The effectiveness of robotic rehabilitation for the functional recovery of the upper limb in post-stroke patients: a systematic review
La efectividad de la rehabilitación robótica para la recuperación funcional del miembro superior en pacientes post-ictus: una revisión sistemática

*Stefano Fiore, **Andrea Battaglino, ***Pierluigi Sinatti, ***,*****Eleuterio A. Sánchez-Romero, ***,*****Iván Ruiz-Rodriguez, **Marcello Manca, **Stefano Gargano, **Jorge Hugo Villafañe
*Università degli Studi di Torino (Italy), ** IRCCS Fondazione Don Carlo Gnocchi (Italy), ***Universidad Europea de Madrid (Spain), ****Universidad Europea de Canarias (Spain), *****Sociedad Española de Disfunción Craneomandibular y Dolor Orofacial (Spain)

Abstract. Stroke is a significant contributor to global mortality and disability, and it is typically classified as a neurological disorder. A key component of stroke rehabilitation is improving upper limb function to reduce impairments and disabilities and their impact on activities of daily living. In the last few years, robot-assisted therapy (RT) arises as a novel and expanding approach in poststroke rehabilitation, which utilizes robotic devices to facilitate the recovery of motor function and task-oriented training. The aim of this systematic review, conducted through MEDLINE, CINAHL and EMBASE consultation, was to investigate the association between functional outcomes of the upper limb in patients with stroke after-effects and the use of robotic rehabilitation.
The results of the included studies have highlighted the impact of robot-assisted rehabilitation, whether integrated with traditional physiotherapy, on several clinical outcomes such as pain, spasticity, motor function, hand and finger function and cognitive abilities. The introduction of the robot-assisted intervention, coupled with traditional treatment, maybe a valuable approach to improving quality of life and enhance not only motor function but also the cognitive ability of stroke patients, especially whether focusing on the early phase of stroke recovery with a high potential impact on clinical practice.
Keywords: Stroke; Upper limb; Robotic rehabilitation; Neurological disorders; robot-assisted therapy;

Resumen. El accidente cerebrovascular es un contribuyente significativo a la mortalidad y discapacidad global, y generalmente se clasifica como un trastorno neurológico. Un componente clave de la rehabilitación del accidente cerebrovascular es mejorar la función de las extremidades superiores para reducir las deficiencias y discapacidades y su impacto en las actividades de la vida diaria. En los últimos años surge la terapia asistida por robot (RT) como un enfoque novedoso y en expansión en la rehabilitación post-ictus, que utiliza dispositivos robóticos para facilitar la recuperación de la función motora y el entrenamiento orientado a tareas. El objetivo de esta revisión sistemática, realizada a través de la consulta de MEDLINE, CINAHL y EMBASE, fue investigar la asociación entre los resultados funcionales del miembro superior en pacientes con secuelas de ictus y el uso de rehabilitación robótica.
Los resultados de los estudios incluidos han resaltado el impacto de la rehabilitación asistida por robot, ya sea integrada con la fisioterapia tradicional, en varios resultados clínicos como dolor, espasticidad, función motora, función de manos y dedos y habilidades cognitivas. La introducción de la intervención asistida por robot, junto con el tratamiento tradicional, puede ser un enfoque valioso para mejorar la calidad de vida y mejorar no solo la función motora sino también la capacidad cognitiva de los pacientes con accidente cerebrovascular, especialmente si se centra en la fase temprana de la recuperación del ictus con un alto potencial de impacto en la práctica clínica.
Palabras clave: Accidente cerebrovascular; miembro superior; rehabilitación robótica; Desórdenes neurológicos; terapia asistida por robot;

Introduction

Stroke is one of the main factors contributing to death and disability worldwide (Monasta et al., 2022). Globally, in 2019, there were 12.2 million incident strokes and 101 million prevalent strokes, 143 million DALYs due to stroke, and 6.55 million deaths from stroke. Stroke is the second cause of death and the third cause of death and disability worldwide (as expressed by disability-adjusted life-years lost - DALYs) (Collaborators, 2021; Villafane et al., 2018).

A stroke is classically characterized as a neurological deficit attributed to an acute focal injury of the central nervous system by a vascular cause (Hood and Klima, 2021). A key component of stroke rehabilitation is improving upper limb function to reduce impairments and disabilities. These upper limb impairments include numbness or weakness, difficulty moving and coordinating the arms, hands, and fingers, and have a negative impact on ADL

(activities of daily living) (Bissolotti et al., 2016; Borboni et al., 2017; González and Sedlacek, 2021). Conventional poststroke rehabilitation, including constraint-induced movement therapy (CIMT), mental practice, mirror therapy, interventions for sensory impairment, and a relatively high dose of repetitive task practice may be effective (Borboni et al., 2017; Pillastrini et al., 2016; Pollock et al., 2014; Taveggia et al., 2016b).

In the last few years, technology-supported training is emerging to help therapists, patients, and the health system. Particularly, robot-assisted therapy (RT) is a novel and expanding approach in poststroke rehabilitation, which utilizes robotic devices to facilitate the recovery of motor function and task-oriented training (Chien et al., 2020; Hernández Niño et al., 2022; Villafane et al., 2016; Villafane et al., 2017).

Robotic devices allow to facilitate the patients and they can control the complexity of a motor task. The benefits of

robotic rehabilitation affect both therapists and patients: robot-assisted therapy can increase treatment compliance by way of introducing games or interactive upper-limb tasks and patients can train independently with less supervision from therapists (Aguirre-Cardona and Mendoza-Espinel, 2022; Chien et al., 2020; Saraiva et al., 2022; Taveggia et al., 2016a).

