

Review

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Therapeutic robots for post-stroke rehabilitation

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Abstract: Stroke is a prevalent, severe, and disabling health-care issue on a global scale, inevitably leading to motor and cognitive deficits. It has become one of the most significant challenges in China, resulting in substantial social and economic burdens. In addition to the medication and surgical interventions during the acute phase, rehabilitation treatment plays a crucial role in stroke care. Robotic technology takes distinct advantages over traditional physical therapy, occupational therapy, and speech therapy, and is increasingly gaining popularity in post-stroke rehabilitation. The use of rehabilitation robots not only alleviates the workload of healthcare professionals but also enhances the prognosis for specific stroke patients. This review presents a concise overview of the application of therapeutic robots in post-stroke rehabilitation, with particular emphasis on the recovery of motor and cognitive function.

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Introduction

Stroke is a prevalent, severe, and disabling health-care issue on a global scale. With the increasing elderly population, stroke has emerged as a major challenge in China [1, 2]. A cross-sectional study of 676,394 participants aged over 40 revealed that in mainland China in 2020, the estimated overall prevalence, incidence, and mortality rates of stroke were 2.6 %, 505.2 per 100,000 person-years, and 343.4 per 100,000 person-years, respectively [1]. Stroke ranked as the third leading cause of death after malignant tumors and heart disease. Furthermore, years of life lost (YLLs) per 100,000 population due to stroke increased by 14.6 %; YLLs attributed to stroke rose from the third highest among all causes in 1990 to the highest in 2017 [3].

Stroke inevitably results in motor and cognitive deficits. Motor deficits following a stroke are well-recognized among the array of post-stroke symptoms, profoundly impacting motor functions of the face, arms, and legs [4]. These deficits encompass a spectrum of manifestations, including compromised motor control, muscle weakening or contractures, alterations in muscle tone, joint laxity, heightened spasticity, reflex escalation, coordination depletion, and the emergence of abnormal gait [5–7]. Post-stroke cognitive impairment (PSCI) is defined as cognitive deficits emerging 3–6 months after an incident stroke. It consists of cognitive impairments such as aphasia or memory deficits due to strategic infarcts in the specific lesion site, like the hippocampi, thalami, and key cortical regions [8]. Globally, PSCI significantly contributes to post-stroke morbidity and mortality [8].

In addition to the medication and surgical interventions during the acute phase, rehabilitation treatment is a critical component of stroke care in favor of patients' prognosis [9, 10]. The conventional stroke rehabilitation methods mainly consist of physical therapy (PT), occupational therapy (OT), and speech therapy (ST) [11]. For instance, well-defined PT is capable of effectively improving upper and lower limb movement ability [12, 13], gait [14], balance and functional ability [15, 16], and even mental and cognitive

function [17, 18]. Similarly, OT may slightly improve performance in activities of daily living and global cognitive performances like sustained visual attention, working memory, and flexible thinking [19, 20]. Meanwhile, ST has shown effectiveness for people with aphasia following stroke in terms of improved functional communication, reading, writing, and expressive language [21–23]. However, despite all these well-established methods, many stroke survivors still suffer from severe residual disability which deeply impairs their daily functional ability. This is probably partly due to the insufficient therapy dose, low patient engagement and motivation, and a lack of objective feedback required to achieve significant improvements in function [11].

In recent decades, stroke rehabilitation interventions utilizing various technologies such as exercise games, robotic assistive systems, virtual and augmented reality, wearable sensors, and smartphone apps have emerged. The use of technology has been shown to be highly effective in improving functional mobility and independence in stroke patients by reducing the labor cost of task-based training, increasing patient motivation, monitoring functional progress in time, and providing appropriate guidance [11]. Among these technologies, rehabilitation robotics play an important role in several areas of stroke rehabilitation, including motor function recovery, balance and gait improvement, cognitive function recovery, and neurologic plasticity [24–31]. Their addition to conventional neurological rehabilitation has proven to be effective and valuable in post-stroke management [32].

This review provides a comprehensive overview of the application of therapeutic robots in post-stroke rehabilitation, with a special focus on motor and cognitive function recovery.

Concept and categories of therapeutic robots for post-stroke rehabilitation

Therapeutic robots for post-stroke rehabilitation serve as clinical tools designed to automatically facilitate labor-intensive, repetitive training process, especially during the early stages of neurologic recovery when patients will likely need significant weight support. Robotic technology can increase training duration and frequency while reducing the need for as many assisting therapists as possible [33, 34].

The most commonly used therapeutic robots in clinical practice are employed for specific durations within rehabilitation programs. They aim to enhance particular functions through the application of robotic devices, which seek

to expand and improve an individual’s abilities by restoring their capacity of movement. These robots are commonly utilized as robotic therapy aids to support patients with manipulative disabilities, rather than functioning purely as assistive devices, within the scope of human–robot interactions [34].

Therapeutic rehabilitation robotics can be classified in various ways based on different criteria. Firstly, they can be classified as upper-limb robots and lower-limb robots, depending on the affected area [35]. Secondly, two primary categories of robots have been defined based on the mode of human–machine integration, namely exoskeletons and end-effector devices [33]. Exoskeleton robots feature a direct one-to-one correspondence between each joint in the robot and its human counterpart [36]. Serving as orthotic structures, these devices bear a resemblance to external bones, forming a limb-encompassing structure akin to a scaffold. The device’s segments align with the anatomical divisions of the human limb, and its rotational axis essentially mirrors that of the human limb [37]. The soft robotic glove is distinct from other exoskeletons in that it employs soft actuators instead of hard ones, specifically designed for functional hand rehabilitation [38]. In contrast, end-effector robots generate movement through their most distal segment without a one-to-one joint correspondence [36]. When the end-effector moves, it alters the limb’s position at the connection point and indirectly affects other limb segments, leading to interaction torques in each limb segment that the device cannot fully determine [39]. Figure 1 shows the categories of therapeutic rehabilitation robotics.

