Robot-Assisted Rehabilitation of Hand Paralysis After Stroke Reduces Wrist Edema and Pain: A Prospective Clinical Trial

Alberto Borboni, Eng, MSc, PhD,[a] Jorge H. Villafañe, PhD, MSc, PT,[b] Chiara Mullè, MD,[c] Kristin Valdes, OTD, OT, CHT,[d] Rodolfo Faglia, MD,[a] Giovanni Taveggia, MD,[c] and Stefano Negrini, MD[b,e]

Abstract

Objective: The purpose of this study was to determine whether passive robotic-assisted hand motion, in addition to standard rehabilitation, would reduce hand pain, edema, or spasticity in all patients following acute stroke, in patients with and without hand paralysis.

Methods: Thirty-five participants, aged 45 to 80 years, with functional impairments of their upper extremities after a stroke were recruited for the study from September 2013 to October 2013. One group consisted of 16 patients (mean age ± SD, 68 ± 9 years) with full paralysis and the other groups included 14 patients (mean age ± SD, 67 ± 8 years) with partial paralysis. Patients in the both groups used the Gloreha device for passive mobilization of the hand twice a day for 2 consecutive weeks. The primary outcome measure was hand edema. Secondary outcome measures included pain intensity and spasticity. All outcome measures were collected at baseline and immediately after the intervention (2 weeks).

Results: Analysis of variance revealed that the partial paralysis group experienced a significantly greater reduction of edema at the wrist ($P = .005$) and pain ($P = .04$) when compared with the full paralysis group. Other outcomes were similar for the groups.

Conclusion: The results of the current study suggest that the partial paralysis group experienced a significantly greater reduction of edema at the wrist and pain when compared with the full paralysis group. The reduction in pain did not meet the threshold of a minimal clinically important difference. (J Manipulative Physiol Ther 2016;xx:0-10)

Key Indexing Terms: *Hand; Rehabilitation; Robotics*

Introduction

A stroke (or cerebrovascular accident) is a sudden ischemic or hemorrhagic episode that disturbs generation and integration of neural commands from the sensorimotor areas of the cortex.[1] As a consequence, the ability to selectively activate muscle tissues to perform movement is reduced.[2] One of the many possible consequences of disturbed neural command generation of the sensorimotor cortex is impairment of arm and hand functioning.[3,4]

Cerebrovascular diseases are the third cause of mortality and the second cause of long-term disability in Western countries.[4,5] Sixty percent of those individuals who survive a stroke exhibit a sensory or motor deficit of the hand, or both, and should undergo rehabilitation in an attempt to optimize recovery of the upper extremity.[4,6] Restoration of arm and hand mobility is essential for independent performance of activities of daily living.[2,4] A prompt and effective rehabilitation approach is essential[7] to obtain maximum recovery of the impaired limb to prevent tendon shortening, spasticity,[8] and pain.Recent technological advances have facilitated the use of robots as tools to assist patients in the rehabilitation process to maximize patient outcomes.[9] Several groups have developed robotic tools for upper limb rehabilitation of the shoulder and elbow.[10] These robotic

[a] Mechanical and Industrial Engineering Department, University of Brescia, Brescia, Italy.
[b] IRCCS Don Gnocchi Foundation, Milan, Italy.
[c] Habilita, Istituto Clinico Ospedale di Sarnico, Sarnico, Bergamo, Italy.
[d] Gannon University, Ruskin, FL.
[e] Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy.
Corresponding author: Jorge Hugo Villafañe, PT, MSc, PhD, Regione Generala 11/16, Piossasco, 10045, Italy. Tel.: +39 011 9065495, +39 339 5857563; fax: +39 011 9065495.
(e-mail: *mail@villafane.it*).
Paper submitted April 17, 2014; in revised form September 20, 2016; accepted September 27, 2016.
0161-4754

http://dx.doi.org/10.1016/j.jmpt.2016.10.003

tools assist the patient with carrying out exercise protocols and may help restore upper limb mobility.[2,11] The most commonly reported treatment approaches provided by rehabilitation robots are:

- *Assisted passive limb movement:* A robotic device moves a patient's arm.
- *Assisted active limb movement:* A robotic device helps patients to execute movements they would not be able to fully execute with their current muscle strength.
- *Resisted active limb movement:* A robotic device resists a patient's active movement.
- *Assisted/resisted bimanual exercise:* A robotic device recognizes an active movement of a patient's unaffected limb and reproduces it (mirroring) on the patient's affected limb with an assisted active or passive limb movement.[2]

The complexity of wrist and finger articulations delayed the development of dedicated rehabilitation robots until the introduction in 2003 of the first tool based on continuous passive motion (CPM) technology, which was followed by several other solutions with various levels of complexity and functionality.[12] Continuous passive motion was first introduced by the Canadian surgeon R. B. Salter.[7] Salter focused the emerging technology on a wide range of pathologies restricting movement of joints. The CPM technique, when applied to orthopedic pathologies, can reduce postoperative pain, enhance local arterial and venous circulation, reduce perspiration, accelerate the return to normal movements, and reduce serious complications caused by intra- and extra-articular adhesions.[7] The use of CPM has also been reported to reduce edema and articular effusion,[13] thus shortening hospital stays.[14]

Continuous passive motion is a therapy in which a joint is passively moved according to a predetermined sequence for a defined length of time. The external forces causing the joint movement should never overcome physiological joint stiffness and should strictly respect any degrees of freedom of the joint being treated.

Continuous passive motion treatment has also been found to be effective in patients with neurologic disorders. A study on a group of patients with chronic hemiplegia who used CPM reported a reduction in spasticity of the distal extremity of the upper limb.[15] Other studies report that CPM is effective in reducing hand edema,[13] particularly in patients with flaccid hemiplegia in the subacute phase.[16]

A recent review of the mechanisms for motor relearning reported that factors such as attention and stimuli (reinforcement) are crucial during learning, which indicates that motor relearning can take place in patients with neurologic disorders even when only passive stimulation is applied.[17] Additionally, another review reported the benefits of CPM for stretching and upper limb passive mobilization for patients with stroke but indicated CPM treatment requires further research.[18]

This purpose of this study was to determine whether passive robotic-assisted hand motion, in addition to standard rehabilitation, reduces hand pain, edema, or spasticity after acute stroke, in patients with and without hand paralysis.

