group to account for the effects of undergoing any kind of intervention. Due to the data's retrieval from routine clinical care, a number of patients were lost to follow-up, resulting in missing data. Moreover, the patients were assessed repeatedly, which may have caused observer effects, also referred to as the Hawthorne effect. Another potential limitation involves the routine surgical procedures being evaluated: namely, for some patients, the postoperative treatment and training were carried out by the same therapist who did the assessments. Ideally, there should have been an independent assessor who was not involved in the postoperative training and treatment to avoid overreporting. The inclusion of various CNS diagnoses in the present study clearly affects heterogeneity and may somewhat limit generalisability to clinical practice. The study aimed, however, to evaluate a treatment strategy for disabling spasticity, independent of spasticity origin of the muscles targeted for surgery. The MAS was selected as the outcome measure to be analysed across the groups collapsed due to its frequent use in spasticity research. Measuring spasticity is difficult since it has no direct measures, but also because test results can be influenced by factors like temperature, stress and fatigue. The use of reliable and valid outcome measures and separate primary outcome measures for each regimen could potentially reduce systematic bias in the present study.

As a complementary qualitative approach, it would be valuable to hear the patients' own views, how they experience the treatment and the transfer of effects into their daily lives. The endpoint in the present study was six months, and this is relatively short when studying the development of surgical interventions. It remains to be seen whether the gains are sustained over the long term for more than a subgroup of patients. Finally, future studies should aim to address these limitations with the use of a longitudinal and controlled design.

Conclusion

This study provides data in support of a feasible treatment algorithm for spasticity-correcting surgery in patients with disabling UL spasticity. The algorithm may be used to guide patient expectations and may facilitate the tailored selection of UL rehabilitation goals based on the individual patient's capacity for improvement.

Funding

We thank the following funding agencies for supporting the study: the Swedish state under the agreement between the Swedish government and the county councils (the ALF agreement, 725241), the Local Research and Development Board for Gothenburg and Södra Bohuslän, and the Promobilia Foundation.

Appendix I. Outcome measures used in each treatment regimens to assess the outcome of spasticity-correcting surgery listed according to the International Classification of Functioning, Disability and Health.

Outcome measure	HFR	LFR	NFR
Body function			
Goniometer			
AROM	x	x	
PROM	x	x	x
Hand-opening scale			
active	x	x	
passive	x	x	x
resting position	x	x	x
MAS	x	x	x
Jamar, grip strength	x	(x)	
Pinch gauge, pinch strength	x	(x)	
VAS			
pain intensity	x	x	(x)
spasticity	x	x	(x)
Basic Activities			
Cylindertest subtest 1-4	x	x	x *
GRT	x	(x)	
Complex Activities			
VAS			
appearance	x	x	(x)
arm-hand function	x	x	(x)
COPM P/S	x	(x)	
ArmA			
A (passive)	x	x	x
B (active)	x	x	(x)

HFR= High-functioning regimen, LFR=Low-functioning regimen, NFR= Non- functioning regimen, PROM=Passive Range of Motion, AROM= Active Range of Motion, MAS= Modified Ashworth Scale, VAS= Visual Analog scale, GRT= Grasp and Release Test, COPM P= Canadian Occupational Performance Measure *Performance*, COPM S= Canadian Occupational Performance Measure *Satisfaction*, ArmA= Arm Activity Measure, ArmA A= passive subscale, ArmA B= active subscale. *subtest 4.

Appendix II. Changes from baseline to 6 months in secondary outcome measures for patients in the HFR (n=18).

