Feasibility and efficacy of a robotic device for hand rehabilitation in hemiplegic stroke patients: A randomized pilot controlled study

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Abstract
Objective: The purpose of the study was to evaluate the feasibility and efficacy of robot-assisted hand rehabilitation in improving arm function abilities in sub-acute hemiplegic patients.
Design: Randomized controlled pilot study.
Setting: Inpatient rehabilitation centers.
Participants: Thirty hemiplegic stroke patients (Ashworth spasticity index <3) were recruited and randomly divided into a Treatment group (TG) and Control group (CG).
Interventions: Patients in the TG received intensive hand training with Gloreha, a hand rehabilitation glove that provides computer-controlled, repetitive, passive mobilization of the fingers, with multisensory feedback. Patients in the CG received the same amount of time in terms of conventional hand rehabilitation.
Main outcome measures: Hand motor function (Motricity Index, MI), fine manual dexterity (Nine Hole Peg Test, NHPT) and strength (Grip and Pinch test) were measured at baseline and after rehabilitation, and the differences, (Δ) mean(standard deviation), compared between groups.
Results. Twenty-seven patients concluded the program: 14 in the TG and 13 in the CG. None of the patients refused the device and only one adverse event of rheumatoid arthritis reactivation was reported. Baseline data did not differ significantly between the two groups. In TG, ΔMI 23(16.4), ΔNHPT 0.16(0.16), ΔGRIP 0.27(0.23) and ΔPINCH 0.07(0.07) were significantly greater than in CG, ΔMI 5.2(9.2), ΔNHPT 0.02(0.07), ΔGRIP 0.03(0.06) and ΔPINCH 0.02(0.03) [p=0.002, p=0.009, p=0.003 and p=0.038, respectively].
Conclusions: Gloreha Professional is feasible and effective in recovering fine manual dexterity and strength and reducing arm disability in sub-acute hemiplegic patients.

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Introduction

Upper limb recovery, particularly that of the hand, is complex in patients with cerebral stroke and requires an intensive approach. The focus of rehabilitation is on improving upper limb function and reducing long-term disability. The objective of physiotherapy is to train the arm through repetitive functional activities, paying particular attention to strength, coordination and speed. The need for intensive training has prompted, in the past two decades, the development of rehabilitation robots. Robotic systems can provide repetitive, reproducible, interactive forms of physical therapy that can be quantified. The results are very promising, showing that robot-assisted therapy is safe and well tolerated and that it has a positive impact on motor impairments.

Regarding upper limb rehabilitation, several research groups have developed robotic devices to provide passive and/or active movements. Initially, research concentrated on the more proximal portion of the arm; the development of devices for the hand took longer due to the complexity of wrist and finger movements. Use of robotic devices appears to reduce the motor deficit of the arm and affected hand and to improve hand function both at the wrist and fingers. Hence, the evidence supporting specific robot-assisted rehabilitation of the hand is very promising even if further study is required. In particular, evidence is limited about the benefit of passive exercises and mobilization of the hemiplegic upper limb following stroke, and further research is called for. Current evidence does not show whether robotics are more or less effective or harmful when compared with hands-on physiotherapy.

In this study we used Gloreha Professional, a new hand rehabilitation glove that provides computer-controlled, repetitive and passive mobilization of the fingers, with multisensory feedback. The hypothesis was that rehabilitation with this device could be not inferior in comparison with hands-on physiotherapy. The purpose of this study was to evaluate: 1) the feasibility of this new device, 2) its efficacy in improving arm function abilities, and 3) the costs involved in using it, in the rehabilitation of patients with stroke in the subacute phase.

Methods

This was a prospective, randomized controlled pilot study registered at ClinicalTrials.gov website: NCT02628418 on 12 September 2015. Post-stroke patients admitted for inpatient rehabilitation to the Neurological Rehabilitation of the Salvatore Maugeri Foundation, Lumezzane, Brescia and Habilita Hospital, Sarnico, Bergamo, Italy between May 2013 and January 2014 were screened for enrolment.

