# Recovery of hand function with robot-assisted therapy in acute stroke patients: a randomized-controlled trial

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**In the last few years, not many studies on the use of robot-assisted therapy to recover hand function in acute stroke patients have been carried out. This randomized-controlled observer trial is aimed at evaluating the effects of intensive robot-assisted hand therapy compared with intensive occupational therapy in the early recovery phases after stroke with a 3-month follow-up. Twenty acute stroke patients at their first-ever stroke were enrolled and randomized into two groups. The experimental treatment was performed using the Amadeo Robotic System. Control treatment, instead, was carried out using occupational therapy executed by a trained physiotherapist. All participants received 20 sessions of treatment for 4 consecutive weeks (5 days/week). The following clinical scales, Fugl-Meyer Scale (FM), Medical Research Council Scale for Muscle Strength (hand flexor and extensor muscles) (MRC), Motricity Index (MI) and modified Ashworth Scale for wrist and hand muscles (MAS), were performed at baseline (T0), after 20 sessions (end of treatment) (T1) and at the 3-month follow-up (T2). The Barthel Index was assessed only at T0 and T1. Evidence of a significant improvement was shown by the Friedman test for the FM [experimental group (EG): $P=0.0039$, control group (CG): $P<0.0001$], Box and Block Test (EG: $P=0.0185$, CG: $P=0.0086$), MI (EG: $P<0.0001$, CG: $P=0.0303$) and MRC (EG: $P<0.0001$, CG: $P=0.001$) scales. These results provide further support to the generalized therapeutic impact of intensive robot-assisted treatment on hand recovery functions in individuals with acute stroke. The robotic rehabilitation treatment may contribute toward the recovery of hand motor function in acute stroke patients. The positive results obtained through the safe and reliable robotic rehabilitation treatment reinforce the recommendation to extend it to a larger clinical practice. *International Journal of Rehabilitation Research* 00:000–000 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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## Introduction

The most important motor deficit in acute stroke survivors is represented by the paresis of the affected side and patients with upper extremity paresis show scarcities in motor control (Alt Murphy *et al.*, 2011) and motor function (Broeks *et al.*, 1999), with limitations in daily functions (Lai *et al.*, 2002). As is known, the hand is required in everyday activities such as eating, manipulating objects, or handwriting, and the loss of hand dexterity is a serious common result of a cortical lesion because of cerebrovascular disease (Sale *et al.*, 2012). A great number of activities of daily living (ADLs) involves the use of the upper extremities and the hands; retraining reach and grasp skills is critical for the return to a full quality of life (Schweighofer *et al.*, 2012). Recovery of hand function is essential to improve the quality of life of stroke survivors. It has already been shown that the abilities that are lost or affected by stroke depend on the extent, the type (ischemic or hemorrhagic), and the location of the brain damage.

The main goal in hand rehabilitation is to relearn basic skills such as eating, dressing, and walking and the effectiveness of interventions on conditions leading to long-term disability is a complex task as the outcome depends on many interacting factors (Wallace *et al.*, 2010; Franceschini *et al.*, 2012). Occupational therapy (OT) aims to enable patients to achieve health, well-being, and life satisfaction through participation in occupation and specifically aims to promote recovery through the use of purposeful activities. Legg *et al.* (2006) showed in their meta-analysis that OT interventions in patients with stroke reduce the chances of a poor outcome in terms of deterioration in the ability to perform ADLs and have a beneficial effect on the patient's ability to perform personal ADLs and extended ADLs.

In stroke recovery, the last few years have shown the advantage of robot therapy in performing an intensive motor tasks-based training and to provide a high number

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of task-specific movements by supporting and guiding repetition of the impaired limb. The number of papers published on robotic therapy has increased rapidly, but it is still not clear whether robot therapy really improves function (Lo, 2012). From a mechanical design point of view, there are two types of robotic devices for upper limb rehabilitation: the end-effector-based and the exoskeleton-based robots. The main advantage of the upper limb robot on the basis of the end-effector system is that it adapts to patients with different body sizes. In contrast, the exoskeleton upper limb robot required various modifications in different patients because they needed an optimal joint adaptation to work correctly.