Outcome measure	n	Baseline Mean (SD) Median (IQR)	6 months Mean (SD) Median (IQR)	Diff Mean (SD) Median (IQR)	MCID	*P*
Body function						
AROM	8	-3.7(10.1)	28.7(32.1)	+32.5(33.4)	+15	**.028**
Supination		.0(-15- .0)	37.5(.0-56.2)	+32.5(5.0-63.7)		**.034**
AROM	9	29.4(49.5)	52.8(27.7)	+23.3(24.5)	+15	**.021**
Wrist extension		45.0(.0-62.5)	60.0(30.0-75.0)	+15.0(7.5-32.5)		**.017**
PROM	7	52.9(31.6)	67.1(32.5)	+14.3(34.0)	+15	.308
Supination		50.0(30.0-80.0)	80.0(50.0-9.00)	+5(.0-30.0)		.206
PROM	8	52.5(36.8)	67.5(29.6)	+15.0(16.7)	+15	**.039**
Wrist extension		65.0(12.5-87.5)	80(45.0-90.0)	+10.0(1.25-23.7)		**.027**
Hand-opening scale,	12	1.2 (.6)	2.7(.9)	+1.4(1.0)	+1	**.000**
Active		1.0(1.0-2.0)	3.0(2.0-3.0)	+2.0(.2-2.0)		**.006**
Hand-opening scale,	11	2.9(1.0)	3.7(.5)	+0.8(0.9)	+1	**.011**
Passive		3.0(2.0-4.0)	4.0(3.0-4.0)	+1.0(.0-2.0)		**.024**
Hand-opening scale,	7	.4(.8)	1.7(.5)	+1.3(.7)	+1	**.004**
Resting position		.0(.0-1.0)	2.0(1.0-2.0)	+1.0(1.0-2.0)		**.024**
Pain intensity	15	.9(2.1)	0.6(1.4)	-0.2(2.1)	-2	.650
VAS		.0(.0-.0)	.0(.0-.0)	±.0(.0-.0)		.686
Spasticity	4	7.2(1.5)	3.5(1.9)	-3.7(3.0)	-2	.091
VAS		7.9(5.7-8.0)	4.0(1.5-5.0)	-3.9(-.7- -6.5)		.109
Basic Activities						
Grip strength (kg)	13	14.4(8.6)	10.5(5.4)	-3.9(4.5)	-20%	**.009**
		12.0(9.0-20.0)	8.0(7.0-14.0)	-3.0(-1- -5.5)		**.006**
Pinch strength (kg)	11	3.7(1.9)	3.9(2.0)	+.0(1.2)	-20%	.596
		3.5(2.7-4.5)	3.5(2.7-5.0)	-.5(-.7- .8)		.928
Cylindertest (mm)	14	20.0(28.8)	39.3(38.7)	+19.3(29.2)	+20	**.028**
One-handed		.0(.0-35.0)	35.0(.0-65.0)	±.0(.0-40.0)		**.028**
Cylindertest (mm)	11	31.8(33.7)	64.5 (32.4)	+32.7(29.0)	+20	**.004**
Adapted one-handed		30.0(.0-60.0)	70.0(50.0-90.0)	+40.0(0.0-50.0)		**.012**

Cylindertest (mm)	11	64.5(53.5)	92.7(40.5)	+28.2(30.9)	+20	**.013**
Two-handed		.0(.0-100.0)	100.0(60.0-120.0)	+20.0(.0-50.0)		**.011**
Cylindertest (mm)	13	89.2(23.6)	104.6(18.5)	+15.4(15.1)	+20	**.003**
Adapted two-handed		90.0(75.0-100.0)	100.0(90.0-120.0)	+20.0(.0-30.0)		**.009**
Complex Activities						
Appearance	11	2.3(3.2)	.6(1.2)	-1.7(2.9)	-2	.087
VAS		.0(0.0-5.0)	.0(.0-1.0)	±.0(.0- -4)		.078
Arm/hand function	14	3.0(1.6)	5.1(1.7)	+2.1(2.1)	+2	**.002**
VAS		3.0(1.9-4.1)	5.5(.0-6.1)	+2.4(.7-3.1)		**.005**
ArmA	13	12.3(4.9)	8.1(4.2)	-4.1(6.9)	-3	.050
A (passive activities)		12.0(9.0-15.0)	9.0(4.5-11.0)	-2.0(.0- -9)		**.045**
ArmA	12	34.7(7.3)	26.7(11.5)	-8.0(9.6)	-2	**.015**
B (active activities)		35.5(27.5-42.2)	26.0(16.2-36.5)	-6.5(.2- -14)		**.023**
COPM	17	2.9(1.2)	5.1(2.1)	+2.1(2.1)	+2	**.001**
Performance		2.8(2.0-3.6)	5.3(3.6-7.1)	+2.3(.4- 3.2)		**.002**
COPM	17	2.5(1.4)	4.8(2.2)	+2.3(2.4)	+2	**.001**
Satisfaction		2.3(1.5-3.4)	3.6(3.1-6.7)	+2.0(0.5- 4.5)		**.004**

SD = Standard deviation; IQR = Interquartile range; MCID= minimal clinical important difference, PROM=Passive Range of Motion, AROM= Active Range of Motion, VAS= Visual Analog scale, COPM = Canadian Occupational Performance Measure, ArmA= Arm Activity Measure ArmA A= passive subscale, ArmA B= active subscale). Statistical analyses of changes in mean scores were made with paired-sample T-test and analyses of changes in median scores were made with Wilcoxon signed rank test. p-values<0.05 were considered significant and are presented in bold numbers.