The protocol was approved by the Review Board of the two Hospitals and was carried out in conformity with the principles stated in the Declaration of Helsinki. All patients gave their written informed consent.

Eligible patients were randomly assigned, following a simple randomization procedure (computerized random numbers) conducted independently of the study investigators, to Treatment group or Control group, on a 1:1 ratio. To minimize bias we used consecutive enrolment and central randomization. Due to the nature of the trial, it was not possible to blind patients and healthcare personnel. But the outcome assessors and data analysts were blinded.

To standardize the physiotherapy approach in the two hospitals, we carried out joint training of staff, organizational meetings and planning before commencing patient enrolment.

Inclusion criteria were: age > 18 years, patients affected by stroke from cerebral ischemia or hemorrhage that had occurred ≤ 30 days before, with
Ashworth\textsuperscript{18} spasticity index $< 3$. Exclusion criteria were: orthopedic limitation (amputations, irreducible articular limitations, advanced osteoarthritis, active rheumatoid arthritis); peripheral nerve injury; uncontrolled inflammation; severe cognitive and behavioral disorders; neurodegenerative and neuromuscular diseases; Ashworth spasticity index $\geq 3$.

The degree of independence and need-of-assistance in basic activities of daily living was measured at enrolment and at the end of the study with the Functional Independence Measure scale (FIM),\textsuperscript{19} an 18-item ordinal scale rated from 1 (total dependence) to 7 (total independence) per item; 13 items of this scale, the sub-scale Motor-FIM, were used to evaluate motor disability.

The Ashworth spasticity index was measured both at enrolment and at the end of the study.

**Interventions**

**General rehabilitation.** All patients underwent basic rehabilitation following the guidelines\textsuperscript{6} according to the Bobath concept.\textsuperscript{20} A personalized rehabilitation program for each patient was designed by a team of specialists (physicians, speech therapist, and physiotherapists). Specific goals were set by the rehabilitation team on a patient-by-patient basis before beginning the study. Rehabilitation started the day after admission. The program was performed from Monday to Saturday over a period of about 6 weeks.

**Hand rehabilitation.** The specific hand intervention consisted of a total of 30 sessions, lasting 40 min/day, for 5 days/week. In Control Group, the affected hand was passively moved by the physiotherapist. The activities were:

1. Flexion-extension of the fingers (10 min).
2. Thumb opposition with the other fingers keeping the forearm in supine position (10 min).
3. Adduction and abduction of the fingers (10 min).
4. Global movement of the hand consisting in reaching for a 0.5 l empty bottle of water, taking hold of it, simulating the pouring of water into a glass, and then putting the bottle down and letting go of it (10 min).

In Treatment Group, the affected hand was passively moved by the glove Gloreha Professional (Idrogenet, Lumezzane, Italy).\textsuperscript{17,21} Each training session consisted of six parts:

1. A sequence of 17 cycles of movements including digital joint flexion/extension exercises, from the thumb to the fifth finger (7 min).
2. A sequence of 23 cycles of movements for 7 min (counting from one to five).
3. A sequence of 70 cycles of movements including thumb-finger opposition movements from the 2nd to the 5th finger (7 min).
4. A sequence of 28 cycles of movements including wave-like finger movements (7 min).
5. A sequence of 42 cycles of movements including fist opening/closing (7 min).
6. A sequence of 20 cycles of movements including flexion-extension of the fingers alternated with flexion-extension of the thumb (5 min).