Thirdly, rehabilitation robots for therapy can be classified into two main categories: traditional and virtual reality (VR), depending on the level of interaction between the user and the virtual environment. Within the VR category, there are further distinctions between non-immersive and immersive VR [40]. Traditional methods primarily facilitate interaction between the patient and the robot or between the patient and the real world supported by the robot. In contrast, VR technology enables user engagement in a virtual realm. This is achieved by capturing the patient’s movements, integrating them into the virtual world, and providing multisensory feedback [41]. VR allows the customization of practice intensity and feedback in a dynamic

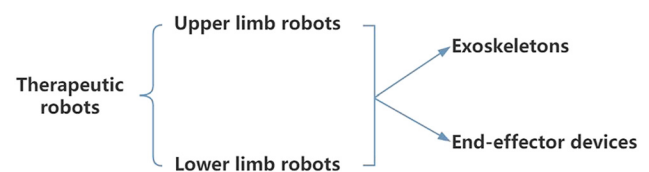


Figure 1: The categories of therapeutic rehabilitation robotics.

environment, fostering interactive and engaging experiences for personalized movement retraining treatments [42]. Non-immersive VR allows users to observe and interact with a virtual environment using devices that do not completely override sensory perception [43]. On the other hand, immersive VR has the ability to simulate complex real-world environments, which enhances the sense of presence and makes users feel as if they are genuinely within a virtual environment. This increases the likelihood of user interaction with stimuli presented by the computer and related devices that produce visual, auditory, and haptic sensations [40]. Currently, there is a hotpot research topic on VR-based environmental simulation rehabilitation systems, providing multi-sensory experiences and facilitating realistic human–computer interactions [44]. These systems are capable of simulating a variety of realistic environments, such as different weather conditions, complex road conditions, and travel scenarios, among others [45].

Many of the robots utilized in clinical or research environments are tailored to adult dimensions, making them unsuitable for children [46]. Consequently, robots specifically intended for children have been meticulously crafted to cater to the diverse height and size specifications associated with varying age groups among children [47]. Similarly, rehabilitation robots designed for children can be based on both the site of action, distinguishing between upper and lower limb robots, and their design, differentiating between exoskeletons and end-effector devices [48].

Rehabilitation robotics in upper limb function

Numerous studies, with a participant pool exceeding 1,000, have assessed the efficacy of hand and arm training using robotic assistance in comparison to traditional therapeutic approaches [49, 50]. The results consistently indicate significant benefits in terms of upper limb recovery, strength, motor control, and activities of daily living (ADL) when rehabilitation is assisted by robots [51]. Figure 2 illustrates the commonly used upper limb rehabilitation robotics used in our daily clinical practice at our center.

In randomized controlled trials, the prevalent choice has been end-effector devices, with only limited representation of exoskeleton robots. Upper-limb rehabilitative robotics encompass the comprehensive rehabilitation of the trunk, shoulder, elbow, wrist, forearm, and finger. Most robots designed to enhance upper extremity functionality possess three degrees of freedom, affording distinct rotational

capacity at the shoulder, elbow, and wrist within the sagittal plane. For the restoration of hand function, wearable glove-like devices are commonly employed in targeted therapeutic approaches.

The primary upper-limb robotic feedback mode utilized is force feedback, with some machines also incorporating visual feedback and audio feedback. These modes serve distinct yet complementary functions. Force feedback is crucial for providing resistance in muscle strengthening and assistance for individuals with limited mobility [52]. Visual feedback offers essential guidance for precise movement execution, real-time monitoring for therapists, and motivational elements for patients [53]. Additionally, gamified elements within the realm of visual feedback are integrated to make the rehabilitation process engaging and enjoyable. Gamified visual feedback not only provides guidance but also transforms exercises into interactive experiences, encouraging patient participation in their therapy [54, 55].

The subjects in the trials encompassed a broad spectrum of ages, excluding only adolescents and children below 18 years. Stroke progression among the subjects encompassed the acute, sub-acute, and chronic phases. In most cases, the experimental designs included an intervention group that used an upper-limb robot, either alone or in conjunction with conventional rehabilitation techniques. The control group engaged exclusively in traditional rehabilitation methods. A limited number of investigations sought to evaluate the relative efficacy of distinct rehabilitation robot types. Importantly, all trials adhered to an intervention period lasting no more than 15 weeks.

Effect on muscle and joint function of upper limb

The upper extremity robot did not demonstrate statistically significant advantages in augmenting patients' upper extremity muscle strength and mitigating spasticity. However, it yielded a notably favorable effect in ameliorating upper extremity muscle synergies and enhancing Range of Motion (ROM).

In terms of enhancing muscle strength, upper extremity rehabilitation robots exhibited limited effectiveness and did not show a distinct advantage. For instance, a study involving 16 participants who underwent 20 rehabilitation sessions using a novel myoelectric robotic system designed to facilitate wrist mobility in stroke survivors did not yield significant enhancements in muscle strength [56]. In another study by Lee KW et al. [57] no significant differences in muscle strength measured by Manual Muscle Test