Appendix III. Changes from baseline to 6 months in secondary outcome measures for patients in the LFR (n=27).

Outcomes measure	n	Baseline Mean (SD) Median (IQR)	6-months Mean (SD) Median (IQR)	Diff Mean (SD) Median (IQR)	MCID	P
Body function						
AROM	12	2.5(26.7)	43.7(27.9)	+41.2(33.8)	+15	**.001**
Supination		7.5(-15.0- 23.7)	45(20-67.5)	+47.5(6.2-63.7)		**.005**
AROM	12	15.2(38.2)	41.2(31.9)	+25.8(25.8)	+15	**.005**
Wrist extension		20.0(2.5-33.7)	40.0(22.5-75.0)	+25.0(.0- 48.7)		**.011**
PROM	15	44.3(39.2)	74.3(19.3)	+30.0(28.5)	+15	**.001**
Supination		60.0(25.0-70.0)	80.0(70.0-90.0)	+20.0(5.0-45.0)		**.002**
PROM	12	51.2(35.4)	72.9(24.0)	+21.7(23.3)	+15	**.008**
Wrist extension		60.0(32.5-76.2)	90.0(52.5-90.0)	+25.0(10.0-37.5)		**.020**
Hand-opening scale	13	1.1(1.0)	2.5(1.0)	+1.4(1.0)	+1	**.000**
Active		1.0(.0-2.0)	2.0(2.0-3.0)	+2.0(.5-2.0)		**.004**
Hand-opening scale	14	3.3(1.0)	3.8(.6)	+.5(.8)	+1	**.029**
Passive		4.0(2.0-4.0)	4.0(4.0-4.0)	±.0(.0-1.0)		**.038**
Hand-opening scale	7	.3(.5)	1.7(.9)	+1.4(.8)	+1	**.003**
Resting position		.0(.0-1.0)	2.0(1.0–2.0)	+2.0(1.0–2.0)		**.023**
Pain intensity	23	1.8(2.8)	.4(.9)	-1.4(2.5)	-2	**.011**
VAS		.0(.0-4.0)	.0(.0-.0)	±.0(.0- -4.0)		**.017**
Spasticity	5	5.6(2.6)	3.8(2.6)	-1.8(.8)	-2	**.009**
VAS		4.0(3.5-8.4)	3.0(1.5-6.5)	-1.8(-1.0- -2.5)		**.042**
Grip strength (kg)	15	7.1(4.0)	5.0(3.2)	-2.1(3.7)	-20%	**.045**
		6.0(4.0-9.6)	5.0(2.0-8.0)	-.6(.5- -6.0)		.102
Pinch strength (kg)	17	2.4(1.3)	2.5(1.4)	+.1(1.2)	-20%	.750
		2.5(1.5-3.0)	2.2(1.5-3.6)	+.2(.5- -.4)		.494
Basic Activities						
GRT	20	24.6(23.8)	34.1(29.5)	+9.4(15.6)	+6	**.014**
		19.0(.0-45.3)	29.0(6.3-54.0)	+6.0(.0-22.2)		**.015**
Cylindertest (mm)	15	.0(.0)	8.7(18.1)	+8.7(18.1)	+20	.084
One-handed		.0(.0-.0)	.0(.0-.0)	±.0(.0-.0)		.102