Several reviews and meta-analyses have assessed the effectiveness of robotic therapy in comparison with conventional therapy, but the wide variety of devices and protocols may explain the heterogeneity of results (Lo, 2012; Mehrholz *et al.*, 2012).

Recently, Lo (2012) confirmed in their review that the results of a meta-analysis of robotic literature show that a number of pilot studies or case series have been carried out to illustrate proof of concept or clinical feasibility. However, there have not been many larger randomized-controlled trials (RCTs) investigating the clinical efficacy and reliability of these devices or even their clinical safety and tolerability (Lo, 2012). In particular, extensive RCTs are needed to clarify the relationship between impairment and function, besides a classification of the outcome measures, as both these have important implications for the role of robotic systems in rehabilitation. Rehabilitation robotic systems for upper extremities have the potential to deliver large doses of motor training in a cost-effective manner. Numerous robotic devices for the recovery of hand function with various levels of complexity and functionality have been developed over the last 10 years. The human hand is a complex neuromuscular and sensorimotor apparatus with a 21 degrees-of-freedom (DOFs) skeleton actuated by 29 skeletal muscles. These robotic devices range from simple instruments that support single joint movements to mechanisms with as many as 18 DOFs that can support multijoint movements at the wrist and fingers (Balasubramanian *et al.*, 2010). Until now, stroke survivors in the chronic stage are largely the most involved in robot therapy studies, whereas there has been much less research on the robot-assisted rehabilitation of stroke survivors in the acute and subacute phases. Balasubramanian *et al.* (2010) identified 30 devices for hand function, but among these, only eight were tested in clinical trials that showed an improvement in the functional use of the affected hand. Recently, Lum *et al.* (2012) discussed the impairments in hand function after stroke and presented the works on robot-assisted approaches. Clinical testing has shown that robotic hand training can improve movement ability and performance on functional scales mostly in chronic stroke patients, but it is still unclear which is the most appropriate population in terms of time since stroke (acute and/or subacute and/or chronic) and/or whether robot-assisted movement has advantages over unassisted movement or conventional therapy.

The main objective of the randomized-controlled observer-blind trial (RCT) presented in this article was to evaluate the effects of intensive robot-assisted hand therapy compared with intensive OT in acute stroke patients at their first event and in the early phase of recovery after stroke, with a 3-month follow-up.

## Patients and methods

### Participants

This study was a RCT. Eligible hemiparetic acute stroke survivors (Péter *et al.*, 2011) at their first stroke were recruited consecutively. The study included only patients enrolled $30 \pm 7$ days after the event onset, with solely ischemic or hemorrhagic lesions. Diagnosis was confirmed by means of a computed tomography scan and/or an MRI. Inclusion criteria for all patients were as follows: first acute event of cerebrovascular stroke, unilateral paresis, ability to understand and follow simple instructions, ability to remain in a sitting posture, mini Mental State Examination score more than 20, muscle strength in finger flexion and extension more than 2 (movement without gravity) evaluated with Medical Research Council, and absence of sensory impairment evaluated using a neurological test.

The following exclusion criteria were identified: bilateral impairment, severe sensory deficits in the paretic upper limb, posterior circulation, cognitive impairment or behavioral dysfunction that would influence the ability to comprehend or perform the experiment, refusal or inability to provide informed consent, other current severe medical problems, history of endogenous depression or serious psychiatric disorders and severe visual deficits, patients younger than 18 years or older than 80 years of age, previous cerebrovascular disease, and cognitive disorders such as neglect and upper limb apraxia.

The local ethical committee center approved the study and all patients provided informed consent to the investigation.

### Procedures

After providing written informed consent, stroke survivor inpatients with a first-ever ischemic monohemispheric were divided randomly using specific software into two groups: experimental group (EG) and control group (CG).