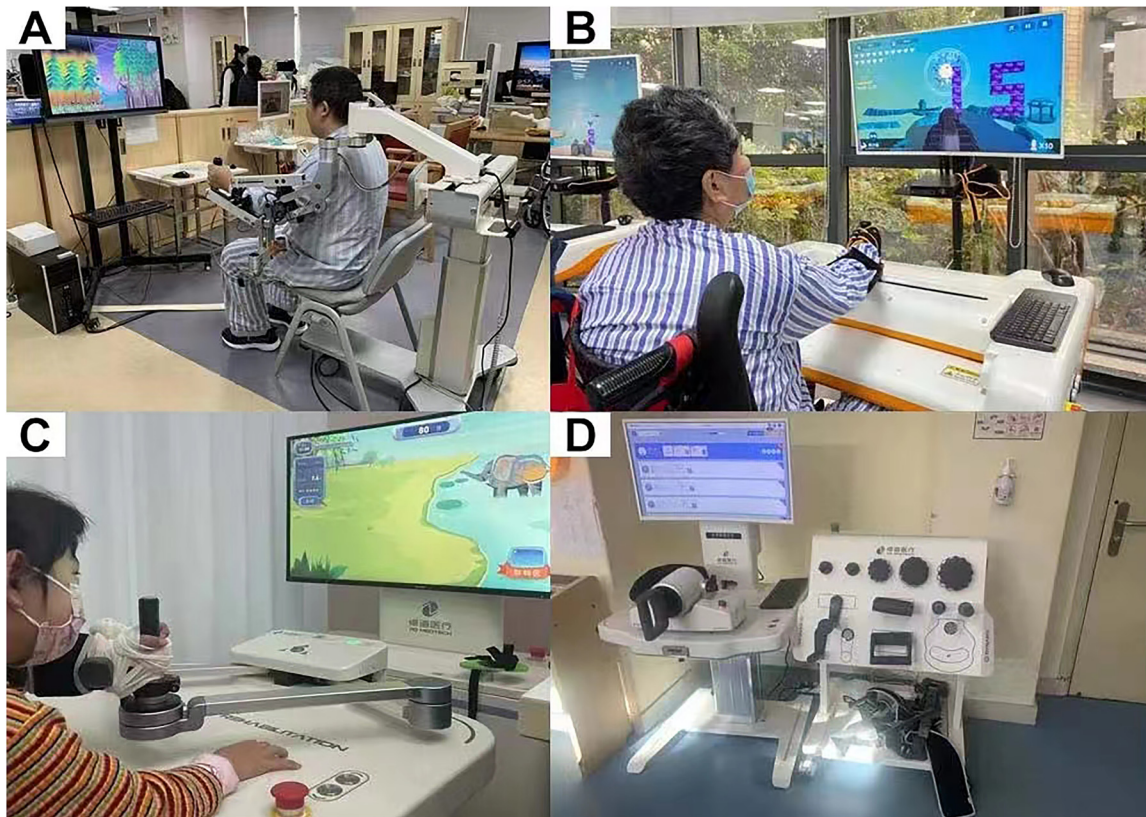


Figure 2: Common upper limb rehabilitation robotics used in daily clinical practice at our center. (A) Armed[®] Spring three-dimensional upper limb training and evaluation system, Hocoma, Switzerland; (B) M2 upper-limb intelligent isokinetic trainer, Shanghai Fourier Intelligence, China; (C) arm guide upper-limb rehabilitation training system, Shanghai Zhuodao Medical, China; (D) Dynaxis upper-limb rehabilitation training system, Shanghai Zhuodao Medical, China.

(MMT) were reported between adding planar robot-assisted game training to conventional training alone. Conventional training, led to a greater improvement in wrist joint flexion compared to robotic training after a two-week intervention.

Conversely, upper extremity robots have demonstrated efficacy in improving muscle synergy of upper extremity muscles in individuals recovering from stroke. In stroke patients, flexor synergy patterns represent coordinated muscular actions resulting from concurrent muscle contractions [58, 59]. These synergies can hinder their movements and affect daily activities such as reaching and self-care. In the study conducted by Takahashi and colleagues [60, 61], a six-week adjunct robotic therapy regimen yielded more significant enhancements in upper extremity flexor synergy motor function when compared to adjunct self-guided rehabilitation. Lencioni's team [62, 63] recruited 40 individuals in sub-acute and chronic stages following a stroke and found significant improvements in axial-to-proximal muscle synergies, comprising shoulder and elbow coordination, in the group receiving robotic-assisted training for four weeks, as opposed to the control group undergoing standard

care arm-specific physiotherapy. Nevertheless, both treatments had negative effects on the control of the distal district [63].

Rehabilitation robots have the potential to improve both active and passive upper extremity ROM compared to conventional therapy alone. Patel et al. [64] reported that an additional 8 h of intensive VR-based robotics upper-limb training initiated within the first month post-stroke may promote greater gains in wrist active ROM. In addition, robot-assisted therapy demonstrated significant effectiveness in improving passive ROM in the upper limb, including shoulder flexion/extension, abduction, intra/extra rotation, and elbow extension, after six months of treatment follow-up instead of at the end of initial treatment [65]. However, a study showed improvement in elbow extension confirmed just after four weeks, with a total of 900 min of robot-assisted training intervention [62].

As for spasticity control, upper extremity robots have also played a role. It is reported that upper extremity robots whether combined with hand functional electrical stimulation or not, demonstrate limited impact on upper extremity

spasticity in comparison to conventional therapeutic approaches [49, 66]. However, some studies have shown that the combination of robotic training and botulinum toxin treatment, resulted in a pronounced reduction in spasticity [67, 68]. Likewise, the application of focal muscle vibration in conjunction with robotic neurorehabilitation, may be helpful in the management of upper-limb spasticity among chronic stroke patients [69].

Effect on the functional activity of upper limb

The effectiveness of upper extremity rehabilitation robots in facilitating functional activities of the upper extremity in stroke patients remains uncertain. The Fugl-Meyer Upper Extremity (FMA-UE) scale, widely recognized for evaluating impairments in stroke patients [70], has been employed in most studies to examine reflex activity, muscle strength, and upper extremity movement control in post-stroke hemiplegic individuals [71, 72]. The general consensus is that robot-assisted therapy, with or without EMG use, does not provide noticeable benefits when compared with conventional or task-oriented training [66, 73–75], especially in the domain of motor function [49]. However, the use of rehabilitative robot-assisted therapies in combination with VR systems has shown relatively optimistic results, suggesting improved upper extremity function compared with traditional rehabilitation therapy alone [64, 76]. The combination of robotics, virtual reality tasks, and neuromuscular electrical stimulation (NMES) has also demonstrated feasibility and preliminarily effectiveness in enhancing upper extremity function among individuals with chronic stroke (≥ 3 months) [77].

Furthermore, when rehabilitation robots are employed alongside complementary therapeutic modalities, promising therapeutic benefits are observed. Bilateral robot-assisted mirror therapy has been found to be more effective than conventional standard mirror therapy in augmenting upper extremity motor function, as indicated by the FMA-UE motor subscale [78]. Similarly, robot-assisted therapy combined with task-specific training has shown superior results in upper extremity motor function and improvements in quality of life, as measured by the FMA-UE motor subscale and the Stroke Impact Scale, compared with robot-assisted therapy combined with impairment-oriented group intervention [79].

The impact of rehabilitation robots on upper extremity motor function and independence in activities of daily living varies depending on the specific functional area and the type of rehabilitation used. In comparison to the FMA-UE, the Wolf Motor Function Test places a greater emphasis on

evaluating upper extremity movement ability [80, 81]. When rehabilitation robots prioritize the rehabilitation of finger function, they hold the potential to significantly enhance the upper-limb capabilities of stroke patients [25], including improved movement duration during functional tasks [75]. On the other hand, when rehabilitation robots do not target finger function, their effectiveness in enhancing upper-limb motor function is not significantly superior to intensive conventional arm training or self-guided training, whose items are determined by therapists [60, 66].

In the realm of enhancing unilateral gross manual dexterity as measured by the Box and Block Test [82], the integration of robotic upper extremity therapy and conventional rehabilitation or functional electrical stimulation, focusing on the shoulder, elbow, forearm, and wrist, has demonstrated clear superiority over sole reliance on conventional therapy when addressing the needs of acute or sub-acute stroke patients [25, 66].