Cylindertest (mm)	17	12.3(20.5)	25.9(29.4)	+13.5(25.7)	+20	**.046**
Adapted one-handed		.0(.0-30.0)	30.0(.0-40.0)	±.0(.0-30.0)		**.035**
Cylindertest (mm)	12	27.5(39.8)	45.0(48.3)	+17.5(35.4)	+20	.115
Two-handed		.0(.0-47.5)	40.0(.0-77.5)	±.0(.0-37.5)		.141
Cylindertest (mm)	19	54.7(25.2)	76.8(32.5)	+22.1(18.4)	+20	**.000**
Adapted two-handed		60.0(40.0-60.0)	80.0(60.0-100.0)	+20.0(10.0-30.0)		**.001**
Complex Activities						
Appearance	16	2.7(3.4)	1.0(1.7)	-1.7(2.7)	-2	**.020**
VAS		1.0(.0-6.5)	.0(.0-2.5)	-.5(.0- -2.7)		**.015**
Arm hand function	20	2.0(1.6)	3.9(1.9)	+1.9[1.1-2.7]	+2	**.000**
VAS		1.5(.6-3.0)	4.0(3.0-5.0)	+1.7(.2-3.9)		**.001**
ArmA	21	9.8(6.1)	4.6(4.7)	-5.2(4.5)	-3	**.000**
A (passive)		10.0(5.5-13.5)	3.0(1.0-8.5)	-4.0(-1.5- -9.5)		**.000**
COPM	20	2.1(1.0)	4.4(1.7)	+2.3(1.3)	+2	**.000**
Performance		1.8(1.4-2.5)	4.7(2.7-5.8)	+2.3(1.0-3.5)		**.000**
COPM	20	1.7(0.8)	4.5(1.6)	+2.7[1.9-3.6]	+2	**.000**
Satisfaction		1.4(1.0-2.4)	4.7(2.6-6.0)	+2.8(1.2-4.6)		**.000**

SD = Standard deviation; IQR = Interquartile range; MCID= minimal clinical important difference, PROM=Passive Range of Motion, AROM= Active Range of Motion, VAS= Visual Analog scale, GRT= Grasp and Release Test, COPM = Canadian Occupational Performance Measure, ArmA= Arm Activity Measure ArmA A= passive subscale. Statistical analyses of changes in mean scores were made with paired-sample T-test and analyses of changes in median scores were made with Wilcoxon signed rank test. p-values<0.05 were considered significant and are presented in bold numbers.

Appendix IV. Changes from baseline to 6 months in secondary outcome measures for patients in the NFR (n=13).

Outcome measure	n	**Baseline** **Mean (SD)** **Median (IQR)**	**6-months** **Mean (SD)** **Median (IQR)**	**Diff** **Mean (SD)** **Median(IQR)**	**MCID**	**P**
Body function						
PROM	5	28.0(40.8)	45.0(36.4)	+17.0(18.6)	+15	.110
Supination		.0(.0-70.0)	45.0(10.0-80.0)	+20.0(.0-32.5)		.102
PROM	7	54.3(31.7)	68.6(17.7)	+14.3(22.1)	+15	.138
Wrist extension		60.0(30.0-80.0)	70.0(60.0-90.0)	+25.0(-10.0- 30.0)		.115
Hand-opening scale	5	2.0(1.9)	3.6(.5)	+1.6(1.3)	+1	.056
Passive		3.0(.0-3.5)	4.0(3.0-4.0)	+1.0(0.5-3)		.063

Pain intensity	5	2.4(3.4)	.0(.0)	-2.4(3.4)	-2	.186
VAS		.0(.0-6.0)	.0(.0-.0)	±.0(.0- -6)		.180

SD = Standard deviation; IQR = Interquartile range; MCID= minimal clinical important difference, PROM=Passive Range of Motion, VAS= Visual Analog scale. Statistical analyses of changes in mean scores were made with paired-sample T-test and analyses of changes in median scores were made with Wilcoxon signed rank test. p-values<0.05 were considered significant.