The following clinical outcomes were performed at baseline (T0), at the end of treatment (T1), and at the 3-month post-treatment follow-up visit (T2): Fugl-Meyer Scale (FM) (Lindmark and Hamrin, 1988), Medical Research Council Scale for Muscle Strength (hand flexor

and extensor muscles) (MRC) (Riddle *et al.*, 1987), Motricity Index (MI) (Paternostro-Sluga *et al.*, 2008), modified Ashworth Scale for wrist and hand muscles (MAS) (Sommerfeld *et al.*, 2012), Box and Block Test (BB) (Page *et al.*, 2012), and Barthel Index (Page *et al.*, 2012). Primary outcomes were the FM and the BB. The secondary outcomes were MI and MAS. A blinded trained occupational therapist not involved in the research treatment performed all assessments. All the above scales were validated.

## Therapeutic intervention

All participants underwent inpatient rehabilitation consisting of at least 3 h/day of physiotherapy according to individually tailored exercise scheduling. In addition to standard rehabilitation, eligible patients were randomized and received 40 min daily sessions of either experimental (EG) or control treatment (CG) according to the random allocation outcome.

### *Experimental group*

Each patient was asked to perform 20 sessions (4/5 days a week for 4/5 weeks) of robot-assisted hand therapy using the Amadeo Robotic System (Tyromotion GmbH, Graz, Austria). The end-effector-based Amadeo Robot has five DOFs and provides the motion of one or all five fingers through a passive rotational joint placed between the fingertip and an entity that moves laterally (the thumb has two passive rotational joints). All five translational DOFs are independent and provide an almost entire coverage of the fingers' workspace. The interface between the human hand and the machine is achieved thanks to elastic bands or plasters and the wrist is restrained from movement by a Velcro strap (Sale *et al.*, 2012).

Each session lasted 40 min (30 min of hand training and 10 min of passive upper limbs mobilization). According to our previous paper, the exercises were carried out as follows: (i) continuous passive motion therapy (the hand is stimulated in continuous passive motion therapy modality for 5 min); (ii) assisted therapy (the hand motion is assisted by the robot and adjusted to the individual limit of function and performance of each patient for 10 min); and (iii) balloon (active training in a virtual environment by carrying out various target-oriented tasks for 10 min).

Passive movement speeds were selected according to patients' ability. The difficulty of each exercise was increased day by day according to the hand motor improvements of the single patient. In particular, the therapist may select from a number of different modules, according to the progress made during therapy, and may also choose between completely passive, assisted, or active variations. Resting time (1 min) within an inter-session exercise was allowed according to individual needs. The hand flexion and extension strengths were performed by the robot at the end of treatment and during the assessment session. The limit of the movement can be set for each individual finger; single fingers can be excluded altogether or limited. In this way, the therapist can react optimally to each and every constraint that a patient has. The patient's paretic wrist is placed in a custom-made support (available for both arms) attached to the robot. The therapist designs a specific rehabilitation program for each individual.

### *Control group*

Each participant received 20 sessions (4/5 days a week for 4/5 weeks) of OT in addition to standard treatment. Each participant received personalized OT training in a separate room, with only one participant per therapist. In particular, patients received OT for a 40-min therapy session each working day (i.e. five times a week), conducted one on one by an occupational therapist for 4 consecutive weeks. A treatment protocol was developed for each patient and was focused exclusively on recovery of hand function. According to international standards, the OT activities consisted of different purposeful kinetic activities with unimanual or bimanual tasks, with or without ADL activities.

The occupational therapist could offer passive, active-assistive, or active training, as deemed appropriate for the patient's ability. Tasks and activities were focused on reducing upper limb activity limitations identified at baseline assessment and targeted three occupational performance goals identified by the parents. Planning activities required task analysis and development of guidelines for grading to challenge patients with varying capabilities.

During the study, EG and CG patients did not receive any supplemental or additional concomitant upper limb treatment. Each missed session was retrieved. In both groups, participants who did not retrieve sessions and interrupted treatment for more than 3 consecutive days were excluded from the study.