Activities of daily living independence can be measured by the Barthel Index or the modified Barthel Index [83, 84]. When juxtaposed with conventional therapeutic approaches, rehabilitation robots utilizing end-effector, specifically targeting the shoulder and elbow, whether employed in isolation or in conjunction with hand functional electrical stimulation, exhibited no discernible enhancement in the attainment of upper extremity independence in the context of activities of daily living independence [49, 57, 66]. Nonetheless, Iwamoto et al. [85] revealed that the amalgamation of an exoskeletal upper-limb robot with occupational therapy results in a notable enhancement in Activities of Daily Living (ADL) function, particularly in the context of dressing, as evaluated through the Barthel Index, among acute stroke patients.

Hemiplegic shoulder pain (HSP), a common complication after stroke [86], can negatively impact a patient's upper extremity movement [87]. Relieving hemiplegic shoulder pain can have a positive effect on improving upper limb function in stroke patients. Upper extremity robotics has the potential to relieve HSP. Serrezuela et al. [88] showed that robotic-assisted physiotherapy using an exoskeleton with 4 degrees of freedom was more effective than conventional physiotherapy alone. Similarly, Kim et al. [89] demonstrated that robotic therapy plus conventional therapy, which provided passive movement and stretching in the coronal plane, effectively reduced HSP compared with conventional therapy. In another study of robotic therapy combined with traditional therapy, Aprile et al. [90] found that a set of end-effector devices providing active motor training was effective in relieving HSP. However, there was no significant difference between the groups when compared to traditional therapy alone.

Rehabilitation robotics in lower limb function

Lower-limb rehabilitation robots, developed in recent years, play a crucial role in extensively aiding stroke patients by enhancing motor function in paralyzed limbs. These robots facilitate structured and effective training for improving motor function in affected extremities [91]. Figure 3 illustrates the common lower-limb rehabilitation robotics in daily clinical practice at our center.

Most randomized controlled trials have utilized exoskeleton robots, either alone or with combined end-effector devices [28, 29, 92–100]. Additionally, there have

been studies involving gait robots based on the end-effector principle [101, 102], where a vest supports the patient's weight, and their feet are fastened to the system using two platforms to simulate gait movements [103]. Lower-limb rehabilitative robotics target the trunk, hips, knees, ankles, and feet. The majority of robots designed to improve patients' walking or stair-climbing abilities in the lower extremities offer three degrees of freedom, allowing independent rotation at the hip joint, knee joint, and ankle joint in the sagittal plane. Certain robotic systems incorporate harnesses to assist patients in bearing a portion of their body weight while walking within the device [28, 104]. Research has demonstrated the effectiveness of this approach in enhancing the straight-line walking ability of

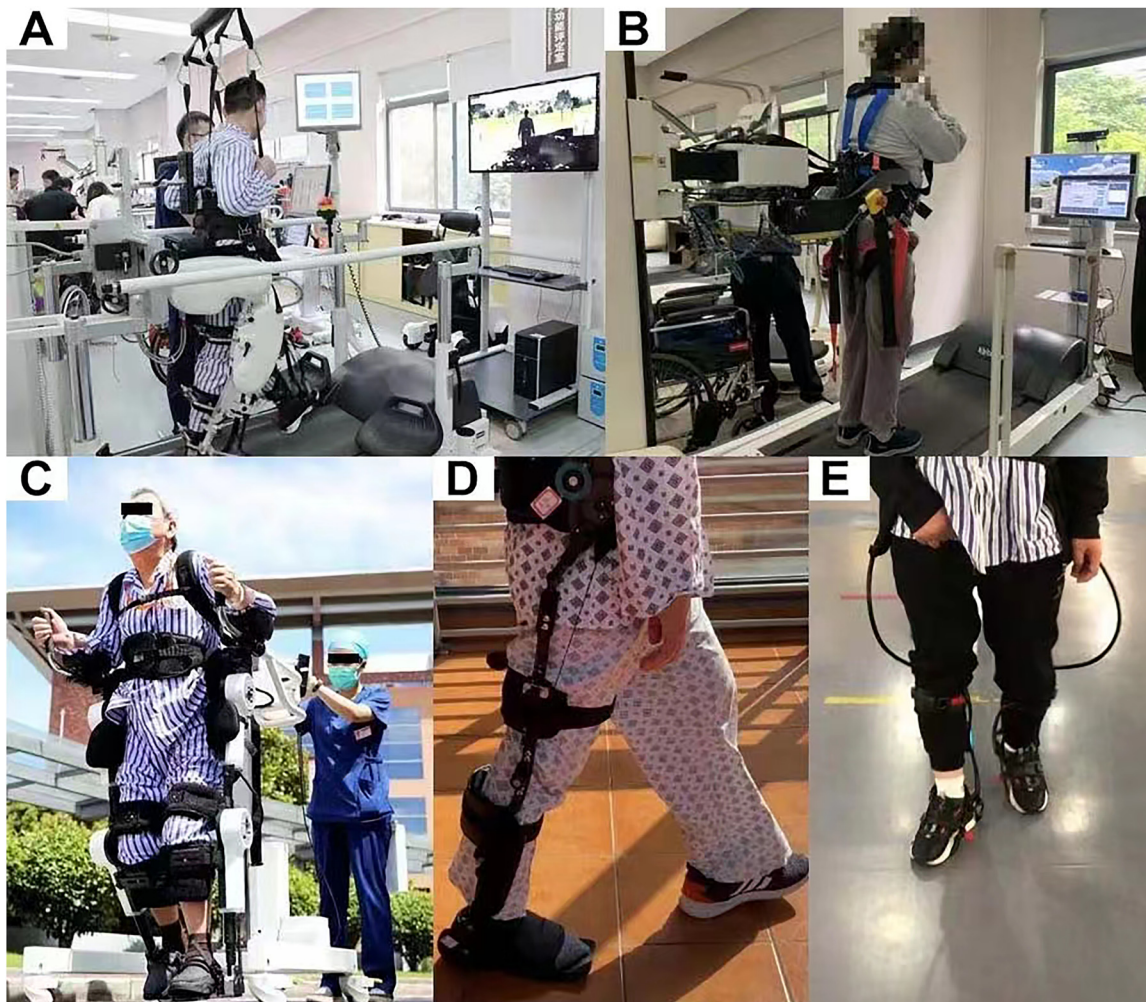


Figure 3: Common lower limb rehabilitation robotics in daily clinical practice at our center. (A) Lokomat® lower-limb rehabilitation robot, Hocoma, Switzerland; (B) Natura Gait 1 weight-loss gait training system, Shanghai Electric Intelligent Rehabilitation Medical, China; (C) exoskeleton walking rehabilitation device, Hangzhou Chengtian Technology, China; (D) Kickstart® walking assistance system, Shanghai Yiran Rehabilitation Equipment, China; (E) muscle armor, Suzhou Yuanye Technology, China.

patients with chronic stroke, especially when utilizing 30 % weight bearing [105]. The primary feedback mode used in most robotic systems is force feedback, with some machines also integrating visual feedback modalities.