Methods

Trial Design

We conducted a double-blind clinical trial without randomization of subjects. Informed consent was obtained from all participants, and procedures were conducted according to the Declaration of Helsinki (Protocol No. GLO01). The ethics committee of the Azienda Sanitaria Locale of Bergamo, Italy, approved the study. The study has been registered at the Current Controlled Trials website as NCT01936298. The protocol can be accessed at http://clinicaltrials.gov/.

Participants

Thirty-five participants aged 45 to 80 years were recruited from the Department of Neurologic Rehabilitation, Istituto Clinico Habilita, Sarnico, Bergamo, Italy, for the study from October to December 2013. All subjects were in the acute phase following their stroke. All patients had functional impairments of their upper extremity after the stroke. A neurologist established the diagnosis of acute phase of stroke. One group, P-ROM (passive range of motion), consisted of 16 patients (mean age ± SD, 68 ± 9 years) with full paralysis of the wrist and fingers who could not voluntarily initiate and control finger and wrist extension movement. The other group, A-ROM (active range of motion), consisted of 14 patients (mean age ± SD, 67 ± 8 years) with partial paralysis of the wrist and fingers who had difficulty in voluntarily initiating and controlling finger and wrist extension movements. Each patient underwent subjective and physical examinations performed by a physician experienced in neurologic conditions and rehabilitation to evaluate inclusion and exclusion criteria. To be included in the study, participants had to meet the following criteria: they had to be in the acute phase of stroke (<12 months postonset)[19]; this had to be their first stroke episode; they could not have a history of peripheral nerve injury or musculoskeletal disease (eg, arthritis, musculotendinous injury, or bone fracture) in the affected upper extremity; there could be no contracture of the affected wrist or fingers (Modified Ashworth Scale score <3)[20]; and they could have no history of any invasive procedure (botulinum toxin type A) for the treatment of spasticity for at least 6 months before the start of this study.[21] Participants in the P-ROM group had paralysis of the wrist and fingers and inability to voluntarily initiate and control finger and wrist extension movements. Those in the partial paralysis (A-ROM) group had to have partial paralysis of the wrist and fingers and difficulty in voluntarily initiating and controlling finger and wrist extension movements[19] (capable of voluntarily extending the wrist to 20° against gravity from a flexed position as measured by

goniometry).[22] Participants with unstable medical disorders, active complex regional pain syndrome, severe spatial neglect, aphasia, or cognitive problems were excluded.[21]

None of the individuals in this study had received prior interventions poststroke. Therefore, they were naïve to the treatment they received. Participants were not treated with diuretics, analgesics, muscle relaxants, or anti-inflammatory drugs for 24 hours prior to the examination.

Study Setting

The work was carried out at the Department of Neurological Rehabilitation at the Istituto Clinico Habilita in Sarnico, Italy.

Interventions

Main Features of the Robotic Device. Gloreha (Idrogenet, Brescia, Italy) was designed by the first author with his team at the University of Brescia (Italy) and prototyped by Polibrixia, Brescia Italy. The Velcro fastenings and glove were manufactured by Spidi Sport Srl, Vicenza, Italy. The device was first presented at an Italian conference[23-25] and a complete description of the system can be found in the literature[26] (Fig 1). Two main modules with well-defined mechanical characteristics constitute the glove. One is the actuator, where forces, speeds, and displacements originate; this module may be considered the engine of the glove, and it is located on the upper side of the forearm, close to the wrist (and to the impaired hand) and yet separated from it. The transmission is composed of several elastic transmissions that are moved by an actuator and properly transmit displacement, speed, and forces to one or more impaired fingers during a rehabilitation session. Although the actuator module has a rigid and defined structure and is fixed to the forearm section of the glove, the "transmission" module has in fact a labile and extended structure, as it has to reach all 5 fingers (1, some, or all might be impaired and in need of rehabilitation) up to their tips and move them in an effective and reliable manner. This is indeed the critical part of the glove: it has to be flexible, adoptable to an impaired hand anatomy, and still capable of fulfilling its "transmission" task in an efficient manner. The glove is not (apart from the disposable and optional glove mentioned before) a structure fully covering an impaired hand like a second skin, but it is a sequence of sectors that links one to the other through elastic transmissions, which remain on the back side of an impaired hand/finger and reflect and follow the hand anatomy in terms of its natural parts and articulations. Each sector, to be effective in movement actuation and transmission, is fixed to the corresponding anatomic part of the impaired hand or finger by a Velcro fastening, thus allowing a precise fit on a flaccid or an edematous (or both) hand or finger. The brace is initially affixed to the forearm, then the first finger, and then all other fingers.

Fig 1. *Wearable glove/orthosis.*

The movement transmission was a critical aspect of glove design, as it had to be flexible and capable of[1] eliminating any risk of mechanical overstress caused by possible malfunctioning of a glove component, on an impaired hand or finger often presenting with articular rigidity and pain[2]; adapting to different hand and finger sizes; and[3] leaving, for medical reasons, the hand palm, and inner part of fingers free.