## Data analysis

A preliminary descriptive analysis was carried out to check the normal distribution of patients' clinical and instrumental data using the Shapiro–Wilk test. The Kolmogorov–Smirnov test was used to assess the difference between the samples at T0. Unless collected variables showed a normal distribution, parametric statistical tests were used. A repeated measure analysis of variance model was carried out using time as a within-group factor to evaluate within-group changes over time. The Friedman test was used to analyze ordinal data in the different evaluation sessions within each patient group. In the presence of significant main effects, the Wilcoxon signed-rank test was performed to determine the location of any important difference between time points. The $\alpha$

level for significance was set at $P$ value less than 0.05 for the first level of analysis.

## Results

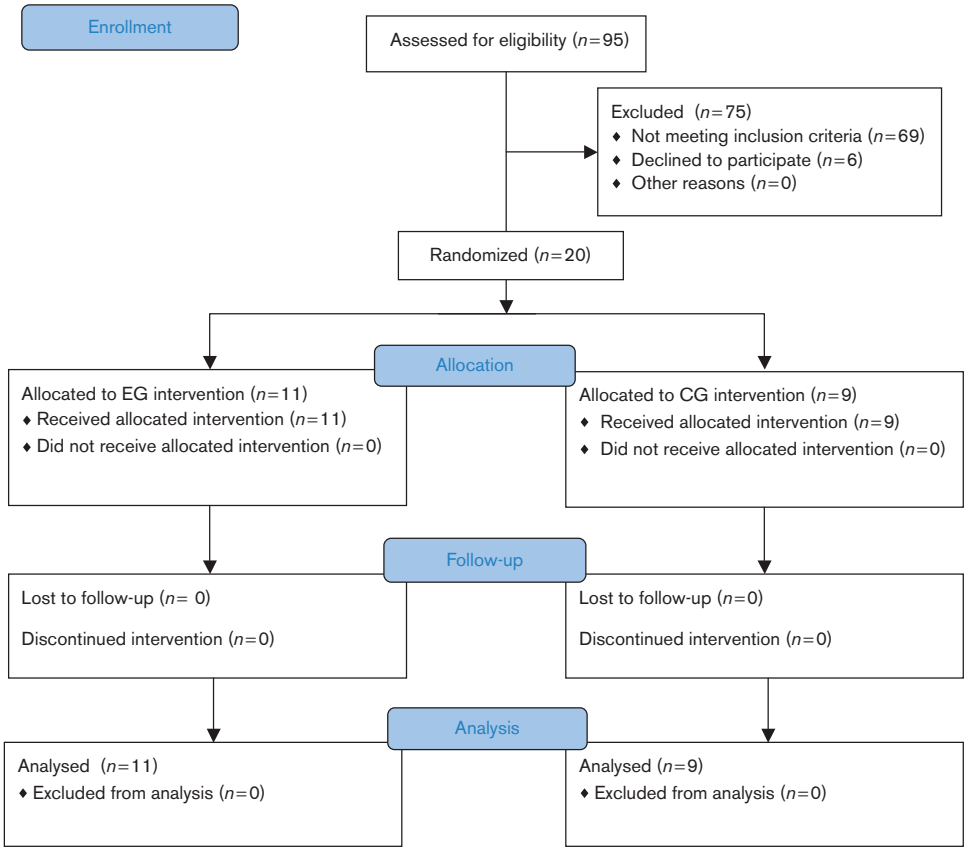
Ninety-five patients were screened; 20 fulfilled the inclusion criteria and were assigned randomly to the groups as follows: 11 to the robot-assisted therapy (EG) and nine to the OT (CG) (Fig. 1). The distribution of the study participants ($N = 20$) by age, sex, and main clinical and demographical characteristics did not show significant differences in the Kolmogorov–Smirnov test between the EG and the CG (Table 1). No dropouts were recorded during treatment and all participants fulfilled the protocol (compliant participants, $N = 20$). Table 2 summarizes the observed mean ± SD and other statistical results for all tests as they were measured on the compliant participants at T0 ($N = 20$), T1 ($n = 20$), and T2 ($N = 20$). Clinical improvements that fulfilled the protocol were found in EG and CG patients. In particular, using the Friedman test, a statistically significant improvement in EG for the FM ($P = 0.0039$), the BB ($P = 0.0185$), MI ($P < 0.0001$), and MRC ($P < 0.0001$) was found. A statistically significant increase in the MAS score in EG was found ($P = 0.0025$). Similar to EG, the Friedman test showed statistically significant improvements in CG for the FM ($P < 0.0001$), BB ($P = 0.0086$), MI (CG: $P = 0.0303$), and MRC (CG: $P = 0.001$) (Fig. 2).