The study subjects encompassed individuals across all age groups, excluding adolescents and children under 18 years old. Stroke progression among the subjects spanned acute, sub-acute, and chronic phases. The majority of experimental designs included an intervention group utilizing the robot as an intervention, either with or without traditional rehabilitation methods, and a control group using traditional rehabilitation methods exclusively. A limited number of studies aimed to compare the effectiveness of different types of rehabilitation robots. All trials had an intervention period of no longer than eight weeks.

Effect on muscle and joint function of lower limb

End-effector devices that act on the ankle joint have shown significant benefits in improving the ROM and mobility of the ankle in chronic stroke patients. Yoo et al. [106] developed the Robotic Ankle Stretching, a system for ankle stretching, and found that using this system led to increased ROM compared to using a stretching board. Yeung et al. [107] demonstrated that improved ankle mobility positively impacted gait independence, motor recovery, and walking speed. They observed a considerable increase in the angle of the tilted affected foot from the ground during initial contact and an extension of the affected hip while standing due to robot-assisted ankle-foot-orthosis (AFO) treatment when compared to passive AFO. However, exoskeleton robots have not shown the same level of effectiveness in improving lower-limb ROM. Lin et al. [94] conducted a study with 40 patients with sub-acute stroke, randomly assigning them to receive either conventional rehabilitation alone or combined with 15 robot-assisted gait training (RAGT) sessions. They observed significant changes in active ROM within the groups, but no difference between groups was found.

Lower-limb rehabilitation robots do not appear to be effective in improving the spasticity status of the lower limbs. The Modified Ashworth Scale (MAS) is commonly used to assess lower-limb spasticity in stroke patients [108]. A novel robot-assisted AFO did not produce significant changes in MAS between groups and within groups when compared to sham robot-assisted AFO after treatment [107]. Li et al. [93] discovered that patients who underwent robot-assisted gait training with exoskeletons for 4 weeks did not experience greater improvements in MAS than those who received traditional training. Tamburella et al. [109] demonstrated a

decrease in spasticity only at the knee joint when employing robot-generated joint torque biofeedback post-treatment, but no significant variances were identified among the groups at the conclusion of the training when comparing it with biofeedback based on online biological electromyographic information. Notably, one study indicated that robot-assisted practice of gait and stair climbing did not provide any benefits in reducing lower extremity (LE) muscle tone in nonambulatory stroke patients [101]. However, Park et al. [110] suggested that utilizing an inventive humanoid robot capable of coordinating inter-limb movement between the ankle, knee, and hip joints, can significantly increase active and resistive forces in these joints compared with physical therapy. They observed that resistive stiffness in the hip extension, knee extension, ankle dorsiflexion, and ankle plantarflexion muscles had a moderate correlation with spasticity, suggesting that RAGT might help reduce spasticity, stiffness, and abnormal synergistic (extensor) gait patterns in the lower limbs. In summary, further research is necessary to confirm the efficiency of the lower limb rehabilitation robots for lower limb spasticity.

Few RCTs have investigated the effects of lower limb rehabilitation robots on muscle strength. Only Lin et al. [94] reported significant changes within the RAGT intervention group, but no significant difference in manual muscle test (MMT) scores were found between the intervention and control groups where using conventional rehabilitation.

Effect on the functional activity of lower limb

Generally, therapeutic robots designed for lower limb rehabilitation have generated mixed evidence regarding their effectiveness in improving active functional movement of the lower limbs. The Fugl-Meyer Assessment of Lower Extremity (FMA-LE) is a widely used standard for assessing motor function after stroke [70, 111, 112]. Results regarding the effectiveness of RAGT compared with the conventional rehabilitation, as measured by FMA-LE, have varied. Some researchers have reported significant improvements in the RAGT group [28, 94], while others have not found substantial differences between the two groups [93, 96, 107]. When it comes to assessing walking ability, the Functional Ambulation Classification (FAC) of stroke patients in the acute or sub-acute phase showed improvements following RAGT, but no significant difference was observed between experimental and control groups [96, 100]. However, Hesse et al. [101] argued that the extent of FAC improvement in the RAGT group outweighed that of the control group. In chronic stroke patients, Yeung et al. [107] demonstrated that robotic gait training with a robotic ankle-foot orthosis

featuring ankle dorsiflexion support improved FAC scores after five training sessions and at the three-month follow-up. Furthermore, Mayr et al. [95] concluded that an early treatment protocol involving conventional physical therapy in addition to RAGT is not superior to that of adding conventional gait training intervention for improving locomotion in non-ambulatory stroke patients, as measured by the modified Emory Functional Ambulation Profile. Ogino T's research team found that Global Rating of Change (GRC) scales, which evaluate the impact of an intervention [113], significantly increased at the 1-month follow-up and 3-month follow-up compared to the baseline in the Gait Exercise Assist Robot (GEAR) group [98, 99]. In summary, the efficacy of lower-limb rehabilitation robots in enhancing lower limb motor function remains unclear.

In terms of lower limb coordination and balance among stroke patients, Kim et al. [28] found a significant improvement in coordination function within the RAGT group compared to the conventional training group. However, studies on the effectiveness of rehabilitation robots for lower limb rehabilitation on balance function have not consistently yielded positive results. In terms of balance in the standing position, rehabilitation robotic therapy showed improvement only within the group, with no significant differentiation between the groups compared to conventional therapy [94, 114]. Regarding balance whilst walking, exoskeleton robots designed for the lower limbs, whether or not they incorporated visual feedback, did not demonstrate superior outcomes as measured by Time Up and Go test (TUG) [100, 114]. Ogino et al. [98] demonstrated that the mean changes in TUG were significantly higher in the GEAR group compared to the treadmill group during week 4, compared to baseline (week 0). However, there was no significant effect in the long term, as there was no difference between the groups from baseline (week 0) to the 1-month follow-up (week 8) and baseline (week 0) to the 3-month follow-up (week 16).