Kinematic Aspects of the Device. Referring to Figure 2, the principal movements of a finger can be described by Eq. (1), where l_{DP}, l_{MP}, and l_{PP} are the phalanx segment lengths, and θ_{MCP}, θ_{PIP}, and θ_{DIP} are the joint angles.[27]

$$\begin{cases} x' = l_{DP}\cos(\theta_{MCP}+\theta_{PIP}+\theta_{DIP}) + l_{MP}\cos(\theta_{MCP}+\theta_{PIP}) \\ \qquad +l_{PP}\cos(\theta_{MCP}) \\ y' = l_{DP}\sin(\theta_{MCP}+\theta_{PIP}+\theta_{DIP}) + l_{MP}\sin(\theta_{MCP}+\theta_{PIP}) \\ \qquad +l_{PP}\sin(\theta_{MCP}) \end{cases} \tag{1}$$

A flexible rod with length l moves the fingertip to which it is connected through a hinge and a subsequent rigid L-shaped element having lengths h and f (Fig 2). Testing has indicated excessive flexion of the rod can cause excessive stroke of actuators, mechanical overstress, and can result in a risk of injury to patients with jerky movements. The shapes of the rod were also aesthetically unacceptable. Changes were made to the rectilinear slides mounted on some sections of the glove. The slides are now conveniently long so that the rod does not hunch while gliding through them, which appears to have solved the problem.

Kinematic analysis of correct dimensioning of the movement transmission system proceeds by fixing a position of a finger as identified by the angles θ_{MCP}, θ_{PIP}, and θ_{DIP}, by determining the positions of the main points of the system and by imposing adequate kinematic constraints to the rod. This analysis allows the flexible rod in a spatial

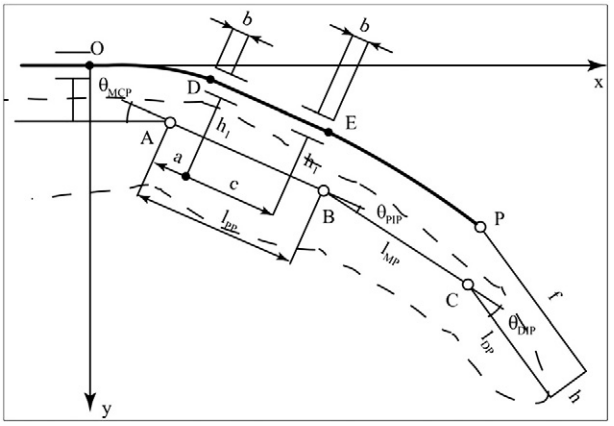

Fig 2. *Kinematic scheme of finger and orthosis.*

configuration; in particular, the positions of points D, E, and P may be determined by Eqs. (2)-(4).

$$\begin{cases} x_D = x_A + a\cos(\theta_{MCP}) + h_1\cos\left(\theta_{MCP}-\dfrac{\pi}{2}\right) \\ \quad +b\cos(\theta_{MCP}-\pi) \\ y_D = y_A + a\sin(\theta_{MCP}) + h_1\sin\left(\theta_{MCP}-\dfrac{\pi}{2}\right) \\ \quad +b\sin(\theta_{MCP}-\pi) \end{cases} \tag{2}$$

$$\begin{cases} x_E = x_A + (a+c)\cos(\theta_{MCP}) + h_1\cos\left(\theta_{MCP}-\dfrac{\pi}{2}\right) \\ \quad +b\cos(\theta_{MCP}) \\ y_E = y_A + (a+c)\sin(\theta_{MCP}) + h_1\sin\left(\theta_{MCP}-\dfrac{\pi}{2}\right) \\ \quad +b\sin(\theta_{MCP}) \end{cases} \tag{3}$$

$$\begin{cases} x_P = \; x_A + l_{PP}\cos(\theta_{MCP}) + l_{MP}\cos(\theta_{PIP}+\theta_{MCP}) + \\ \quad +l_{DP}\cos(\theta_{DIP}+\theta_{PIP}+\theta_{MCP}) + \\ \quad +h\cos\left(\theta_{DIP}+\theta_{PIP}+\theta_{MCP}-\dfrac{\pi}{2}\right) + \\ \quad +f\cos(\theta_{DIP}+\theta_{PIP}+\theta_{MCP}-\pi) \\ y_P = \; y_A + l_{PP}\sin(\theta_{MCP}) + l_{MP}\sin(\theta_{PIP}+\theta_{MCP}) + \\ \quad +l_{DP}\sin(\theta_{DIP}+\theta_{PIP}+\theta_{MCP}) + \\ \quad +h\sin\left(\theta_{DIP}+\theta_{PIP}+\theta_{MCP}-\dfrac{\pi}{2}\right) + \\ \quad +f\sin(\theta_{DIP}+\theta_{PIP}+\theta_{MCP}-\pi) \end{cases} \tag{4}$$

Polynomial splines of minimum degree are used[28] compatibly with constraints adopted to represent the flexible rod sections between the main points calculated with Eqs. (2)-(4). In particular, the coordinates of points H belonging to arcs OD, DE, and EP are represented by Eqs. (5)-(7), and must comply with bounds indicated by Eqs. (8)-(10).

$$y = u\cdot x^3 + v\cdot x^2 + w\cdot x + z \tag{5}$$

$$y = w\cdot x + z \tag{6}$$

$$y = v\cdot x^2 + w\cdot x + z \tag{7}$$

$$y(0)=0,\;\; y(x_D)=y_D,\;\; y'(0)=0,\;\; y'\left(x_D^-\right)=y'\left(x_D^+\right) \tag{8}$$

$$y(x_D)=y_D,\quad y(x_E)=y_E \tag{9}$$

$$y(x_E)=y_E,\quad y(x_P)=y_P,\quad y'\left(x_E^-\right)=y'\left(x_E^+\right) \tag{10}$$

As the adopted rod is extremely flexible and inextensible, the arch length function allows it to calculate the arch formed by the rod section outside the guide O (Fig 2). This result links a fingertip position with the geometric variable describing actuator movement and calculates the actuator stroke required to move the system. In particular, at point H of the flexible rod, the arch OH length is described by Eq. (11), where y(x) is a point on the rod, as shown in Eq. (12).