## Discussion

The principal issues of this study may be summarized as follows: effectiveness of intensive robot-assisted hand therapy as a rehabilitation treatment in acute stroke patients and comparison of the results, in terms of gain in clinical scales, between patients who underwent robot therapy and those who underwent an intensive OT treatment.

After stroke injury, about 80% of patients at 3 weeks after stroke showed total or partial dependence in ADLs and about 30% of these at 6 months to 5 years (Shah *et al.*, 1990). Immediately after stroke, therefore, the main goal is to restore function following the injury, with the aim of achieving the best quality of life (Langhorne and Pollock, 2002). A rehabilitative program should maximize functional independence, promote resumption of the patients' pre-existing lifestyle, reintegrate patients into the home and community, enhance quality of life, and facilitate psychological and social adaptation (Legg *et al.*, 2007).

**Fig. 1**




Study consort. CG, control group; EG, experimental group.

**Table 1 Distribution of the study participants by age, sex, and main clinical characteristics**

| | Control group ($n=9$) | Experimental group ($n=11$) |
|---|---|---|
| Dropouts | 0 | 0 |
| Compliants | 9 | 11 |
| Sex | | |
| Female | 3 | 3 |
| Male | 6 | 8 |
| Etiology | | |
| Hemorrhagic | 2 | 3 |
| Ischemic | 7 | 8 |
| Lesion side | | |
| Right | 4 | 3 |
| Left | 5 | 8 |
| Age (mean±SD) | 72.56±8.98 | 67.0±12.4 |

**Table 2 Observed mean±SD of all tests and results**

| | T0 | T1 | T2 |
|---|---|---|---|
| Motricity Index | | | |
| Control group | 61.25±19.40 | 75.63±17.52 | 76.50±17.30 |
| Experimental group | 37.55±21.96 | 55.64±30.33 | 60.18±29.66 |
| Fugl-Meyer Test | | | |
| Control group | 78.63±15.15 | 98.13±16.90 | 97.13±14.58 |
| Experimental group | 56.09±17.79 | 73.27±27.02 | 71.64±28.81 |
| MRC | | | |
| Control group | 5.750±2.121 | 7.25±23.18 | 7.875±2.588 |
| Experimental group | 3.182±2.639 | 5.818±2.601 | 6.091±2.773 |
| Ashworth Scale | | | |
| Control group | 3.125±3.796 | 2.250±2.915 | 3.625±3.335 |
| Experimental group | 6.364±3.957 | 4.727±4.101 | 5.636±4.610 |
| Box and Block Test | | | |
| Control group | 5.0±7.194 | 9.111±12.02 | 12.33±14.77 |
| Experimental group | 2.091±4.7 | 9.091±13.50 | 16.09±18.87 |

MRC, Medical Research Council Scale for Muscle Strength (hand flexor and extensor muscles).

An important role, to achieve maximum independence in ADLs, is represented by recovery of the hand motor that often remains strongly impaired.