Robotic devices for arms training can be differentiated into end-effector robots and exoskeletons: end-effector robot consent to a more limited range of movements because end-effector robots' joints are not the same as those in a human limb. So these devices don't allow the upper limb intersegmental control; exoskeletons offer a larger range of motion compared to end-effector robots and they can be used in the early phase of rehabilitation as they don't require significant motor abilities (Bertani et al., 2017; Villafane et al., 2018).

There is evidence comparing the use of robotic rehabilitation with traditional upper limb rehabilitation methods for recovering manual dexterity after a stroke (Rodgers et al., 2019), that concluded that robot-assisted arm training was as effective as conventional therapy.

According to all these considerations, the present systematic review conducted by experts in the field aimed to analyze the evidence and methodological quality of published experimental studies on the efficacy of robotic rehabilitation for functional recovery of the upper extremity in post-stroke patients.

Methods

This is a systematic review of studies investigating or reporting an association between functional outcomes of the upper limb in patients with stroke after-effects and the use of robotic rehabilitation. PRISMA guidelines were followed during the design, search, and reporting stages of this systematic review. The protocol was registered on PROSPERO CRD42022379697.

Search strategy

The electronic literature search was conducted in the following databases from their inception until October 1, 2022: MEDLINE, CINAHL, and EMBASE. The keywords "Stroke", "Upper limb", "Robotic rehabilitation", "Neurologic disorders", and "robot-assisted therapy," were used combined with Boolean operators, and MeSH terms, and completing the searching operation with manual research by a search methodology expert. Additional records were searched through other sources to complement the database findings (manual search of reference lists). Two authors (S.F. and A.B.) performed the search and evaluated the abstracts independently for potential eligibility and subsequently full-text publications for eligibility. A third author (J.H.V.) resolved discrepancies (Villafane, 2022). Each researcher reviewed the title and the abstract of all the articles, selecting the relevant ones according to inclusion and exclusion criteria.

The search strategy was restricted to human research, including only randomized controlled trials (RCTs).

Population, intervention, control, and outcomes

The selected studies' participants had to be male or female aged over 18 years old with the first episode of stroke (both vascular or ischemic) without any other peripheral nerve lesion or musculoskeletal disorders in the affected arm. Robot-assisted therapy was the analyzed intervention compared with usual care. The selected outcome was pain, spasticity, and quality of life. Priority was given to using these outcome measurements based on our expectation that most of the studies we included would report on them. One scale was not prioritized over another to measure the same variable. It was not a requirement that a study title explicitly states its intention to analyze these variables to be included in our analysis. If measurements for the primary outcome of activities of daily living (ADL) were accessible, data obtained using the Barthel Index or the Functional Independence Measure (FIM) were considered acceptable indicators.

Studies selection

After the independent titles and abstracts screening of the identified studies by two authors (S.F. and A.B.), full texts of the potentially relevant articles were retrieved. All disagreements between the reviewers were settled with another author (J.H.V.). The manual search of relevant studies' references was applied to retrieve additional articles. Exclusion criteria based on study design were systematic reviews, meta-analyses, letters, case reports, editorials, and comments. The studies that included subjects under 18 years of age affected by cognitive disorders, systemic diseases, aphasia/apraxia/neglect, and unstabled vertebral fractures were excluded.

Data extraction

Two authors (S.F. and A.B.) conducted the extraction independently. A third author (J.H.V.) resolved discrepancies. Reviewers were not blinded to information regarding authors, the journal, or the outcomes for each article reviewed. A standardized form was used to extract data concerning study design, number and mean age of participants, year and country of publication, setting, expectation association with outcome, clinical outcome measures, and reported findings. The form was developed according to the direction of the Cochrane Handbook for Systematic Reviews of Interventions.

Quality assessment

RCTs' methodological quality was evaluated using the PEDro scale. The PEDro scale is an 11-item scale designed for rating the methodological quality of RCTs. Each item that is satisfied on the scale contributes one point to the total possible score of 10 points.24 Version 2 of the Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to assess the risk of bias in randomized clinical trials included

in the present study (Pereira-Pedro et al., 2023). RoB 2 evaluates a set of domains of bias, focussing on different aspects of trial design, conduct, and reporting.

Results

Study selection

At first, 929 articles were identified through the database search. Once duplicates were excluded, the titles and abstracts of the remaining unique articles were analyzed. To conclude, full-text articles were analyzed to verify their eligibility for inclusion in this review (Daunoraviciene et al., 2018; Franceschini et al., 2020; Hsieh et al., 2011; Hwang et al., 2012; Liao et al., 2012; Linder et al., 2015; Sale et al., 2014a; Sale et al., 2014b; Susanto et al., 2015; Timmermans et al., 2014; Villafane et al., 2018). Eleven studies were finally selected for inclusion in this review. The flow diagram of the review process can be found in Figure 1.

Quality assessment

To evaluate the quality of all clinical trials, randomized and non-randomized, used the PEDro scale. All the trials reviewed resulted in good quality (scores between 6 and 8). No articles resulted in fair quality (score 4–5). The PEDro scale results are reported in Table 1.
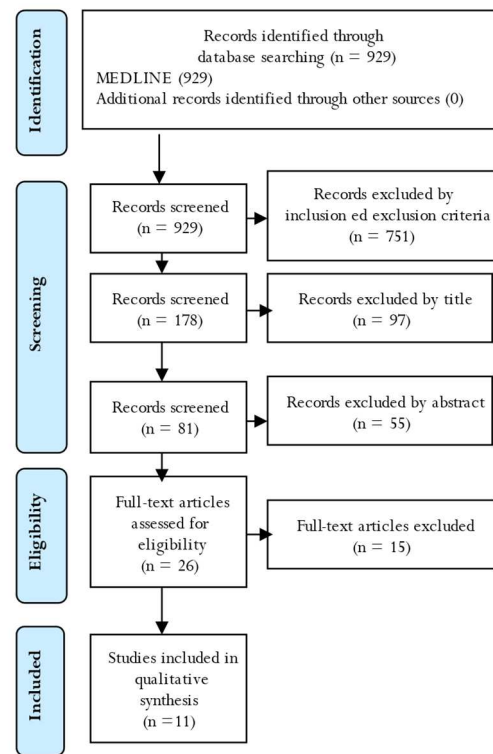