$$s_H = \int_0^{x_H}\sqrt{1+y'(x)^2}\,dx \tag{11}$$

$$y(x) = \begin{cases} u_1\cdot x^3 + v_1\cdot x^2, & H\in OD \\ w_2\cdot x + z_2, & H\in DE \\ v_3\cdot x^2 + w_3\cdot x + z_3, & H\in EP \end{cases} \tag{12}$$

The rod excursion inside the guide can be determined by calculating the position of P and the length of the arch s^0, as described in Eq. (13),

$$s^0 = \int_0^{x_P^0}\sqrt{1+y'(x)^2}\,dx \tag{13}$$

when the orthosis is idle and by appropriately fixing values of the angles θ_{MCP}, θ_{PIP}, and θ_{DIP}; the desired range of motion (ROM) is imposed and the length of the arch s_{Max} is calculated always with the appropriate values of angles θ_{MCP}, θ_{PIP}, and θ_{DIP} in Eq. (14);

$$s^{Max} = \int_0^{x_P^{Max}}\sqrt{1+y'(x)^2}\,dx \tag{14}$$

eventually the actuator stroke can be determined as the difference between the two arch lengths in Eq. (15).

$$c = s^{Max} - s^0 \tag{15}$$

Further dimensioning and material choice are omitted in this article.

The participants in both groups, full and partial paralysis, were treated by one clinician with postgraduate orthopedic physiotherapy training and more than 8 years of clinical experience in the management of musculoskeletal disorders. Patients in both groups received two treatment sessions daily for 2 weeks. The patients did not take any drugs or perform any procedures that might have affected spasticity during the study period.

All patients received the same intervention. Each patient used the Gloreha (Idrogenet, Lumezzane, BS, Italy) device for passive mobilization of the hand for 1½ hours in the morning and afternoon. Each of the patient's fingers was

hooked to individual thimbles connectable through a nylon thread to a device fixed on the glove that interfaced with a hybrid system (compressed air and oil), allowing flexion–extension of the fingers. In the morning, the robotic device moved each finger individually for half an hour in total. In the afternoon, the index, long, ring, and small fingers were passively moved together, and only the thumb was moved individually for half an hour in total.

In addition to the passive robotic-assisted hand motion, all patients underwent a standard rehabilitation program consisting of 1 hour of interventions for 2 sessions, 5 days per week, that included both physical and occupational therapy. Rehabilitation interventions were standard interventions received after a stroke: including active ROM, passive ROM, tone inhibition, gait training, and facilitation techniques. The rehabilitation physical and occupational therapists were blinded to all data that was collected for the study. Each patient attended 20 sessions over a period of 2 weeks (10 sessions per week).

Outcomes

The outcome measures were assessed at baseline and after completion of the 2-week intervention. All outcomes measures were captured at baseline (preintervention) and immediately after intervention (postintervention) by an assessor blinded to group assignment. The sequence of testing for the outcome measures was randomized among participants.

Assessment of the patient's response to therapy was monitored with the following assessment tools: perimeter edema of the wrist, maximum hand circumference (MHC) and hand circumference joint,[29] visual analog scale (VAS),[30,31] Modified Ashworth Scale for Grading Spasticity (MAS)[32,33] to measure spasticity, and ROM with a goniometer[34,35]; raters reviewed charts using Clinical Global Impression[36,37] criteria to assess severity of illness.

Pain Intensity. The intensity of hand pain was assessed with a VAS.[38] The VAS is a 100-mm line anchored with a 0 at one end, representing no pain, and 100 at the other end, representing the worst pain imaginable.[30] The VAS was selected as the primary outcome measure based on its ability to detect change (minimal clinically important difference, 20 mm).[39,40]

Hand Edema. Edema reduction was a secondary outcome. The wrist and hand measurements included wrist circumference, the close measurement that follows wrist contour at the minimum girth measurement (including the styloid processes); MHC, the closed measurement that follows a hand contour at the maximum at the base of the hand (maximum bulge of the palm including the thumb thenar muscles); and hand contour (HC), the close measurement that follows hand contour at the distal palmar crease. The measurements were performed with a flexible tape around the perimeter of each corresponding section of the hand in the vertical plane when the hand and wrist was positioned horizontally, resting on a flat surface. The techniques of measurements were as per guidelines in NASA-1024 (1978).[41]

Modified Ashworth Scale. Hand spasticity was a secondary outcome measure. The MAS is used to test resistance to passive movement about a joint with varying degrees of velocity within a range from 0 to 4, with 6 choices.[32]

Assessment of spasticity included flexion and extension movements around the upper limb (shoulder, elbow, wrist, and fingers), with the patient in resting position. Spasticity was defined as a MAS score ≥ 1 for any of the passive movements performed, in accordance with most previous studies on spasticity after stroke.[33]

Sample Size

A priori sample size calculation was performed to determine the necessary number of subjects needed for this study and was based on the results of a previous pilot study.[42]

Similarity of Interventions

All study participants received the same intervention.

Statistical Methods

Data were analyzed using SPSS Version 19.0 (SPSS, Chicago, IL). Intention-to-treat analysis was not performed because all subjects completed the study. Group data were summarized using means and standard deviations. The Kolmogorov–Smirnov test confirmed the normality of the distribution of the data, so a repeated-measures analysis of variance (ANOVA) was used to determine the differences in the A-ROM and P-ROM groups with time (preintervention and postintervention) as the within-subject factor and group (both groups) as the between-subject factor. The main hypothesis of interest was the group × time interaction. Between-group differences were expressed as mean differences with 95% confidence intervals (CIs). Between-group effect sizes were calculated using Cohen's d coefficient.[43] An effect size >0.8 was considered large, that of 0.5 moderate, and a size <0.2 small.[43] Spearman's rank correlation coefficient (r) was used to evaluate the relationship between the VAS and the other parameters evaluated. The r values were interpreted according to Domholdt's recommendations.[44] Statistical analysis was conducted at a 95% confidence level, and a P value $< .05$ was considered to indicate statistical significance.