**Outcome measures**

1. **Feasibility.** The feasibility of the device was assessed in terms of the number of patients who completed the program; side effects (the physiotherapist was required to report any adverse events occurring during the study in regard to the use of Gloreha Professional); and the level of operator difficulty for the physiotherapist in managing the device, assessed by visual analogue scale (VAS) (0 extremely simple - 10 extremely difficult).\textsuperscript{22}

2. **Efficacy.** The device’s efficacy in improving functional abilities was measured by the following tests at enrolment and at the end of the study in both groups:

   - Motricity Index\textsuperscript{23} used to measure the ability to activate a muscle group to move a body segment through a range of motion and resist external force. The upper extremity motricity index includes pinch grasp, elbow flexion, and shoulder abduction. The total upper extremity score involved adding one to the sum of the
three actions (each score 0-33) with a maximum possible score=100.

- Nine Hole Peg Test, a measure of coordination and mono-manual dexterity. It consists in collecting 9 pegs and inserting them into holes in a wooden base within a 50-sec time limit. The score is the average number of pegs inserted/tests performed.

- The Grip and Pinch test, a measure of strength, was performed with a hydraulic dynamometer (Jamar Plus+, Sammons Preston) according to the standard procedure described by Mathiowetz. For each evaluation, the mean value of 3 tests normalized for body mass index (BMI) was calculated.

- The Arm disability was assessed of the study with the Quick version of the Disabilities of the Arm, Shoulder, and Hand (Quick-DASH) questionnaire. The Quick-DASH is a 19-item ordinal scale with a 5-level rating of items from 1 (no difficulty) to 5 (unable to do). Quick-DASH can be subdivided into an 11-item (abilities and symptoms) and an 8-item optional work module and sports/performing arts module. In the 11-item subscale, the subject defines the ability to perform some actions (8 items) and the intensity of some symptoms (3 items), referring to the previous week. The total score range is from 19 (no disability) to 95 (full disability).

3. **Cost analysis.** Costs were calculated in terms of the time required by healthcare personnel, using the average cost per hour of a physiotherapist per total number of rehabilitation treatments per patient and in terms of the time required by physiotherapist to take care that the robotic device working correctly during the sessions. The energy cost of the instrument was insignificant. The equivalent cost of the device for the period of patient treatment was calculated incorporating depreciation over a period of 5 years (20% per year). The capital cost of the device was 30000€. We considered 67 potential patients treatable per year (8 patients/day for 30 days of treatment considering 250 days/year). Indirect costs were not considered because these were common to both groups.

**Statistical analysis**

Statistical analysis was carried out with Graph Pad Prism 4 version 4.03 and MedCalc version 11.4.2. The normality of variables was assessed using the Shapiro–Wilk test. To compare groups at baseline, the Mann-Whitney-Wilcoxon test for continuous variables was used. Student’s paired t-test was used for within-group comparisons between baseline and after 30 days of all continuous variables. The differences between groups in the delta improvement (posttest -pretest) were compared by analysis of variance (ANOVA). All reported P values were two-sided.

**Results**

Patient recruitment and flow, excluded patients and reasons for exclusion are noted in Figure 1. Table 1 shows clinical characteristics of the study group at admission. Hospital length of stay was 72 (17) days in Control Group and 69 (17) days in Treatment Group (p=0.56). Patients performed 4.6 (0.6) sessions/week of general rehabilitation in Control Group and 4.5 (0.5) sessions/week in Treatment Group (p=0.36). All patients were right-handed, so the treated hand was not always the dominant one.

After inpatient rehabilitation, in both groups both FIM [Control Group: 58 (32), p=0.001; Treatment Group: 79 (31), p=0.0005] and Motor-FIM [Control Group: 35 (24), p=0.001; Treatment Group: 53 (25), p=0.0005] scores showed a significant increase compared to baseline.