References

1. Bethoux F (2004) Spasticity patients: special considerations. Seminars in Pain Medicine 2: 36-42.
2. Zorowitz DR, Gillard JP, Brainin JM (2013) Poststroke spasticity: Sequelae and burden on stroke survivors and caregivers. Neurology 80: 45-52.
3. Wedekind C, Lippert-Grüner M (2005) Long-term outcome in severe traumatic brain injury is significantly influenced by brainstem involvement. Brain Inj 19: 681-684.
4. Holtz KA, Lipson R, Noonan VK, Kwon BK, Mills PB (2017) Prevalence and effect of problematic spasticity after traumatic spinal cord injury. Arch Phys Med Rehabil 98: 1132-1138.
5. Malhotra S, Pandyan AD, Day CR, Jones PW, Hermens H (2009) Spasticity, an impairment that is poorly defined and poorly measured. Clin Rehabil 23: 651-658.
6. Lance JW (1980) The control of muscle tone, reflexes, and movement: Robert Wartenberg Lecture. Neurology 30: 1303-1313.
7. Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, et al. (2005) Spasticity: clinical perceptions, neurological realities and meaningful measurement. Disabil Rehabil 27: 2-6.
8. Burns AS, Lanig I, Grabljevec K, Wayne New P, Bensmail D, et al. (2016) Optimizing the management of disabling spasticity following spinal cord damage: The ability network-An international initiative. Arch Phys Med Rehabil 97: 2222-2228.
9. Waljee JF, Chung KC (2018) Surgical management of spasticity of the thumb and fingers. Hand Clin 34: 473-485.
10. Pajaro-Blázquez M, Maciejasz P, McCamley J, Collantes-Vallar I, Rymer WZ (2014) Challenges in measurement of spasticity in neurological disorders. In: Pons J, Torricelli D (editor). Emerging therapies in neurorehabilitation 2014: 117-145.
11. Ward AB (2003) Long-term modification of spasticity. J Rehabil Med 2003: 60-65.
12. Turner-Stokes L, Ward A (2002) Botulinum toxin in the management of spasticity in adults. Clin Med 2: 128-30.
13. Chung BPH (2018) Stratification of stroke rehabilitation: Five-year profiles of functional outcomes. Hong Kong Physiother J 38: 141-147.
14. Francis HP, Wade DT, Turner-Stokes L, Kingswell RS, Dott CS, et al. (2004) Does reducing spasticity translate into functional benefit? An exploratory meta-analysis. J Neurol Neurosurg Psychiatry 75: 1547.
15. Khan F, Amatya B, Bensmail D, Yelnik A (2019) Non-pharmacological interventions for spasticity in adults: An overview of systematic reviews. Ann Phys Rehabil Med 65: 265-273.
16. Rhee PC (2011) Surgical Management of upper extremity deformities in patients with upper motor neuron syndrome. J Hand surg Am 44: 223-235.
17. Graham LA (2013) Management of spasticity revisited. Age Ageing 42: 435-441.
18. Wangdell J, Fridén J (2016) Rehabilitation after spasticity-correcting upper limb surgery in tetraplegia. Arch Phys Med Rehabil 97: 136-143.
19. Petuchowksi J, Kieras K, Stein K (2018) Rehabilitation strategies following surgical treatment of upper extremity spasticity. Hand Clin 34: 567-582.
20. Gohritz A, Friden J (2018) Management of spinal cord injury-induced upper extremity spasticity. Hand Clin 34: 555-565.
21. Mertens P SM (2001) Surgical management of spasticity. In: Barnes MP JGe (editor). Upper motor neurone syndrome and spasticity: Clinical management and neurophysiology 2001: 239-265.
22. Gras M, Leclercq C (2017) Spasticity and hyperselective neurectomy in the upper limb. Hand Surg Rehabil 36: 391-401.
23. Gschwind CR, Yeomans JL, Smith BJ (2019) Upper limb surgery for severe spasticity after acquired brain injury improves ease of care. J Hand Surg E 44: 898-904.
24. Tafti MA, Cramer SC, Gupta R (2008) Orthopaedic management of the upper extremity of stroke patients. J Am Acad Orthop Surg 16: 462-470.
25. Wangdell J, Bunketorp-Kall L, Koch-Borner S, Fridén J (2016) Early active rehabilitation after grip reconstructive surgery in tetraplegia. Arch Phys Med Rehabil 97: 117-25.
26. Bergfeldt U, Stromberg J, Ramstrom T, Kulbacka-Ortiz K, Reinholdt C (2020) Functional outcomes of spasticity-reducing surgery and rehabilitation at 1-year follow-up in 30 patients. J Hand Surg E 45: 807-812.
27. Negrini S (2015) Application of the TIDieR checklist to improve understanding and replicability of studies in physical and rehabilitation medicine. Eur J Phys Rehabil Med 51: 667-668.
28. Bohannon RW, Smith MB (1987) Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther 67: 206-207.
29. Fleuren JF, Voerman GE, Erren-Wolters CV, Snoek GJ, Rietman JS, et al. (2010) Stop using the Ashworth Scale for the assessment of spasticity. J Neurol Neurosurg Psychiatry 81: 46-52.
30. Alibiglou L, Rymer WZ, Harvey RL, Mirbagheri MM (2008) The relation between Ashworth scores and neuromechanical measurements of spasticity following stroke. J Neuroeng Rehabil 5: 18.
31. Wuolle KS, Van Doren CL, Thrope GB, Keith MW, Peckham PH (1994) Development of a quantitative hand grasp and release test for patients with tetraplegia using a hand neuroprosthesis. J Hand Surg Am 19: 209-218.