Results

Between October and December 2013, 35 consecutive patients ($n = 35$) with acute-phase stroke were screened for eligibility criteria. A total of 16 subjects (8 females, 8 male, aged 50–77 years) presenting with A-ROM satisfied all eligibility criteria and agreed to participate. Also agreeing to participate were the 14 age and sex-matched participants in the

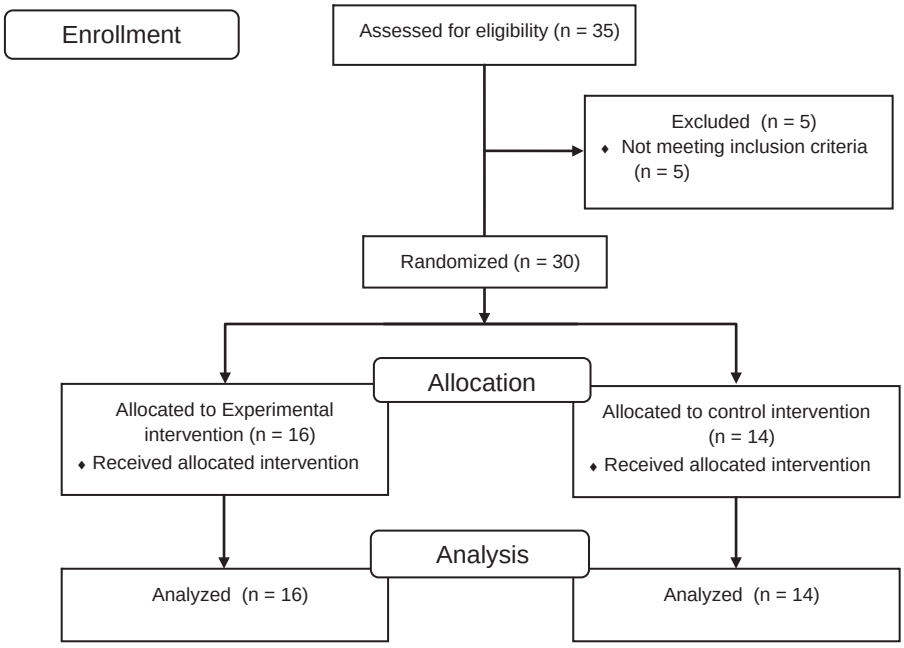

Fig 3. *Flow diagram.*

P-ROM group (7 females, 7 male, aged 54–83). Fifty-three percent of all subjects exhibited unilateral stroke in their left (nondominant) hand.

Five subjects were eliminated from the study after originally being included. The reasons for ineligibility were: medically instability (uncontrolled hypertension, arrhythmia) (n = 3), and active complex regional pain syndrome (n = 2) (Fig 3). Baseline features of both groups were similar for all variables (Table 1). No adverse effects were detected during or after treatment, and none of the subjects started diuretic therapy during the study.

Table 1. *Baseline Demographics for Both Groups*

Basal Metabolic Data	A-ROM (n = 16)	P-ROM (n = 14)
Age, y	67 ± 8	68 ± 9
Female sex, n (%)	8 (50.0)	7 (50.0)
Event, n (%)		
Ischemic ictus	10 (75.0)	12 (71.4)
Hemorrhagic ictus	4 (25.0)	4 (28.6)
Time from event, acute (d)	43 ± 24	58 ± 42
Affected upper limb, n (%)		
Right	8 (50)	8 (57.1)
Left	8 (50)	6 (42.9)

d, day; *A-ROM,* active range of motion; *P-ROM,* passive range of motion; *y,* year.

Primary Outcomes: Pain

The mean pain score of the A-ROM group decreased from 3.7 ± 2.3 to 2.7 ± 2.1. The mean pain score of the P-ROM group remained unchanged at 0.5 ± 0.5. The VAS revealed a significant time factor (F[1.0] = 5.2; P = .04, partial η = 0.286) and group × time interaction (F[1.0] = 5.2, P = .04, partial η = 0.286) in the A-ROM group. Post hoc analysis revealed significant differences between the 20 sessions for the A-ROM group (P = .01) but not for the P-ROM group (P > .05). There was a statistically significant difference between the groups (P < .005). Between-group effect size was large (d = 1.42) after the intervention. The data are summarized in Table 2.

Secondary outcomes

Edema (circumference). In the A-ROM group, edema in the affected wrist measured 18.5 ± 0.7 cm and decreased after treatment by 5.4%. In contrast, in the P-ROM group, the edema in the affected hand measured 19.5 ± 1.2 cm and remained unchanged. The 2 × 2 mixed-model ANOVA indicated a significant group × time interaction (F[1.0] = 6.127, P = .03, partial η = 0.4), but not for time (F[1.0] = 0.245, P = .6, partial η = 0.02), for wrist edema. Post hoc analysis revealed significant differences between the 20 sessions for the P-ROM group (P = .005), but not for the A-ROM group (P > .05). There was no significant difference between the groups (P > .05). Between-group effect size was large (d = 1.41) after the intervention.

In the A-ROM group, MHC and HC edema in the affected hand measured 20.3 ± 0.4 and 18.5 ± 0.7 cm and decreased after treatment by 2.5% and 2.7%, respectively. Similarly, in the P-ROM group, MHC and HC edema in the affected hand measured 24.0 ± 2.8 and 21.4 ± 1.4 cm and decreased after treatment by 2.1% and 1.9%, respectively.