The Ashworth spasticity index in the various areas did not change significantly compared to baseline in either group after inpatient rehabilitation. The index was respectively 0.46 (0.52) in Control Group (p=1) and 0.57 (0.85) in Treatment Group (p=1) of finger flexor, 0.15 (0.37) in Control Group (p=1) and 0.07 (0.27) in Treatment Group (p=0.5) for opponents of the thumb, and 0.46 (0.66) in Control Group (p=0.31) and 0.71 (0.73) in Treatment Group (p=0.75) for wrist flexors.
Figure 1. Flow chart of the study.
1. Feasibility outcome. Twenty-seven patients completed the 30 sessions of the program: 13 in Control Group and 14 in Treatment Group. Three patients did not complete the program: 2 in Control Group due to an acute hospital transfer for infection, and 1 in Treatment Group due to reactivated rheumatoid arthritis.

In Treatment Group, the degree of difficulty with managing the device was evaluated daily by the physiotherapist by VAS. We compared the mean of the values reported on the first 3 days with the mean of values reported in the last 27 days. The mean VAS score for the first three days was 5.13 (1.6) vs. 1.16 (0.26) for the last 27 days, i.e. the device became ‘simple to use’ from day 4 on in all patients. The time commitment of the physiotherapist decreased from 24 (8.5) min in the first 3 days to 11 (1.1) min in the last 27 days. No patient refused the device.

2. Efficacy outcome. Table 2 shows the comparison of the assessments of the paretic side pre versus post intervention in the two groups. Motricity Index, Nine Hole Peg Test, Grip and Pinch test - strength normalized for BMI of the paretic upper limb, were similar at baseline between the two groups (respectively \( p=0.31 \), \( p=0.88 \), \( p=0.60 \) and \( p=0.25 \)) but improved significantly after inpatient rehabilitation only in Treatment Group. Quick-DASH, similar at baseline between the two groups (\( p=0.74 \)), showed a significant decrease in score only in Treatment Group.

Also Table 2 shows the changes between pre and post-intervention for the various outcome parameters.

3. Cost analysis
   Treatment group. The cost of a physiotherapist € 0.40/minute. Considering the mean time consumed in the first three days and in the last 27 days, the cost of the physiotherapist for the complete 30-day cycle of treatment with the Gloreha Professional device was: \( (24 \text{ min} \times €0.40/\text{min} \times 3 \text{ days}) + (11 \text{ min} \times €0.40/\text{min} \times 27 \text{ days}) = € 147.60/\text{patient} \). The cost of device calculated for the 30-day period of treatment was: € 89.60/\text{patient}.

Table 1. Clinical characteristics of the study group at admission.

<table>
<thead>
<tr>
<th></th>
<th>Control Group (n=15)</th>
<th>Treatment Group (n=15)</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, ( n ) (%)</td>
<td>7 (47)</td>
<td>7 (47)</td>
<td>0.72</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>73 (14)</td>
<td>72 (14)</td>
<td>0.41</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>25.3 (6.2)</td>
<td>26.3 (3.4)</td>
<td>0.34</td>
</tr>
<tr>
<td>Days from acute event to inclusion, mean (SD)</td>
<td>17.8 ± 7.9</td>
<td>15.2 ± 6.8</td>
<td>0.34</td>
</tr>
<tr>
<td>Ischemic stroke, ( n ) (%)</td>
<td>9 (60)</td>
<td>10 (67)</td>
<td>0.58</td>
</tr>
<tr>
<td>Hemorrhagic stroke, ( n ) (%)</td>
<td>6 (40)</td>
<td>5 (33)</td>
<td>0.34</td>
</tr>
<tr>
<td>Cortical stroke, ( n ) (%)</td>
<td>7 (47)</td>
<td>5 (33)</td>
<td>0.34</td>
</tr>
<tr>
<td>Subcortical stroke, ( n ) (%)</td>
<td>8 (53)</td>
<td>10 (67)</td>
<td>0.34</td>
</tr>
<tr>
<td>Dominant Limb:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Right</td>
<td>15</td>
<td>15</td>
<td></td>
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<tr>
<td>Paretic side:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Right, ( n ) (%)</td>
<td>5 (33)</td>
<td>4 (27)</td>
<td></td>
</tr>
<tr>
<td>- Left, ( n ) (%)</td>
<td>10 (67)</td>
<td>11 (73)</td>
<td></td>
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<tr>
<td>Ashworth spasticity index of:</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>- Finger flexor, mean (SD)</td>
<td>0.46 (0.52)</td>
<td>0.29 (0.61)</td>
<td>0.35</td>
</tr>
<tr>
<td>- Opponents of the thumb, mean (SD)</td>
<td>0.23 (0.44)</td>
<td>0.21 (0.43)</td>
<td>0.96</td>
</tr>
<tr>
<td>- Wrist flexors, mean (SD)</td>
<td>0.54 (0.66)</td>
<td>0.50 (0.52)</td>
<td>0.98</td>
</tr>
<tr>
<td>FIM, mean (SD)</td>
<td>43.5 (26.5)</td>
<td>52.7 (30)</td>
<td>0.32</td>
</tr>
<tr>
<td>Motor-FIM, mean (SD)</td>
<td>23.5 (18.6)</td>
<td>28.2 (23.4)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