Figure. 1 Flow diagram based on PRISMA statement

Table 1.
Characteristics of the included studies

Author, y.	Design of the study	Aim of study	Characteristics of the participants	Interventions	Outcome measures	Results	Conclusions	The methodological quality of clinical studies
Villafañe JH, et al. (2018)	RCT	The study aims to determine the effectiveness of robot-assisted movement in addition to traditional physiotherapy (PT) and occupational therapy (OT) versus the additional time spent in PT and OT on hand stroke patients' paralysis on function, motor strength, spasticity, and pain	32 subjects Exp group 16 subjects 67 y M/F = 11/5 Ctrl group 16 subjects 70 y M/F = 10/6	All patients underwent a standard rehabilitation approach consisting of both PT and OT. In addition, Exp group received experimental treatment using the hand Gloreha while the Ctrl group received an additional PT and OT	NIHSS Functional ability BI Spasticity MAS Motor strength MI QuickDASH The intensity of hand pain VAS At baseline and after treatment	Significant time factor but not for group-by-time interaction for NIHSS, BI, MI, and QuickDASH. Clinically and statistically significant differences between the baseline and 3 weeks for outcome scores, except for the MAS scores, for both the Exp group and Ctrl group. Hand Pain Intensity VAS revealed a significant effect of time but not for the group-by-time interaction. Significant within-group differences for the exp group but not for the ctrl group	The robot-assisted treatment may contribute toward the recovery of hand motor function in acute stroke patients	*PEDro score 7*
Linder SM, et al. (2015)	Randomized controlled clinical trial	This study aimed to determine the effects of home-based robot-assisted rehabilitation coupled with a home exercise program compared with	99 subjects Exp group 51 subjects 59.4 y ± 13.6 M/F = 31/20 Ctrl group 48 subjects 55.5 y ± 12.6 M/F = 33/15	Exp group: robot-assisted therapy + home exercise program Ctrl group: home exercise program	Quality of life SIS Depression CES-D At baseline and after treatment	Baseline SIS scores did not differ significantly across groups for any of the SIS domains. Changes in SIS domain scores from baseline to EOT did not differ significantly across the two groups. However, participants in both groups improved significantly on	The results of this study indicate that a robot-assisted intervention coupled with a home exercise program and a home exercise program alone administered using a telerehabilitation	*PEDro score 7*

		a home exercise program alone on depression and quality of life in people after a stroke				the CES–D and SIS domain scores, except Memory and Mood For CES- D changes were significant for the Ctrl group but not for the Exp group	model may be valuable approaches to improving quality of life and depression in people after stroke	
Daunoraviciene K, et al. (2018)	Randomized controlled trial	The study aims to determine the effectiveness of robot-assisted training in the recovery of stroke-affected arms using an exoskeleton robot Armeo Spring compared to conventional therapy	34 subjects Exp group 17 subjects 65.88 y ± 4.87 M/F = 11/6 Ctrl group 17 subjects 65.47 y ± 4.05 M/F = 11/6	Both groups received treatment lasting for 30 minutes 5 days a week. Ctrl group patients additionally performed conventional functional rehabilitation. In the Exp group, conventional treatment of the affected arm was substituted with Armeo Spring training	Functional independence Modified FIM Sensorimotor impairment FMA of UL Depression and anxiety HAD (D/A) Global cognitive function ACE-R Measure of muscle tone MAS ROM assessment of the shoulder, elbow and wrist At baseline and after treatment	All patients showed similar UL impairment results and changes in kinematic data. *Exp group*: significant increase in ACE-R and modified FIM scores. *Exp group*: significant increase in ROM from baseline in both the shoulder and elbow; however, the ROM in the wrist did not differ meaningfully. Increase in elbow and wrist muscle tone after treatment in both groups	This study showed that task-oriented robotic training was safe and enhanced not only motor function in the paretic arm but also the cognitive abilities of the stroke patients	*PEDro score 6*
Sale P, et al. (2014)	Randomized controlled trial	The study aims to evaluate the short-time efficacy of intensive robot-assisted therapy compared to usual physical therapy performed in the early phase after stroke onset	53 subjects Exp group 26 subjects 67.7 y ± 14.2 M/F = 15/11 Ctrl group 27 subjects 67.7 y ± 14.2 M/F = 16/11	In addition to the usual rehabilitation consisting of a daily physiotherapy session, the Exp group received robot-assisted therapy while the Ctrl group received the usual therapy	Impairment in stroke patients Upper limb section of the FM MI Spasticity MAS-S and MAS-E Joint excursion pROM shoulder and elbow At baseline, after 15 sessions and at the end of treatment	Exp group: statistically significant improvements in MAS-S and MAS-E. FM improved significantly. Statistically significant improvements in pROM and MI Ctrl group: a not statistically significant decreasing trend of MAS-S and increasing trend of MAS-E. FM improved significantly. Statistically significant improvements in MI and a not statistically significant increase in pROM	Robot-assisted upper limb rehabilitation treatment can contribute to increasing motor recovery in subacute stroke patients. Focusing on the early phase of stroke recovery has a high potential impact on clinical practice	*PEDro score 9*
Franceschini M, et al. (2020)	Randomized controlled follow-up study	This study aims to analyse the long-term effects (6 months follow-up) of upper limb Robot-assisted Therapy (RT) compared to Traditional physical Therapy (TT), in subacute stroke patients	48 subjects Exp group 25 subjects 70.0 y M/F = 12/13 Ctrl group 23 subjects 74.0 y M/F = 14/9	All subjects underwent conventional physiotherapy sessions. In addition Exp group received robot-assisted therapy using a planar end-effector robotic system while the Ctrl group received traditional physical therapy	Impairment in stroke patients Upper limb section of the FM Spasticity MAS-S and MAS-E Joint excursion pROM shoulder and elbow At baseline, end of treatment and 6-month follow-up	Exp group: at T1 significant improvements in FM-UL. MAS-S, MAS-E, and pROM changed significantly Ctrl group: at T1 significant improvements in FM-UL. At T2 significant increase in MAS-S In FM-UL, pROM and MAS-E the improvements obtained at the end of treatment seem to be maintained at 6 months follow-up in both groups. The inter-group analysis of FM-UL values at T1 and T2 demonstrated significant differences in favor of Exp Group	Upper limb Robot-assisted Therapy may lead to a greater reduction of motor impairment in subacute stroke patients compared to Traditional Therapy. The gains observed at the end of treatment persisted over time.	*PEDro score 7*
Sale P, et al. (2014)	Randomized controlled trial	The study aims to evaluate the effects of intensive robot-assisted hand therapy compared with intensive occupational therapy in the	20 subjects Exp group 11 subjects 67.0 y ± 12.4 M/F = 8/3 Ctrl group 9 subjects 72.56 y ±	All participants underwent inpatient rehabilitation consisting of physiotherapy. In addition to standard rehabilitation, the Exp group	FM MRC MI MAS BB BI At baseline, end of treatment and 3-month follow-up	Exp group: statistically significant improvement for the FM, BB, MI and MRC. A statistically significant increase in the MAS score was also found Ctrl group: statistically significant improvements for the FM, BB, MI and	Robotic rehabilitation treatment may contribute toward the recovery of hand motor function in acute stroke patients. The positive results obtained	*PEDro score 7*