The activities of OT in the last few years have proved to be fundamental for the functional recovery of the upper limb and the hand and to promote the ADLs. OT is a fundamental element in the rehabilitation of patients with stroke (Legg *et al.*, 2007). OT is a complex intervention including skilled observation; the use of standardized and nonstandardized assessments of the biological, psychiatric, social, and environmental determinants of health; clarification of the problem; formulation of individualized treatment goals; and the delivery of a set of individualized problem-solving interventions (American Occupational Therapy Association, 1994).

It entails 'use of purposeful activity or interventions designed to achieve functional outcomes which promote health, prevent injury or disability, and which develop, improve, sustain or restore the highest possible level of independence' (Balasubramanian *et al.*, 2010). Legg *et al.* (2007) showed in their meta-analysis that stroke patients who receive OT focused on ADLs, as opposed to no routine OT, are more likely to be independent in those activities. These scientific evidences support the choice of OT as a rehabilitation treatment in the CG.

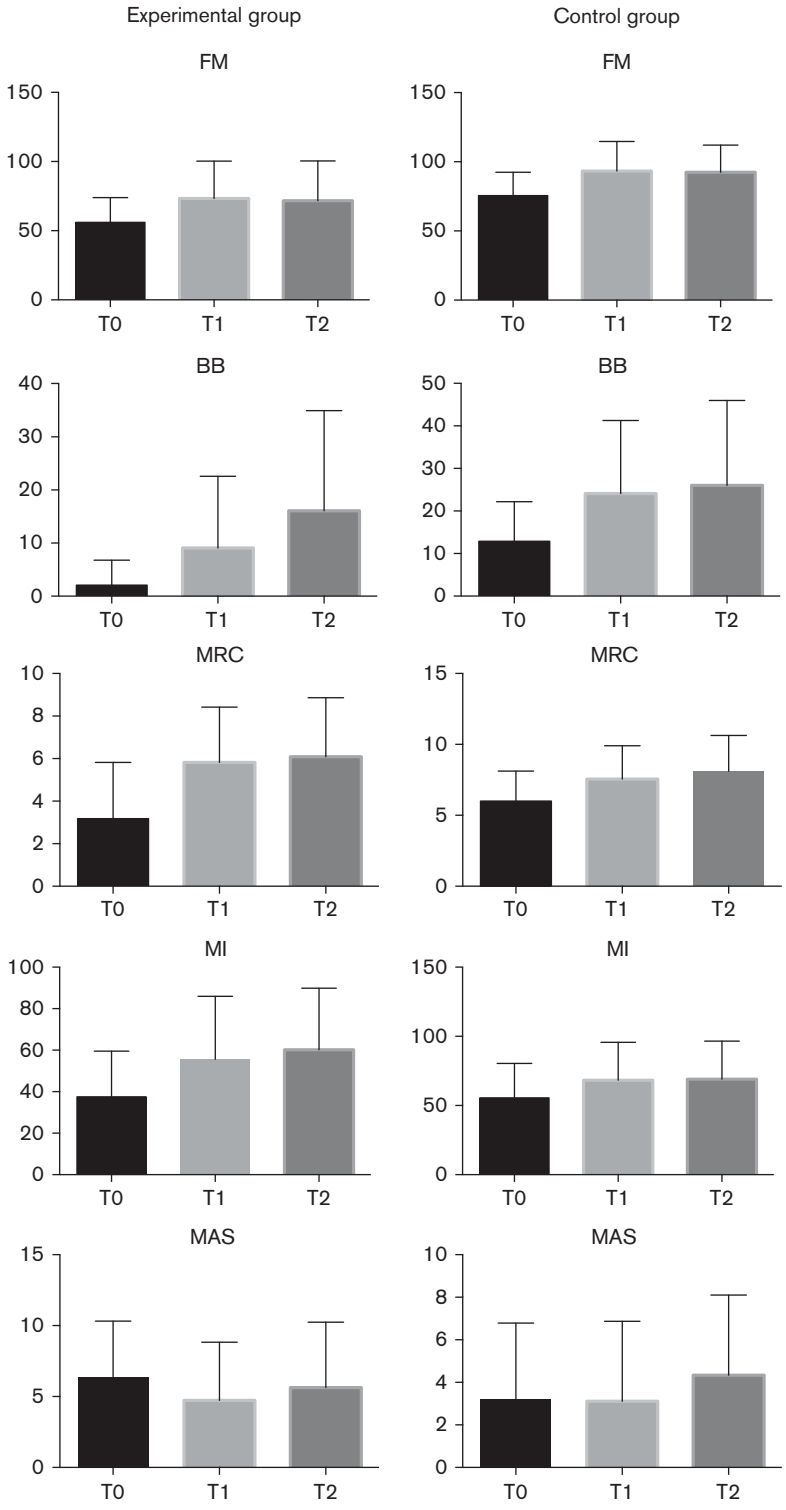
Our results showed that an intensive robot-assisted treatment in acute stroke patients can contribute toward achievement of a significant decrease in motor impairment in the hand as reported by Balasubramanian *et al.* (2010).