BMI, Body Max Index; FIM, Functional Independence Measure.
Table 2. Comparison of the assessments of the paretic side pre- vs. post-intervention in the two groups.

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Treatment Group</th>
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<tbody>
<tr>
<td></td>
<td>Pre-mean (SD)</td>
<td>Post-mean (SD)</td>
</tr>
<tr>
<td>Motricity Index NHPT (pegs/sec)</td>
<td>28.1 (29.8)</td>
<td>33.2 (27.5)</td>
</tr>
<tr>
<td>PINCH (Kg/BMI)</td>
<td>0.19 (0.43)</td>
<td>0.22 (0.14)</td>
</tr>
<tr>
<td>GRIP (Kg/BMI)</td>
<td>0.017 (0.07)</td>
<td>0.04 (0.07)</td>
</tr>
<tr>
<td>Quick DASH</td>
<td>65.6 (11.5)</td>
<td>65.1 (16.4)</td>
</tr>
</tbody>
</table>

Within group p value

Control Group 0.0665 0.2792 0.0854 0.0869 0.8212
Treatment Group 0.0004 0.0024 0.0005 0.0040 0.0048

Changes between pre and post-intervention, mean (95% CI)

Control Group 5.2 (−0.4~10.7) 0.02 (−0.02~0.07) 0.03 (−0.005~0.07) 0.02 (−0.001~0.04) −0.43 (−4.5~3.6)
Treatment Group 23.0 (13.6~32.4) 0.16 (0.09~0.25) 0.27 (0.13~0.41) 0.07 (0.03~0.1) −15.7 (−25.7~−5.8)

Between groups p value

Control group. Considering the time employed to perform the hand rehabilitation, i.e. 40 min/day, the cost of the physiotherapist for the 30 days of treatment was: 40 min x €0.40/min x 30 days = € 480/patient.

Discussion

This randomized pilot study found the feasibility of implementing a new hand rehabilitation glove, Gloreha Professional, that provides computer-controlled, repetitive, passive mobilization of the fingers with multisensory feedback, in sub-acute stroke patients. It showed also efficacy in improving functional parameters of the affected arm. The device was well tolerated by the patients. The program was feasible, in that 93% of patients ended the program and 100% of patients performed all rehabilitation sessions. From the point of view of the health operator, the first three days required a greater time investment for putting the glove on correctly and activating the software and device. During this initial stage, the physical therapist had to adapt the device to the size of each patient’s hand in order to ensure that mobilization was activated correctly. Once the correct positioning of the glove was found, management of the therapy with the Gloreha Professional device was simple and took little time.

Patients in the treatment group significantly improved the motor function of the paretic upper limb (Motricity Index), their coordination and mono-manual dexterity (Nine Hole Peg Test) and strength (Grip and Pinch) in contrast to controls, and the cost savings was considerable - the robot-assisted treatment cost approximately half that of conventional physiotherapy.