		early recovery phases after stroke with a 3-month follow-up	8.98 M/F = 6/3	received robot-assisted hand therapy using the Amadeo Robotic System while the Ctrl group received occupational therapy		MRC	through the safe and reliable robotic rehabilitation treatment reinforce the recommendation to extend it to a larger clinical practice
Susanto EA, et al. (2015)	Pilot randomized controlled trial	The study proposes the use of a robotic device to assist hand and finger function training in stroke patients and it aims to evaluate the potential efficacy of intention-driven robot-assisted fingers training	19 subjects Exp group 9 subjects 50.7 y ± 9.0 M/F = 7/2 Ctrl group 10 subjects 55.1 y ± 10.6 M/F = 7/3	Exp group: stretching and passive mobilization + robot-assisted fingers training Ctrl group: stretching and passive mobilization + non-assisted fingers training	Proximal control of the arm and its dexterity ARAT UE functional ability WMFT and WMFT-FT Motor function, balance, sensations, and joint functions FMA, FMA-SE and FMA-WH At baseline, after 1 week, at the end of treatment and 6-month follow up	Exp group: significant improvements of ARAT, WMFT, WMFT-FT and FMA-SE Ctrl group: Significant improvements of ARAT, WMFT, FMA, FMA-SE and FMA-WH Only the Exp group was able to maintain significant differences in ARAT and FMA-SE scores, six months after training	*PEDro score 7* This study showed the potential efficacy of robot-assisted fingers training for hand and fingers rehabilitation and its feasibility to facilitate early rehabilitation for a wider population of stroke survivors
Liao WW, et al. (2011)	Prospective randomized controlled trial	The study aims to compare the outcome of robot-assisted therapy with dose-matched active control therapy to study functional recovery in chronic stroke patients	20 subjects Exp group 10 subjects 55.51 y ± 11.17 M/F = 6/4 Ctrl group 10 subjects 54.56 y ± 8.20 M/F = 7/3	Exp group: robot-assisted therapy using Bi-Manu-Track robotic arm trainer + training in functional activities Ctrl group: dose-matched active control therapy using occupational therapy	Movements, coordination, and reflexes of the shoulders, elbows, forearms, wrists and hands FMA of UL Basic ADL FIM Amount of use and quality of movement MAL Bimanual ability ABILHAND questionnaire At baseline and after treatment	The Exp group significantly increased motor function, hemiplegic arm activity, quality of movement and bilateral arm coordination compared with the Ctrl group. There was nearly no change in the FIM in the two groups. A significant difference was found in ABILHAND as well	*PEDro score 8* Symmetrical and bilateral robotic practice, combined with functional task training, can significantly improve motor function, arm activity, and self-perceived bilateral arm ability in patients late after a stroke
Hwang CH, et al. (2012)	Prospective randomized clinical trial	The study aims to evaluate individual finger-synchronized robot-assisted hand rehabilitation in stroke patients. The study assessed proximal and distal arm function, and the effect of robot-assisted rehabilitation time on outcomes	15 subjects FTI Group 9 subjects 50.2 y ± 3.7 M/F = 5/4 HTI group 6 subjects 51.3 y ± 3.0 M/F = 4/2	FTI group: active robot-assisted intervention HTI group: early passive therapy followed by active robot-assisted intervention	Fugl-Meyer Scale Grasping force test Pinching force test 2nd metacarpophalangeal joint active ROM Wrist and elbow tone Ashworth Scale At baseline and 2, 4 and 8 weeks after starting therapy	Compared to baseline, both the FTI and HTI groups showed improved results for the wrist and hand sub-portion of the Fugl-Meyer arm motor scale, active movement of the 2nd metacarpophalangeal joint, grasping, and pinching power at each time point (2, 4 and 8 weeks), with a greater degree of improvement for the FTI compared to the HTI group	*PEDro score 7* A four-week rehabilitation using a novel robot that provides individual finger synchronization resulted in a dose-dependent improvement in hand function in subacute to chronic stroke patients
Hsieh YW, et al. (2011)	Pilot randomized controlled trial	The study aims to investigate the effects of higher intensity versus lower intensity robot-assisted therapy relative to conventional rehabilitation	18 subjects Exp group Higher Intensity 6 subjects 56.04 y ± 13.74 M/F = 4/2 Lower intensity 6 subjects 52.45 y ±	Higher intensity exp group: passive range of motion + high intensity robot-assisted therapy + functional activities training Lower intensity exp group:	Movements and reflexes of the shoulder/elbow/forearm, wrist, hand, and coordination and speed FMA of UL Muscle strength of the affected arm MRC scale Amount of use and quality of movement	There were significant differences in motor function and daily performance among the 3 groups. The higher intensity exp group showed better improvement in motor function, muscle strength, the performance of daily activities, and bimanual ability than the other 2	*PEDro score 9* Higher intensity of robot-assisted therapy that assists forearm and wrist movements may lead to greater improvement in motor ability and functional performance in stroke patients