Table 2. *Mean (SD) for Outcomes at All Study Visits for Each Group and Mean (SD) Differences Within Groups* [a]

Group	Preintervention	Postintervention	Change Score	Effect Size CI Within Group	Effect Size CI Between Groups at Postintervention
Pain					
A-ROM	3.7 ± 2.3	2.7 ± 2.1	−1 [b]	0.45 (−0.25, 1.15)	
P-ROM	0.5 ± 0.5	0.5 ± 0.5	0	0	
Between-group difference	−2.5 (−2.1, 1.8) [c]	−1.5 (1.9, −3.9) [c]			1.09 (0.33, 1.86)
Wrist Circumference					
A-ROM	18.5 ± 0.7	17.5 ± 0.7	−1*	1.42 (0.59, 2.25)	
P-ROM	19.5 ± 1.2	19.5 ± 1.2	0	0	
Between-group difference	−1.0 (−3.7, 1.7)	−2.0 (−4.8, 0.8)			2.00 (1.12-2.87)
Maximum Hand Circumference					
A-ROM	20.3 ± 0.4	19.8 ± 0.4	−0.5	1.25 (0.49, 2.01)	
P-ROM	24.0 ± 2.8	23.5 ± 2.7	−0.5	0.18 (−0.56, 0.92)	
Between-group difference	−3.7 (−9.6, 2.1)	−3.7 (−9.6, 2.0)	0		0
Hand Circumference					
A-ROM	18.5 ± 0.7	18.0 ± 0.7	−0.5	0.71 (0, 1.49)	
P-ROM	21.4 ± 1.4	21.0 ± 1.8	−0.4	0.24 (−0.49, 0.99)	
Between-group difference	−2.9 (−5.9, 0.1)	−3.0 (−6.9, 0.9)	−0.1		0.35 (−0.36, 1.07)
Spasticity (MAS Score)					
A-ROM	0.1 ± 0.3	0.3 ± 1.0	0.2	0.27 (−96, 0.42)	
P-ROM	0.6 ± 0.9	0.6 ± 0.9	0	0	
Between-group difference	−0.5 (−1.0, −0.01) [c]	−0.3 (−1.1, 0.4)	0.2		0.27 (−0.44, 0.99)

A-ROM, active range of motion; *CI,* confidence interval; *MAS*, Modified Ashworth Scale; *P-ROM,* passive range of motion.

[a] Data are means ± standard deviations (SD) except for between-group differences which are means and 95% confidence intervals.

[b] Significantly different within group, $P < .05$ (95% CI).

[c] Significant difference between groups, $P < .05$ (95% CI).

For MHC and HC edema, there was no significant finding for time ($F[1.0] = 1.524$, $P = .29$, partial $\eta = 0.28$, and $F[1.0] = 1.524$, $P = .29$, partial $\eta = 0.28$, respectively) or group × time interaction ($F[1.0] = 0.0$, $P = 1.0$, partial $\eta < 0.001$, and $F[1.0] = 0.0$, $P = 1.0$, partial $\eta < 0.001$, respectively) (Table 2). All participants in both groups exhibited changes (decreases) over the 20 treatments. There were no significant differences between the groups ($P > .05$). Between-group effect sizes were small posttreatment ($d < 0.2$).

Spasticity. The 2 × 2 repeated-measures ANOVA did not reveal a significant effect for time ($F[1.0] = 0.871$, $P = .36$, partial $\eta = 0.03$) or group × time interaction ($F[1.0] = 0.871$, $P = .36$, partial $\eta = 0.03$].

Correlations

Spearman's rank correlation coefficients revealed a strong, significant and positive relationship between pain and edema (wrist, MHC, and HC edema) ($r = 0.85$, 0.862, and 0.862, respectively, all $P < .004$) in the P-ROM group, but not for the A-ROM group ($P > .05$). No significant correlation was found between pain and spasticity (Table 3). Finally, no significant correlation was found between edema and spasticity.

Discussion

This purpose of this study was to determine if passive robotic-assisted hand motion, in addition to standard rehabilitation, reduces hand pain, edema, or spasticity in all patients after acute stroke, in patients with and without hand paralysis.

Generalizability

The results of this study may be generalized to stroke patients that have either a right or left hand affected by the stroke and are on average age 67 to 68 ± 9 years of age. The patients could have had either an ischemic or a hemorrhagic stroke on average 43 to 58 ± 42 days prior to the onset of treatment.

Interpretations

The results of the current study suggest that when compared with the P-ROM group, the A-ROM group experienced a large effect size in reduction of edema at the wrist and pain as measured with the VAS score.[43] However, to be of clinical significance, the change in VAS score needed to be 2 points, not 1 point.[39,40]

Hand rehabilitation poststroke is essential in improving mobility of the upper extremity and function. It is possible that a wearable glove may assist with the rehabilitation process and improve hand function. However, future studies are needed to determine this. The emergence of end effector robots that exhibit interesting rehabilitation outcomes for gait training has been reported in the literature[45]; however, there have yet to be any studies examining their benefits in hand

Table 3. *Spearman's Rank Correlation Coefficients Between Pain and the Other Parameters*

Variable	Group	Spearman's *r*	*P* Value
Age	A-ROM	0.5	.67
	P-ROM	0.49	.88
Wrist circumference	A-ROM	0.5	.67
	P-ROM	0.85	.004 [a]
Maximum hand circumference	A-ROM	0.5	.67
	P-ROM	0.862	.003 [a]
Hand circumference	A-ROM	0.5	.67
	P-ROM	0.862	.003 [a]
MAS score	A-ROM	–0.5	.67
	P-ROM	0.572	.05

A-ROM, active range of motion; *MAS*, Modified Ashworth Scale; *P-ROM,* passive range of motion.

[a] Significantly different, $P < .05$ (95% confidence interval).

function, and they have not been able to guarantee safety and natural kinematic motion in acute hand patients.[46] Indeed, this tool has to be effective in terms of actions addressed to an impaired or flaccid hand, has to guarantee high reliability, and has to be easy to use for the patient and therapist. A wearable glove (orthosis) is the only solution offering a satisfactory compromise of these issues.

Limitations

The study has some limitations. Small sample size may have reduced the ability to find a statistically significant difference between groups when in fact one may have existed. In addition, the effect size CI intervals crossed zero when interpreting the effect size between groups at the posttreatment assessment for hand circumference and MAS score changes, indicating that the treatment perhaps had no effect.