Overall, combining RAGT, with or without conventional physical therapy, did not significantly improve spatiotemporal parameters of gait compared to conventional therapy. Gait speed did not demonstrate superiority in interventions involving rehabilitation robots, observed in various speed tests and through the use of gait analyzers [93, 94, 97, 99, 100, 107]. In terms of aerobic capacity and walking endurance, most studies did not show significant benefits [93, 107, 115]. However, Ogino et al. [98] reported higher effectiveness in the 6 min walk test immediately following the intervention, but no lasting differences between the groups at 1-month and 3-month follow-up points. Mizukami et al. [101] found that gait training with a hybrid assistive limb exoskeleton robotic device enhanced the 2 min walk test scores in sub-acute

stroke patients, although the small sample size (8 participants) limits the credibility of this finding. Interestingly, none of the following aspects of RAGT have been shown to provide significant benefits, including toe-out angle, step length, stride length, gait cadence, stride duration, and cycle duration [93, 97, 100]. Ogino's research team found that gait training using the Gait Exercise Assist Robot might be more efficient than treadmill-training in improving the swing phase in subjects with chronic stroke, leading to decreases in hip hiking and excessive hip external rotation, as well as increases in side stride length, side step length, as well as role-physical and social-functioning, as measured by 8-item Short Form Health Survey. However, there was no difference between groups [98, 99].

All the aforementioned studies examined the effectiveness of lower extremity rehabilitation robots as an alternative therapeutic approach to conventional rehabilitation techniques. In recent years, there has been growing interest in exploring innovative treatments that combine robotics and VR to enhance the functionality of stroke patients. This approach has shown significant potential and gained attention as a promising method for treatment. Kayabinar et al. [29] reported that incorporating VR into RAGT resulted in significant differences in single and dual-task gait speeds and cognitive dual-task performance among chronic stroke patients after treatment, even though there were no notable differences when compared to RAGT without VR. Similarly, Bergmann et al. [92] observed that combining VR with RAGT improved the per-session and overall walking time of sub-acute stroke patients while reducing their perceived pressure and tension.

Rehabilitation robotics in cognitive function

The literature on rehabilitation robotics for cognitive function recovery is relatively limited and often closely related to motor function recovery. Aprile et al. [116] conducted an exploratory study revealing notable disparities in attention, processing speed, memory, visuospatial ability, and executive functioning before and after employing robot-assisted rehabilitation. Significant differences also emerged in UE impairments, muscle strength, and ADLs. Bergqvist et al. [117] emphasized the significance of visuospatial/executive function in the long-term outcomes of lower extremity motor function rehabilitation after stroke. They identified a significant association between visuospatial/executive function scores, as measured by Montreal Cognitive

Assessment (MoCA Vis/Ex), and the results of the 6 min walk test (6MWT) in the conventional gait training group. However, this connection was not observed in the robotic gait training group. The study suggested that patients with severely impaired visuospatial/executive could benefit from robotic gait training, as they showed improvement regardless of their visuospatial/executive function.

Furthermore, PC-based cognitive training has the potential to enhance cognitive function in stroke patients. De Luca R's team [118] demonstrated greater cognitive improvement when cognitive PC training was combined with standard neurological rehabilitation, compared to standard neurological rehabilitation alone. In subsequent experiment [119], although no significant difference was found between the experimental group (EG), which underwent traditional cognitive rehabilitation (CR) in addition to PC-based Erica training, and the control group (CG), which only received CR, intragroup comparisons revealed more prominent cognitive improvements in the EG than in the CG.

Additionally, some studies have shown that both upper and lower extremity robotic rehabilitation with VR can be highly efficacy for stroke patients. Especially in terms of cognitive flexibility, shifting skills, visual constructive abilities (attention, memory, visuospatial abilities, and complex commands), and decreased anxiety levels [31, 120].

Finally, one study confirmed that robotic technology used in UE rehabilitation had a positive impact on patients' emotional states by improving their Center for Epidemiological Studies Depression Scale (CES-D) scores after the intervention [32].

Summary and future perspectives

In summary, robotic technology plays a significant role in post-stroke motor and cognitive recovery. The use of rehabilitation robots can relieve clinicians from the burden of intensive training tasks. Leveraging their accuracy and dependability, rehabilitation robots offer an effective means to enhance the outcomes for stroke patients. Future endeavors should prioritize standardized and uniform application of rehabilitation robots in stroke treatment; delve into combining rehabilitation robot training with virtual reality and telemedicine, and concentrate on the research and development of adaptive training technology for rehabilitation robots.

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References

1. Tu WJ, Zhao Z, Yin P, Cao L, Zeng J, Chen H, et al. Estimated burden of stroke in China in 2020. *JAMA Netw Open* 2023;6:e231455.
2. Wu S, Wu B, Liu M, Chen Z, Wang W, Anderson CS, et al. Stroke in China: advances and challenges in epidemiology, prevention, and management. *Lancet Neurol* 2019;18:394–405.
3. Wang YJ, Li ZX, Gu HQ, Zhai Y, Jiang Y, Zhao XQ, et al. China Stroke Statistics 2019: a report from the National Center for Healthcare Quality Management in Neurological Diseases, China National Clinical Research Center for Neurological Diseases, The Chinese Stroke Association, National Center for Chronic and Non-Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention and Institute for Global Neuroscience and Stroke Collaborations. *Stroke Vasc Neurol* 2020;5:211–39.
4. Cauraugh J, Light K, Kim S, Thigpen M, Behrman A. Chronic motor dysfunction after stroke. *Stroke* 2000;31:1360–4.
5. Li S. Spasticity, motor recovery, and neural plasticity after stroke. *Front Neurol* 2017;8:120.
6. Raghavan P. Upper limb motor impairment after stroke. *Phys Med Rehabil Clin N Am* 2015;26:599–610.
7. Basteris A, Nijenhuis SM, Stienen AHA, Buurke JH, Prange GB, Amirabdollahian F. Training modalities in robot-mediated upper limb rehabilitation in stroke: a framework for classification based on a systematic review. *J NeuroEng Rehabil* 2014;11:111.
8. Rost NS, Brodtmann A, Pase MP, van Veluw SJ, Biffi A, Duering M, et al. Post-stroke cognitive impairment and dementia. *Circ Res* 2022;130:1252–71.
9. Hurford R, Sekhar A, Hughes TAT, Muir KW. Diagnosis and management of acute ischaemic stroke. *Pract Neurol* 2020;20:304–16.
10. Zhang T, Zhao J, Li X, Bai Y, Wang B, Qu Y, et al. Chinese Stroke Association guidelines for clinical management of cerebrovascular disorders: executive summary and 2019 update of clinical management of stroke rehabilitation. *Stroke Vasc Neurol* 2020;5:250–9.