| | | | in patients poststroke | 1.98 M/F = 4/2 Ctrl group 6 subjects 54.00 y ± 8.05 M/F = 5/1 | passive range of motion + low intensity robot-assisted therapy + functional activities training Ctrl group: conventional therapy techniques | MAL Bimanual ability ABILHAND At baseline and after the treatment | | groups | |
| Timmermans AA, et al. (2014) | Pilot randomized controlled trial | The study aims to investigate the effectiveness and added value of the Haptic Master robot combined with task-oriented arm-hand training in chronic stroke patients | 22 subjects Exp group 11 subjects 61.8 y ± 6.8 M/F = 8/3 Ctrl group 11 subjects 56.8 y ± 6.4 M/F = 8/3 | Exp group: task-oriented arm training (T-TOAT) with the use of a Haptic Master robot Ctrl group: task-oriented non-robotic arm-hand training (T-TOAT) | ICF body function level FMMA ICF activity level ARAT and MAL ICF participation level EuroQol-5D and SF-36 At baseline, after 4 and 8 weeks and 6-months follow up | Exp group: a significant improvement after training for ARAT. Results were maintained until 6 months after the cessation of the training. A significant improvement after training for MAL. Results were maintained until 6 months after cessation of the training Ctrl group: a significant improvement after training for MAL. Results were maintained until 6 months after the cessation of the training. A significant improvement in the EQ-5D health status (VAS) and a significant improvement in the SF-36 physical health component | Arm-hand performance improved in highly functional chronic stroke patients, after eight weeks of task-oriented training, in both the robot- and the non-technology-supported intervention. However, the use of a Haptic Master robot in support of task-oriented arm training did not seem to have an added value over the video-instructed task-oriented exercises | *PEDro score 9* |

Risk of Bias within and across the studies

The evaluation of the risk of bias of the eleven randomized clinical trials included in this article was realized using the Cochrane risk-of-bias tool for randomized trials (RoB 2.0). Nine articles were at "low risk" of bias (Daunoraviciene et al., 2018; Franceschini et al., 2020; Hsieh et al., 2011; Hwang et al., 2012; Liao et al., 2012; Linder et al., 2015; Sale et al., 2014a; Sale et al., 2014b; Villafane et al., 2018) and the remaining two resulted in "some concerns" (Susanto et al., 2015; Timmermans et al., 2014). The results of the risk of bias are summarized in Figure 2.

Figure 2. Risk of bias assessment via Revised Cochrane risk-of-bias tool for randomized trials (RoB2) of the included studies.

Results of studies

Below are reported the results of the eleven randomized clinical trials included in this review.

1. In the RCT realized by Villafañe et al. (Villafane et al., 2018) authors analyzed the effects of robot-assisted motion and activity in addition to occupational therapy (OT) and physiotherapy (PT) on 32 subjects that suffered a stroke with hand paralysis. The experimental group (EG) (n=16) was treated with 30' of robot-assisted mobilization of the hand and the control group (CG) (n=16) was treated with 30' of PT and OT for three weeks additionally to conventional physiotherapy. Outcomes included the Modified Ashworth Scale, the National Institutes of Health Stroke Scale (NIHSS), a modified version of the Disabilities of the Arm, Shoulder and Hand (QuickDASH), Barthel Index (BI), Motricity Index (MI) and the visual analog scale (VAS). Assessments were realized at the beginning of the study and after three weeks. A notable effect of time interaction was recorded for NIHSS, BI, MI, and QuickDASH after stroke immediately following the treatments (P <0.001). The EG registered a significant improvement in pain compared with the CG after 3 weeks, consisting of a reduction of 11.3 mm in the 100-mm VAS scale, compared with 3.7 mm of the CG. The results of this RCT revealed that in the approach of patients with hand paralysis following stroke, for the treatment of pain and spasticity, robot-assisted mobilization realized in addition to conventional OT and PT is as effective as conventional rehabilitation.