The group with some volitional hand motion had decreased edema in their affected hand both at baseline and after the intervention. It is impossible to quantify the effect of partial hand motion on reduction of edema. All patients had both occupational therapy and physical therapy in addition to the robotic-assisted passive hand mobilization, which could have been the reason there was less edema in the A-ROM group. It is impossible to determine the effect of therapy or robotic passive mobilization in isolation on reduction in hand edema. This study could have benefited from a third control group that received only standard stroke rehabilitation without the robotic intervention.

The absence of one or more follow-up assessments and the limited period of treatment do not provide information on long-term rehabilitation results. Also, a functional objective outcome measure associated with the limited observation time window was not used. Dr. Borboni is a designer of the proposed rehabilitation device and a shareholder in Polibrixia; therefore, there exist elements of study bias. Future studies are needed to determine the correct dosage and long-term benefits of the intervention.

Conclusion

The results of the current study suggest that the A-ROM group experienced a significantly greater reduction of edema at the wrist and pain when compared with the P-ROM group. The reduction in pain did not meet the threshold of a minimum clinically important difference. However, all other outcomes were similar for the 2 groups.

Funding Sources and Conflicts of Interest

Gloreha (Idrogenet, Brescia, Italy) was designed by the first author with his team at the University of Brescia (Brescia, Italy) and prototyped by Polibrixia, Brescia, Italy.

No funding sources and no other conflicts of interest were reported for this study.

Contributorship Information

Concept development (provided idea for the research): A.B., C.M., K.V., R.F., J.H.V, S.N.

Design (planned the methods to generate the results): A.B., C.M., K.V., J.H.V.

Supervision (provided oversight, responsible for organization and implementation, writing of the manuscript): A.B., C.M., K.V., J.H.V.

Data collection/processing (responsible for experiments, patient management, organization, or reporting data): A.B., C.M.

Analysis/interpretation (responsible for statistical analysis, evaluation, and presentation of the results): A.B., J.H.V., R.F., S.N.

Literature search (performed the literature search): A.B., C.M., K.V., J.H.V., R.F., S.N.

Writing (responsible for writing a substantive part of the manuscript): A.B., J.A.C., J.H.V., R.F., S.N.

Critical review (revised manuscript for intellectual content, this does not relate to spelling and grammar checking): A.B., C.M., K.V., J.H.V.

Practical Applications

- Active range of motion group experienced a significantly greater reduction of edema at the wrist when compared with the P-ROM group.
- All of the other outcomes were similar for the groups.
- The proposed device, with its compliant mechanical transmission, may represent an innovative solution to rehabilitation, because the hand can grasp and the orthosis is lightweight.