The clinical protocol is easy and reproducible, and allows the treatment of patients with moderate to severe upper limb paresis. The results in EG confirm those presented in a previous paper, where we showed an improvement in MRC, MAS, FM, and MI. In particular, the results of statistical analyses in EG showed that the gains achieved at the end of treatment were maintained at follow-up. This result is very important because the gain achieved is not exercise and/or time dependent, but could be secondary to reorganization of brain structures (Fazekas *et al.*, 2006). The fingers share one of the largest cortical representation areas in the primary motor area (Hesse *et al.*, 2008). There is neurophysiological evidence in humans that sensory stimulation induces long-term potentiation in the motor cortex and increases corticospinal excitability (Kaehlin-Lang *et al.*, 2002). The treatment of the plegic fingers after stroke is pertinent, given their large cortical representation, with a presumed competition between proximal and distal limb segments for plastic brain territory (Mazzoleni *et al.*, 2013a, 2013b). The gain in the MAS score in EG at the end of the robot-assisted treatment and at follow-up supports the recommendation of Pandyan *et al.* (2003) that passive movements around the joints in nonfunctional patients should start rather early during their rehabilitation program to prevent contractures. Similar to the EG, the CG showed a statistical improvement in FM, BB, MI, and MRC, but not in MAS.

This result is in line with the previous results of meta-analyses on OT. The long immobilization because of paresis could contribute toward the development of finger flexor spasticity. The number of active or passive movements (less in OT) could justify our results. Scientific evidence helps to show that a multifactorial approach and a high-intensity therapy improve recovery of upper limb in stroke rehabilitation (Bovolenta *et al.*, 2011; Mazzoleni *et al.*, 2013a, 2013b), even if passive (Woldag and Hummelsheim, 2002) and active upper limb movements (Mehrholz *et al.*, 2008) seem to improve recovery by their effect on somatosensory input, motor planning, soft tissue properties, and spasticity (Fazekas, 2013).

The focus on the very early phase of stroke recovery makes this research useful to clinical practice. Even if the sample size is small, our results have potential significance in terms of effectiveness and suggest a large clinical use of robot-assisted hand therapy.

**Fig. 2**




Graphics of the results. MAS, modified Ashworth Scale for wrist and hand muscles; BB, Box and Block Test; FM, Fugl-Meyer Scale; MRC, Medical Research Council Scale for Muscle Strength (hand flexor and extensor muscles); MI, Motricity Index.

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The authors declare that they have participated in the conception, design, analysis, and interpretation of the results. They also drafted the manuscript and made its critical revision. In particular, P.S., F.P., C.D., and M.F. participated in the design of the study, the acquisition and analysis of data, and drafted the manuscript. S.M. and V.L., D.G. conceived the study, participated in its design and in the interpretation of data, and helped to draft the manuscript. P.S., S.M., and F.P. were involved in revising the manuscript. All authors read and approved the final manuscript. P.S., V.L., and M.F. all had full access to the data.

### Conflicts of interest

There are no conflicts of interest.

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