2. The purpose of the RCT of Linder et al. (Linder et al., 2015) was to analyze the effectiveness of home-based
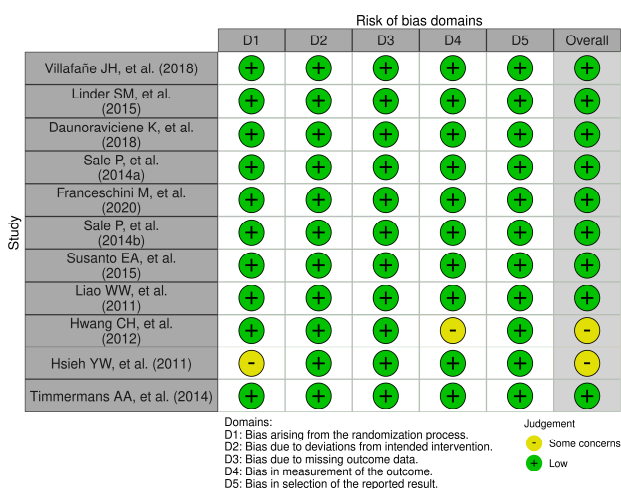
robot-assisted physiotherapy associated with a home physical activity plan in comparison with a home physical activity plan alone on quality of life and depression in 99 patients with stroke. Participants were randomly assigned into a CG, which received a home physical activity plan, or an EG, which received a robot-assisted therapy in addition to the home physical activity plan and participated in 8 weeks of home intervention. Outcomes were assessed with the Stroke Impact Scale (SIS) and the Center for Epidemiologic Studies Depression (CES–D) Scale. The authors observed that SIS domains had adequate reliability during the two assessment periods planned in this study (a >0.75), except the Strength scale at baseline (a 5.62). In addition to that authors observed statistically significant changes in the CES-D Scale for EG and CG both. The results of this RCT showed that robot-assisted physiotherapy in addition to a home physical activity program and a home physical activity program alone may be beneficial treatments for improving the quality of life and depression in people after stroke.

3. The RCT realized by Daunoraviciene et al. (Daunoraviciene et al., 2018) aims to analyze the effects of robot-assisted treatment in the functional rehabilitation of arms in stroke patients using an exoskeleton robot. The RCT was realized on 34 stroke-affected subjects, randomly assigned into an EG (n=17), and trained to use the exoskeleton robot, or a CG (n=17). All patients were evaluated using the Fugl-Meyer Assessment (FMA) of UL recovery after stroke, the modified Functional Independence Measure (FIM) instrument (six-item self-care FIM scale), the Hamilton Rating Scale for Depression (HAD) and the Hamilton Rating Scale for Anxiety, Addenbrooke's Cognitive Examination- Revised (ACE-R) of global cognitive function recovery after stroke, the Modified Ashworth Scale (MAS) as a measure of muscle tone and ROM assessment of the shoulder, elbow, and wrist. Both groups' outcome assessments were measured at the beginning of the study and the end of the intervention. Participants in EG resulted in a greater improvement in upper limb capacity compared to the CG. In conclusion, the results of this RCT showed that robot therapy may produce improvements in the physical capacity of the paretic upper limb and the cognitive faculty of stroke patients.

4. The Sale et al. (Sale et al., 2014a) RCT was realized to analyze the effectiveness of robot-assisted treatment in comparison to traditional PT in 53 stroke subjects. Participants were randomly assigned into two groups, both exposed to standard therapy. The EG received in addition 30 sessions of robot-assisted therapy. Thirty sessions of conventional therapy, however, were applied to the participants of the CG. Assessments were realized at baseline (T0), after 15 sessions (T1), and after the intervention (T2). Outcomes were assessed using the Modified Ashworth Scale-Shoulder (MAS-S), Modified Ashworth Scale-Elbow (MAS-E), the Fugl- Meyer Assessment Scale (FM), Total Passive Range of Motion-Shoulder/Elbow (pROM), and Motricity Index (MI).

Significant improvement was demonstrated in both EG and CG, but a higher improvement was registered in EG. Findings resulted that robot-assisted upper limb therapy may produce significant improvements in physical capacity in subjects that suffered a stroke.

5. The randomized controlled follow-up study of Franceschini et al. (Franceschini et al., 2020) aims to examine the effectiveness of upper extremity robot-assisted rehabilitation compared to traditional PT, in 48 subjects that suffered a stroke. Participants were randomly assigned to an experimental group (EG), where they performed arm rehabilitation using a planar end-effector robotic system, or a control group (CG), consisting of traditional PT (CG). Measurements were realized at baseline (T0), after the intervention (T1), and 6 months following the end of the intervention (T2). Clinical outcomes were assessed using the following scales: Upper Limb part of Fugl-Meyer assessment (FM-UL), total passive Range Of Motion (pROM), Modified Ashworth Scale Shoulder (MAS-S), and Elbow (MAS-E). After the intervention, results showed a significant gain of FM-UL in both groups, while only in EG were found notable improvements in MAS-S, MAS-E, and pROM. After 6 months, only the CG results showed a remarkable increase in MAS-S. In FM-UL, pROM, and MAS-E the improvements registered at T1 seem to be maintained at T2 in both groups. The inter-group analysis of FM- UL values after the treatment and 6 months follow-up demonstrated greater results in favor of EG. The authors concluded that upper extremity robot-assisted rehabilitation may produce better results in motor impairment in subjects with stroke compared to conventional PT.

6. This randomized-controlled observer trial realized by Sale et al. (Sale et al., 2014b) was realized to analyze the effects of robot-assisted hand treatment in comparison with OT in subjects with stroke in the early phases. The trial was conducted on 20 early-phase stroke patients. Participants were randomly assigned into one of two groups: the EG, where the intervention was performed using a robotic system, or the CG where the intervention consisted of OT. Both groups received 20 sessions of treatment, applied 5 days a week for 4 weeks. The following clinical scales were performed: Medical Research Council Scale for Muscle Strength (hand flexor and extensor muscles) (MRC), Motricity Index (MI), modified Ashworth Scale for wrist and hand muscles (MAS), Fugl-Meyer Scale (FM), and Barthel Index. Assessments were performed at baseline, after the treatment, and after 3 months. Significant improvements were registered in EG and results showed that robot-assisted rehabilitation may be beneficial for hand recovery functions in stroke patients in acute phases.