References

1. Song D, Lan N, Loeb GE, Gordon J. Model-based sensorimotor integration for multi-joint control: Development of a virtual arm model. *Ann Biomed Eng.* 2008;36:1033-1048.
2. Prange GB, Jannink MJA, Groothuis-Oudshoorn CGM, Hermens HJ, Ijzerman MJ. Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke. *J Rehabil Res Dev.* 2006;43:171-183.
3. Mehanna R, Jankovic J. Movement disorders in cerebrovascular disease (2013; 12:597) [Correction]. *Lancet Neurol.* 2013;12:733.
4. Mukherjee M, Koutakis P, Siu KC, Fayad PB, Stergiou N. Stroke survivors control the temporal structure of variability during reaching in dynamic environments. *Ann Biomed Eng.* 2013;41:366-376.
5. Mutai H, Furukawa T, Araki K, Misawa K, Hanihara T. Long-term outcome in stroke survivors after discharge from a convalescent rehabilitation ward. *Psychiatry Clin Neurosci.* 2013;67:434-440.
6. Nowak DA. The impact of stroke on the performance of grasping: Usefulness of kinetic and kinematic motion analysis. *Neurosci Biobehav Rev.* 2008;32:1439-1450.
7. Salter RB. Continuous passive motion: from origination to research to clinical applications. *J Rheumatol.* 2004;31: 2104-2105.
8. Andringa AS, Van de Port IG, Meijer JW. Tolerance and effectiveness of a new dynamic hand-wrist orthosis in chronic stroke patients. *NeuroRehabilitation.* 2013;33:225-231.
9. Bishop L, Stein J. Three upper limb robotic devices for stroke rehabilitation: A review and clinical perspective. *NeuroRehabilitation.* 2013;33:3-11.
10. Reinkensmeyer DJ, Schmit BD, Rymer WZ. Assessment of active and passive restraint during guided reaching after chronic brain injury. *Ann Biomed Eng.* 1999;27:805-814.
11. Mazzoleni S, Sale P, Franceschini M, et al. Effects of proximal and distal robot-assisted upper limb rehabilitation on chronic stroke recovery. *NeuroRehabilitation.* 2013;33:33-39.
12. Balasubramanian S, Klein J, Burdet E. Robot-assisted rehabilitation of hand function. *Curr Opin Neurol.* 2010;23: 661-670.
13. Giudice ML. Effects of continuous passive motion and elevation on hand edema. *Am J Occup Ther.* 1990;44:914-921.
14. Brosseau L, Milne S, Wells G, et al. Efficacy of continuous passive motion following total knee arthroplasty: A metaanalysis. *J Rheumatol.* 2004;31:2251-2264.
15. Hu XL, Tong KY, Song R, Zheng XJ, Leung WWF. A comparison between electromyography-driven robot and passive motion device on wrist rehabilitation for chronic stroke. *Neurorehabil Neural Repair.* 2009;23:837-846.
16. Dirette D, Hinojosa J. Effects of continuous passive motion on the edematous hands of 2 persons with flaccid hemiplegia. *Am J Occup Ther.* 1994;48:403-409.
17. Seitz AR, Dinse HR. A common framework for perceptual learning. *Curr Opin Neurobiol.* 2007;17:148-153.
18. Winter J, Hunter S, Sim J, Crome P. Hands-on therapy interventions for upper limb motor dysfunction following stroke. *Cochrane Database Syst Rev.* 2011;6:CD006609.
19. Yamaguchi T, Tanabe S, Muraoka Y, et al. Effects of integrated volitional control electrical stimulation (IVES) on upper extremity function in chronic stroke. *Keio J Med.* 2011;60:90-95.
20. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther.* 1987;67: 206-207.
21. Kim EH, Chang MC, Seo JP, Jang SH, Song JC, Jo HM. The effect of a hand-stretching device during the management of spasticity in chronic hemiparetic stroke patients. *Ann Rehabil Med.* 2013;37:235-240.
22. Fugl-Meyer AR. Post-stroke hemiplegia assessment of physical properties. *Scand J Rehabil Med Suppl.* 1980;7:85-93.
23. Borboni A, Fausti D, Mor M, Vertuan A, Faglia R. Un dispositivo CPM per la riabilitazione della mano. Presented at XX Congresso AIMETA Associazione Italiana di Meccanica Teorica e Applicata, September 12-15, 2011, Bologna, Italy.
24. Borboni A, Aggogeri F, Faglia R. Fast kinematic model of a seven-bar linkage with a single compliant link. In: *Proceedings, ASME 2014 12th Biennial Conference on Engineering Systems Design and Analysis,* ESDA 2014:ESDA2014-20076, V003T17A001.
25. Borboni A, Faglia R, Mor M. Compliant device for hand rehabilitation of stroke patient. In: *Proceedings, ASME 2014 12th Biennial Conference on Engineering Systems Design and Analysis,* ESDA 2014:ESDA2014-20081,V001T03A001.
26. Borboni A, Mor M, Faglia R. Gloreha—hand robotic rehabilitation: design, mechanical model, and experiments. *J Dyn Syst Meas Control.* 2016;138.
27. Chang CW, Kuo LC, Cheng YT, Su FC, Jou IM, Sun YN. Reliable model-based kinematics analysis system for articulated fingers. *Conf Proc IEEE Eng Med Biol Soc.* 2007;2007:4675-4678.
28. Carrera E, Filippi M, Zappino E. Laminated beam analysis by polynomial, trigonometric, exponential and zig-zag theories. *Eur J Mech A/Solids.* 2013;41:58-69.
29. Bell A, Muller M. Effects of kinesio tape to reduce hand edema in acute stroke. *Top Stroke Rehabil.* 2013;20: 283-288.
30. Bialosky JE, George SZ, Bishop MD. How spinal manipulative therapy works: why ask why? *J Orthop Sports Phys Ther.* 2008;38:293-295.
31. Salaffi F, Stancati A, Silvestri CA, Ciapetti A, Grassi W. Minimal clinically important changes in chronic musculoskeletal pain intensity measured on a numerical rating scale. *Eur J Pain.* 2004; 8:283-291.
32. Kong KH, Chua KS, Lee J. Symptomatic upper limb spasticity in patients with chronic stroke attending a rehabilitation clinic: frequency, clinical correlates and predictors. *J Rehabil Med.* 2010;42:453-457.
33. Lundstrom E, Smits A, Terent A, Borg J. Time-course and determinants of spasticity during the first six months following first-ever stroke. *J Rehabil Med.* 2010;42:296-301.
34. American Society for Surgery of the Hand. *The Hand, Examination and Diagnosis*. 2nd ed. Edinburgh/New York: Churchill Livingstone; 1983.
35. Villafane JH, Valdes K. Combined thumb abduction and index finger extension strength: a comparison of older adults with and without thumb carpometacarpal osteoarthritis. *J Manipulative Physiol Therap.* 2013;36:238-244.
36. Busner J, Targum SD, Miller DS. The Clinical Global Impressions scale: errors in understanding and use. *Compr Psychiatry.* 2009;50:257-262.
37. Rothman ML, Hantson LM, Nguyen M, Soo YW, Wessel TC, Beerse B. Reliability and validity of clinical global impression of stroke as a predictor of stroke outcome. *Ann Neurol.* 1998; 44:191.
38. Ferreira-Valente MA, Pais-Ribeiro JL, Jensen MP. Validity of four pain intensity rating scales. *Pain.* 2011;152:2399-2404.
39. Emshoff R, Bertram S, Emshoff I. Clinically important difference thresholds of the visual analog scale: A conceptual model for identifying meaningful intraindividual changes for pain intensity. *Pain.* 2011;152:2277-2282.
40. Farrar JT, Pritchett YL, Robinson M, Prakash A, Chappell A. The clinical importance of changes in the 0 to 10 numeric rating scale for worst, least, and average pain intensity:

analyses of data from clinical trials of duloxetine in pain disorders. *J Pain.* 2010;11:109-118.
41. Mohammad YAA. Anthropometric characteristics of the hand based on laterality and sex among Jordanians. *Int J Ind Ergon.* 2005;35:747-754.
42. Mulè C, Caimmi M, Bianchi P, Taveggia G, Missud S, Molteni F. Applicabilità di un Dispositivo CPM per la Mano in Pazienti Affetti da Stroke: Studio Pilota Multicentrico. Presented at 39th SIMFER Congress, October 16-19, 2011.
43. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.
44. Domholdt E. *Rehabilitation Research: Principles and Applications*. 3rd ed. St. Louis, MO: Elsevier Saunders; 2005.
45. Mehrholz J, Pohl M. Electromechanical-assisted gait training after stroke: A systematic review comparing end-effector and exoskeleton devices. *J Rehabil Med.* 2012;44:193-199.
46. Miranda ABW, Yasutomi AY, Souit C, Forner-Cordero A. Bioinspired mechanical design of an upper limb exoskeleton for rehabilitation and motor control assessment. Presented at 4th IEEE RAS & EMBS International Conference on Biomedical Robotics and Biomechatronics (BioRob), June 24-27, 2012.