These results confirm previous findings that robot-assisted hand rehabilitation in stroke patients can provide more intensive treatment ensuring correct movement patterns, yielding a superior outcome compared to that with conventional treatment.27–29

Arm and hand functions are fundamental for activities of daily living and they are a very important component of quality of life in stroke patients. Hand dysfunction leads to movement limitations and sensory disorders, making it impossible to independently perform a variety of daily tasks.11–14 The degree of
independence of the patients assessed after the rehabilitation period by the FIM and Motor-FIM subscale showed an improvement in both groups, demonstrating the efficacy of both modes of physiotherapy – conventional and robot-assisted. However, arm, shoulder and hand disabilities as measured by QuickDASH decreased significantly only in the robot-assisted group, demonstrating that the treatment with Gloreha Professional was more effective.

Continuous passive motion is a rehabilitative treatment in use for over thirty years. In chronic stroke patients, it reduced the spasticity of the wrist and elbow joints and in patients in the subacute phase, in particular in those with flaccid hand hemiplegia, it reduced edema. The sensorimotor system appears to be activated by passive movement, imagery and observation in severely hemiparetic stroke patients. Seitz et al. showed in fact that perceptual learning occurs not only under training conditions but also in situations of unattended, passive sensory stimulation. Gloreha Professional can be used in a variety of rehabilitation exercises, including sequential and simultaneous flexion-extension of all fingers, functional movements and other movement combinations, and allows the patient to follow, cooperate with and complete the robot-assisted movements thanks to the low impedance of the device (the glove provides no hindrance to the patient’s own movement). Gloreha, thanks to its simple, modular design, can be used in various, prolonged therapies with minimal supervision by the therapist. The association of hand and finger movements with audio-visual effects in order to convey the concept of movement appears to be of particular importance for neurological patients. In fact, auditory feedback seems to aid patient motivation in performing task-oriented motor exercises; providing temporal and spatial information through auditory cues can improve the motor learning process. During the study, we observed that the presence of visual feedback was a further stimulus in patients with left hemi-syndrome suffering from neglect, confirming the findings of Varalta et al. The neuropsychological aspects of post-stroke patients, although not within the scope of this study, represent a vast scenario that could benefit from this type of therapy.

Our analysis of the costs, even if carried out in preliminary fashion in a limited number of patients, indicates that it is possible to carry out an intensive robot-assisted treatment of the hand in hemiplegic patients at lower cost than conventional treatment and without increasing the physiotherapist’s time commitment. The robot as such provides support to the physiotherapist, enabling the physiotherapist to devote more time to patients who cannot be treated with the robot.

There are some study limitations to consider. This is a pilot study carried out in a limited number of patients in only two centers and the number and the type of practice tasks were different between these two groups. Our findings need to be confirmed in a larger randomized controlled study. Furthermore, this device is not applicable to patients with index of hand Ashworth spasticity \( \geq 3 \), which limits its field of application. No follow up data are another limitation of this study. Finally, in some patients active assisted exercise would have been useful, but this function was not present in the version of glove used. At the time of the study the most advanced version of the device was not available yet; this new version will allow to set partial ranges of motion, and the patient can actively complete the movement started by the device.

An intensive hand treatment using a robotic device can be not inferior to a standard treatment performed by the physiotherapist, but more efficient in improving the affected arm in sub-acute stroke patients. Further studies are warranted to confirm our findings in a larger and more representative patient sample.

### Clinical messages

- An intensive hand treatment with an hand rehabilitation glove that provides computer-controlled repetitive, passive mobilization of the fingers with multisensory feedback, can be not inferior to a standard treatment performed by the physiotherapist.
- The hand rehabilitation with Gloreha Professional seems to be feasible and efficient in improving the affected arm and in recovering fine manual dexterity and strength and reducing arm disability in sub-acute hemiplegic patients with a low level of spasticity.
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Conflict of interest
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