7. In the RCT of Susanto et al. (Susanto et al., 2015), the authors proposed the use of robotic devices in hand and finger motor training and they aimed to analyze the effects of intention-driven robot-assisted finger training. The patients of this trial were randomly assigned to an EG with robot-assisted training or to a CG with non-assisted finger

training. In each group, patients realized 20-session training. Outcomes were measured with Action Research Arm Test (ARAT), Wolf Motor Function Test (WMFT) score, its functional tasks (WMFT-FT) sub-score, Fugl-Meyer Assessment (FMA), its shoulder and elbow (FMA-SE) sub-score, and finger individuation index (FII). Results showed a statistically significant difference in the clinical scores for EG and CG after the intervention. However, a significant difference in the ARAT and FMA-SE was maintained only in the EG six months after the intervention. Participants in EG showed greater improvements in The WMFT-FT score compared to CG. The results obtained in this article supported robot-assisted rehabilitation for hands and fingers in stroke patients.

8. The study of Liao et al. (Liao et al., 2012) aimed to analyze the effects of a robot-assisted intervention in comparison with an active control to study functional rehabilitation in patients that suffered a stroke. All 20 participants received either of the two interventions each day, 5 days per week, for 4 weeks. Outcome measures were arm activity ratio and scores on the Fugl-Meyer Assessment Scale, Functional Independence Measure, Motor Activity Log, and ABILHAND questionnaire. The robot-assisted intervention group showed significant results in motor capacity, arm activity, and arm coordination. The results obtained in the experimental group were greater compared with the control group. These findings showed that symmetrical and bilateral robot-assisted intervention can significantly improve arms outcomes in stroke patients.

9. The objective of the RCT of Hwang et al. (Hwang et al., 2012) was to evaluate the effectiveness of robot-assisted hand therapy in stroke-affected subjects. Participants received either 20 sessions of robot-assisted therapy (G1) or 10 sessions of early passive intervention followed by 10 sessions of active robot-assisted therapy (G2). Assessments were realized at the beginning of the study and after 2, 4, and 8 weeks. Results showed statistically significant improvements in G1 and G2 at each measurement. Recorded improvement was greater for participants in G1 compared to the G2 group (P<0.05). These findings showed that finger-synchronized robot-assisted hand therapy, performed for 20 sessions during 4 weeks, provided improvement in hand function in stroke-affected subjects.

10. Hsieh et al. (Hsieh et al., 2011) realized this study to analyze the effects of high-intensity robot training and low-intensity robot training on arm motor function compared to traditional physiotherapy (CG) in 18 stroke-affected people. Participants were randomly assigned to one of these three groups: high-intensity robot training (HG), low-intensity robot training (LG), or CG intervention. Outcome measures were realized at baseline and after the treatment. Primary outcomes were the Medical Research Council scale and the FMA. Notable differences in physical capacity (p=0.04) and daily performance (P = 0.03) resulted in the participants of the 3 groups. The HG showed greater improvement in physical capacity than the LG and

CR intervention groups. Results showed that high-intensity robot training may produce greater improvement in motor capacity and functional performance than low-intensity robot training in stroke-affected people.

11. The aim of the Timmermans study (Timmermans et al., 2014) was to analyze the effects of the Haptic Master robot in combination with task-oriented training in 22 stroke-affected people. Participants were randomly assigned to one of two groups: task-oriented robot-assisted arm-hand intervention group (EG) or task-oriented non-robotic arm-hand control group (CG). The intervention was realized 4 times a week, 2x30' a day for 8 weeks. The EG showed a significant improvement (p=0.008) after intervention on the Action Research Arm Test (ARAT). On the perceived performance assessment (Motor Activity Log (MAL)), both, the EG and CG showed significant differences after intervention (CG p=0.008; EG p=0.013). Only in the CG was found a significant improvement in quality of life (EuroQol-5D p=0.015, SF-36 physical p=0.01). No between-group differences resulted in any of the outcome measures. Findings showed that task-oriented training improved arm-hand outcomes in stroke-affected patients, after 8 weeks, but the use of a Haptic Master robot did not produce additional value.

Discussion

The present systematic review aimed to explore the efficacy of robotic rehabilitation in semiautonomous patients with stroke sequelae. Although all studies presented results of the efficacy of robotic rehabilitation in the reduction of pain and spasticity as well as in the improvement of quality of life (Daunoraviciene et al., 2018; Franceschini et al., 2020; Hsieh et al., 2011; Hwang et al., 2012; Liao et al., 2012; Linder et al., 2015; Sale et al., 2014a; Sale et al., 2014b; Susanto et al., 2015; Timmermans et al., 2014; Villafane et al., 2018), in the study by Timmermans et al. (Timmermans et al., 2014) robotic rehabilitation did not show any additional benefit over usual task-oriented exercise therapy with video-instructions. Nine of the eleven articles included in the review had a "low risk" of bias (Daunoraviciene et al., 2018; Franceschini et al., 2020; Hsieh et al., 2011; Hwang et al., 2012; Liao et al., 2012; Linder et al., 2015; Sale et al., 2014a; Sale et al., 2014b; Villafane et al., 2018), and two of them had "some concerns" (Susanto et al., 2015; Timmermans et al., 2014). The PEDro scale was used to assess the quality of all randomized and nonrandomized clinical trials, with a result of good quality (score between 6-8) in eight of them (Daunoraviciene et al., 2018; Franceschini et al., 2020; Hsieh et al., 2011; Liao et al., 2012; Linder et al., 2015; Sale et al., 2014a; Sale et al., 2014b; Susanto et al., 2015), and excellent quality (score between 9-10) in 3 of them (Hwang et al., 2012; Timmermans et al., 2014; Villafane et al., 2018). While positive results were observed, there are several unanswered questions regarding passive hand manipulation

assisted by robot-assisted intervention. The optimal dose and duration of training are yet to be defined. Further large-scale randomized controlled studies with extended durations are required to confirm the results and establish the long-term benefits of robot-assisted intervention. Objective measures such as wrist accelerometers should be considered to accurately assess compliance and repetitions in future studies.