32. Cambridge-Keeling CA (2002) Range-of-motion measurement of the hand. In: Hunter JM, Mackin EJ, Callahan AD, Skirven TM, Schneider LH, Osterman AL (editor). Rehabilitation of the hand: surgery and therapy. St. Louis: Mosby Company 2002: 169-181.

33. Bakheit AM, Pittock S, Moore AP, Wurker M, Erbguth F, et al. (2001) A randomized, double-blind, placebo-controlled study of the efficacy and safety of botulinum toxin type A in upper limb spasticity in patients with stroke. Eur J Neurol 8: 559-565.

34. Mathiowetz V, Weber K, Volland G, Kashman N (1998) Reliability and validity of grip and pinch strength evaluations. J Hand Surg Am 9: 222-226.

35. Huskisson EC (1974) Measurment of pain. The Lancet 304: 1127-1131.

36. Ashford S, Slade M, Turner-Stokes L (2013) Conceptualisation and development of the arm activity measure (ArmA) for assessment of activity in the hemiparetic arm. Disabil Rehabil 35: 1513-1518.

37. Law M BS, Carswell A, McColl MA, Polatajko H, Pollock N (1998) The Canadian occupational performance measure. Ottawa: CAOT Publications 1998.

38. Reinholdt C (2013) Surgical restoration of grasp control in tetraplegia. [dissertation]. Gothenburg: University of Gothenburg 2013.

39. Tsiampa VA, Ignatiadis I, Papalois A, Givissis P, Christodoulou A, et al. (2012) Structural and mechanical integrity of tendon-to-tendon attachments used in upper limb tendon transfer surgery. J Plast Surg Hand Surg 46: 262-266.

40. Fridén J, Shillito MC, Chehab EF, Finneran JJ, Ward SR, et al. (2010) Mechanical feasibility of immediate mobilization of the brachioradialis muscle after tendon transfer. J Hand Surg Am 35: 1473-1478.

41. Gracies J, Elovic E, McGuire J, Simpson DM (1997) Traditional pharmacological treatments for spasticity - Part 1: Local treatments. Muscle Nerve Suppl 6: 61-91.

42. Coster WJ (2013) Making the best match: selecting outcome measures for clinical trials and outcome studies. Am J Occup Ther 67: 162-170.

43. Andringa A, van de Port I, van Wegen E, Ket J, Meskers C, et al. (2019) Effectiveness of Botulinum Toxin treatment for upper limb spasticity poststroke over different ICF domains: A systematic review and meta-analysis. Arch Phys Med Rehabi 100: 1703-1725.

44. Palazón-García R, Alcobendas-Maestro M, Esclarin-de Ruz A, Benavente-Valdepeñas AM (2019) Treatment of spasticity in spinal cord injury with botulinum toxin. J Spinal Cord Med 42: 281-287.

45. Demetrios M, Gorelik A, Louie J, Brand C, Baguley IJ, et al. (2014) Outcomes of ambulatory rehabilitation programmes following botulinum toxin for spasticity in adults with stroke. J Rehabil Med 46: 730-737.

46. Lee J-M, Gracies J-M, Park S-B, Lee KH, Lee JY, et al. (2018) Botulinum toxin injections and electrical stimulation for spastic paresis improve active hand function following stroke. Toxins 10: 426.

47. Wissel J, Ganapathy V, Ward AB, Borg J, Ertzgaard P, et al. (2016) OnabotulinumtoxinA improves pain in patients with post-stroke spasticity: Findings from a randomized, double-blind, placebo-controlled trial. J Pain Symptom Manage 52: 17-26.