11. Malik AN, Tariq H, Afridi A, Rathore FA. Technological advancements in stroke rehabilitation. *J Pak Med Assoc* 2022;72:1672–4.
12. Huang J, Ji JR, Liang C, Zhang YZ, Sun HC, Yan YH, et al. Effects of physical therapy-based rehabilitation on recovery of upper limb motor function after stroke in adults: a systematic review and meta-analysis of randomized controlled trials. *Ann Palliat Med* 2022;11:521–31.
13. O'Dell MW. Stroke rehabilitation and motor recovery. *Continuum* 2023;29:605–27.
14. van Duijnhoven HJ, Heeren A, Peters MA, Veerbeek JM, Kwakkel G, Geurts AC, et al. Effects of exercise therapy on balance capacity in chronic stroke: systematic review and meta-analysis. *Stroke* 2016;47:2603–10.
15. Pollock A, Baer G, Campbell P, Choo PL, Forster A, Morris J, et al. Physical rehabilitation approaches for the recovery of function and mobility following stroke. *Cochrane Database Syst Rev* 2014;2014: Cd001920.
16. Rahayu UB, Wibowo S, Setyopranoto I, Hibatullah Romli M. Effectiveness of physiotherapy interventions in brain plasticity, balance and functional ability in stroke survivors: a randomized controlled trial. *NeuroRehabilitation* 2020;47:463–70.
17. Yuan S, He Y. Effects of physical therapy on mental function in patients with stroke. *J Int Med Res* 2020;48:300060519861164.
18. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet* 2011;377:1693–702.
19. Gibson E, Koh CL, Eames S, Bennett S, Scott AM, Hoffmann TC. Occupational therapy for cognitive impairment in stroke patients. *Cochrane Database Syst Rev* 2022;3: Cd006430.
20. Legg LA, Lewis SR, Schofield-Robinson OJ, Drummond A, Langhorne P. Occupational therapy for adults with problems in activities of daily living after stroke. *Cochrane Database Syst Rev* 2017;7: Cd003585.
21. Brady MC, Kelly H, Godwin J, Enderby P, Campbell P. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst Rev* 2016;2016: Cd000425.
22. Chiaramonte R, Vecchio M. Dysarthria and stroke. The effectiveness of speech rehabilitation. A systematic review and meta-analysis of the studies. *Eur J Phys Rehabil Med* 2021;57:24–43.
23. Chiaramonte R, Pavone P, Vecchio M. Speech rehabilitation in dysarthria after stroke: a systematic review of the studies. *Eur J Phys Rehabil Med* 2020;56:547–62.
24. Reinkensmeyer DJ, Emken JL, Cramer SC. Robotics, motor learning, and neurologic recovery. *Annu Rev Biomed Eng* 2004;6:497–525.
25. Dehem S, Gilliaux M, Stoquart G, Detrembleur C, Jacquemin G, Palumbo S, et al. Effectiveness of upper-limb robotic-assisted therapy in the early rehabilitation phase after stroke: a single-blind, randomised, controlled trial. *Ann Phys Rehabil Med* 2019;62:313–20.
26. Rodgers H, Bosomworth H, Krebs HI, van Wijck F, Howel D, Wilson N, et al. Robot-assisted training compared with an enhanced upper limb therapy programme and with usual care for upper limb functional limitation after stroke: the RATULS three-group RCT. *Health Technol Assess* 2020;24:1–232.
27. Singh N, Saini M, Kumar N, Srivastava MVP, Mehndiratta A. Evidence of neuroplasticity with robotic hand exoskeleton for post-stroke rehabilitation: a randomized controlled trial. *J NeuroEng Rehabil* 2021; 18:76.
28. Kim HY, Shin JH, Yang SP, Shin MA, Lee SH. Robot-assisted gait training for balance and lower extremity function in patients with infratentorial stroke: a single-blinded randomized controlled trial. *J NeuroEng Rehabil* 2019;16:99.
29. Kayabinar B, Alemdaroglu-Gurbuz I, Yilmaz O. The effects of virtual reality augmented robot-assisted gait training on dual-task performance and functional measures in chronic stroke: a randomized controlled single-blind trial. *Eur J Phys Rehabil Med* 2021; 57:227–37.
30. Hesse S, Werner C, Schonhardt EM, Bardeleben A, Jenrich W, Kirker SG. Combined transcranial direct current stimulation and robot-assisted arm training in subacute stroke patients: a pilot study. *Restor Neurol Neurosci* 2007;25:9–15.
31. Manuli A, Maggio MG, Latella D, Cannavò A, Balletta T, De Luca R, et al. Can robotic gait rehabilitation plus Virtual Reality affect cognitive and behavioural outcomes in patients with chronic stroke? A randomized controlled trial involving three different protocols. *J Stroke Cerebrovasc Dis* 2020;29:104994.
32. Taravati S, Capaci K, Uzumcugil H, Tanigor G. Evaluation of an upper limb robotic rehabilitation program on motor functions, quality of life, cognition, and emotional status in patients with stroke: a randomized controlled study. *Neurol Sci* 2022;43:1177–88.
33. Esquenazi A, Talaty M. Robotics for lower limb rehabilitation. *Phys Med Rehabil Clin N Am* 2019;30:385–97.
34. Yakub F, Md Khudzari AZ, Mori Y. Recent trends for practical rehabilitation robotics, current challenges and the future. *Int J Rehabil Res* 2014;37:9–21.
35. Molteni F, Gasperini G, Cannaviello G, Guanziroli E. Exoskeleton and end-effector robots for upper and lower limbs rehabilitation: narrative review. *PM R* 2018;10:S174–88.
36. Bhardwaj S, Khan AA, Muzammil M. Lower limb rehabilitation robotics: the current understanding and technology. *Work* 2021;69:775–93.
37. Maciejasz P, Eschweiler J, Gerlach-Hahn K, Jansen-Troy A, Leonhardt S. A survey on robotic devices for upper limb rehabilitation. *J NeuroEng Rehabil* 2014;11:3.
38. Li F, Chen J, Zhou Z, Xie J, Gao Z, Xiao Y, et al. Lightweight soft robotic glove with whole-hand finger motion tracking for hand rehabilitation in virtual reality. *Biomimetics* 2023;8:425.
39. Klamroth-Marganska V. Stroke rehabilitation: therapy robots and assistive devices. In: Kerkhof PLM, Miller VM, editors. *Sex-specific analysis of cardiovascular function*. Cham: Springer International Publishing; 2018:579–87 pp.
40. Kim WS, Cho S, Ku J, Kim Y, Lee K, Hwang HJ, et al. Clinical application of virtual reality for upper limb motor rehabilitation in stroke: review of technologies and clinical evidence. *J Clin Med* 2020;9:3369.
41. Schüler T, Santos Lfd, Hoermann S. Harnessing the experience of presence for virtual motor rehabilitation: towards a guideline for the development of virtual reality environments. In: *Proceeding the 10th international conference on disability virtual reality & associated technologies*, Gothenburg, Sweden; 2014;373–6 pp.
42. Merians AS, Jack D, Boian R, Tremaine M, Burdea GC, Adamovich SV, et al. Virtual reality-augmented rehabilitation for patients following stroke. *Phys Ther* 2002;82:898–915.
43. Ventura S, Brivio E, Riva G, Baños RM. Immersive versus non-immersive experience: exploring the feasibility of memory assessment through 360° technology. *Front Psychol* 2019;10:2509.
44. Isaacson BM, Swanson TM, Pasquina PF. The use of a computer-assisted rehabilitation environment (CAREN) for enhancing wounded warrior rehabilitation regimens. *J Spinal Cord Med* 2013;36:296–9.
45. van der Meer R. Recent developments in computer assisted rehabilitation environments. *Mil Med Res* 2014;1:22.
46. Fosch-Villaronga E, Čartolovni A, Pierce RL. Promoting inclusiveness in exoskeleton robotics: addressing challenges for pediatric access. *Paladyn J Behav Rob* 2020;11:327–39.
47. Eguren D, Cestari M, Luu TP, Kilicarslan A, Steele A, Contreras-Vidal JL. Design of a customizable, modular pediatric exoskeleton for