The results of the present review are very similar to those found by Calabrò et al. (Calabro et al., 2021) in their systematic review on robotic rehabilitation of the lower extremities after stroke, concluding that the implementation of robotic rehabilitation in routine treatment protocols represents the future of stroke rehabilitation, pointing out that its feasibility should be improved by new solutions in terms of applicability, and the development of clinical practice guidelines.

A recent systematic review and meta-analysis of 13 clinical trials on the impact of different robotic devices on the recovery of gait abnormalities after stroke [30], concluded that patients who received physiotherapy treatment in combination with robotic devices, such as Lokomat or Gait Trainer, were more likely to achieve better outcomes compared to patients who only received conventional gait training. They determined similar therapeutic effects between the different devices used.

In the present systematic review, only in the studies of Daunoraviciene et al. (Daunoraviciene et al., 2018), Hwang et al. (Hwang et al., 2012), and Timmermans et al. (Timmermans et al., 2014) was robotic rehabilitation used in isolation in the experimental group.

The robotic device used by Villafañe et al. (Villafane et al., 2018) is described as a glove-shaped robotic device for hand rehabilitation called "Gloreha", possessing power generators outside the patient's hand, physically separated from the glove. The device is lighter and safer than others on the market because the mechanical power transmission to the glove is through a flexible beam, which causes the patient's fingers to move independently, in different ranges of motion, and at different speeds. It also visually stimulates the patient during the rehabilitation session because it is equipped with a virtual interface.

The "Hand Mentor" device by Linder et al. [24] has several training modules: the first is designed for the treatment of spasticity, providing prolonged isometric stretching of the wrist flexors as well as visual feedback to the participant that facilitates active inhibition of the wrist and finger flexors. The other modules address various aspects of improving motor control, especially active wrist control. Programming is based on the use of function-focused games in which the goal is to move the hand toward an object in a set amount of time and allow adjustment of speed and force by displaying dynamic targets and variable speeds. Each time a patient completes a level, the session summary is displayed on the screen and stored in that client's encrypted electronic database. Total usage time, usage time in each module, number of repetitions

attempted and successful repetitions, wrist angle, and pneumatic pressure can be recorded. The device consists of a pneumatic pump that facilitates active-assisted wrist and finger movement, and consists of three components: a computerized control box (provides targets with corresponding visual and auditory feedback), an arm unit (stabilizes the forearm so that the user can isolate wrist and finger movement), an arm unit (stabilizes the forearm so that the user can move the wrist and fingers with the aid of the pneumatic pump) and data collection device, and a communications module.

The device used by Daunoraviciene et al. (Daunoraviciene et al., 2018) consists of a flexible spring mechanism to support the weight of the upper limb in an adjustable way in a large three-dimensional workspace that allows it to be used as a real-time input device to the related therapy software (Armeo control). Seven angle sensors (angle sensor resolution <0.2) and a pressure sensor analyze the quality of movement during the rehabilitation session. Continuous adaptation of the weight compensation force to the needs of the subproject is adjusted for the forearm and arm using an instrumented arm orthosis with five degrees of freedom (no robotic actuators) that allows both passive movements, as well as robot-assisted treatment.

Wright et al. (Walker, 2000) tested how different parts of mechanical work help predict training results in stroke patients who finished six sessions of robotic upper extremity rehabilitation (self-guided movement practice) with customized forces and found that the best outcome was obtained when energy activity was increased in the eccentric shoulder and concentric elbow actions. This type of study makes it possible to determine the most important work characteristics for rehabilitation, which constitutes a line of research to improve treatments.

Limitations

We recognize that our sample of included studies was low, but in return, we decided to perform an analysis of only patients with the first episode of stroke (both vascular or ischemic) without any other peripheral nerve lesion or musculoskeletal disorders in the affected arm. It is inherent to neurorehabilitation research to have a low sample size in studies, due to strong inclusion and exclusion criteria. The impact of spontaneous recovery, the development of compensatory strategies, and other factors on motor outcomes and quality of life cannot be precisely determined. Additionally, studies conducted shortly after stroke with a limited number of sessions may not fully capture the potential for motor function improvement, particularly in cases where initial arm control is higher. Spasticity scores may affect the recovery of hand motor function. Nonetheless, the focus on early stroke recovery makes this research relevant to clinical practice.

We could not perform a meta-analysis due to the great heterogeneity of the included studies, which should be considered a limitation of the study.

Practical Applications

The introduction of the robot-assisted intervention, coupled with traditional treatment, maybe a valuable approach to improving quality of life and enhance not only motor function but also the cognitive ability of stroke patients, especially whether focusing on the early phase of stroke recovery with a high potential impact on clinical practice.

Conclusions

Although robot-assisted therapy is more effective than the usual treatments in reducing pain and spasticity and improving quality of life, there is still a lack of information that encourages further research in different areas of robot-assisted therapy like feasibility, safety, efficiency, and long-term follow-ups. However, due to the enormous literary interest in robot-assisted therapy, the latter training modality possesses high potential.

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Conflicts of Interest

The authors declare no conflict of interest.

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