- rehabilitation and mobility. In: 2019 IEEE International Conference on Systems, Man and Cybernetics (SMC), Bari, Italy; 2019:2411–6 pp.
48. Gonzalez A, Garcia L, Kilby J, McNair P. Robotic devices for paediatric rehabilitation: a review of design features. *Biomed Eng Online* 2021; 20:89.
 49. Aprile I, Germanotta M, Cruciani A, Loreti S, Pecchioli C, Cecchi F, et al. Upper limb robotic rehabilitation after stroke: a multicenter, randomized clinical trial. *J Neurol Phys Ther* 2020;44:3–14.
 50. Rodgers H, Bosomworth H, Krebs HI, van Wijck F, Howel D, Wilson N, et al. Robot assisted training for the upper limb after stroke (RATULS): a multicentre randomised controlled trial. *Lancet* 2019;394:51–62.
 51. Johansen T, Sørensen L, Kolskår KK, Strøm V, Wouda MF. Effectiveness of robot-assisted arm exercise on arm and hand function in stroke survivors – a systematic review and meta-analysis. *J Rehabil Assist Technol Eng* 2023;10:20556683231183639.
 52. Payedimarri AB, Ratti M, Rescinito R, Vanhaecht K, Panella M. Effectiveness of platform-based robot-assisted rehabilitation for musculoskeletal or neurologic injuries: a systematic review. *Bioengineering* 2022;9:129.
 53. Zhou Z, Sun Y, Wang N, Gao F, Wei K, Wang Q. Robot-assisted rehabilitation of ankle plantar flexors spasticity: a 3-month study with proprioceptive neuromuscular facilitation. *Front Neurobot* 2016;10:16.
 54. Feingold-Polak R, Barzel O, Levy-Tzedek S. A robot goes to rehab: a novel gamified system for long-term stroke rehabilitation using a socially assistive robot-methodology and usability testing. *J NeuroEng Rehabil* 2021;18:122.
 55. Nizamis K, Athanasiou A, Almpanti S, Dimitrousis C, Astaras A. Converging robotic technologies in targeted neural rehabilitation: a review of emerging solutions and challenges. *Sensors* 2021;21:2084.
 56. Song R, Tong KY, Hu X, Zhou W. Myoelectrically controlled wrist robot for stroke rehabilitation. *J NeuroEng Rehabil* 2013;10:52.
 57. Lee KW, Kim SB, Lee JH, Lee SJ, Kim JW. Effect of robot-assisted Game training on upper extremity function in stroke patients. *Ann Rehabil Med* 2017;41:539–46.
 58. Bhagubai MMC, Wolterink G, Schwarz A, Held JPO, Van Beijnum BF, Veltink PH. Quantifying pathological synergies in the upper extremity of stroke subjects with the use of Inertial measurement units: a pilot study. *IEEE J Transl Eng Health Med* 2021;9:2100211.
 59. Sawner KA, Lavigne JM, Brunnstrom S. *Movement therapy in hemiplegia: a neurophysiological approach*. New York: Lippincott Williams & Wilkins; 1970.
 60. Takahashi K, Domen K, Sakamoto T, Tushima M, Otaka Y, Seto M, et al. Efficacy of upper extremity robotic therapy in subacute poststroke hemiplegia: an exploratory randomized trial. *Stroke* 2016;47:1385–8.
 61. Takebayashi T, Takahashi K, Domen K, Hachisuka K. Impact of initial flexor synergy pattern scores on improving upper extremity function in stroke patients treated with adjunct robotic rehabilitation: a randomized clinical trial. *Top Stroke Rehabil* 2020;27:516–24.
 62. Carpinella I, Lencioni T, Bowman T, Bertoni R, Turolla A, Ferrarin M, et al. Effects of robot therapy on upper body kinematics and arm function in persons post stroke: a pilot randomized controlled trial. *J NeuroEng Rehabil* 2020;17:10.
 63. Lencioni T, Fornia L, Bowman T, Marzegan A, Caronni A, Turolla A, et al. A randomized controlled trial on the effects induced by robot-assisted and usual-care rehabilitation on upper limb muscle synergies in post-stroke subjects. *Sci Rep* 2021;11:5323.
 64. Patel J, Fluet G, Qiu Q, Yarossi M, Merians A, Tunik E, et al. Intensive virtual reality and robotic based upper limb training compared to usual care, and associated cortical reorganization, in the acute and early sub-acute periods post-stroke: a feasibility study. *J NeuroEng Rehabil* 2019;16:92.
 65. Franceschini M, Mazzoleni S, Goffredo M, Pournajaf S, Galafate D, Criscuolo S, et al. Upper limb robot-assisted rehabilitation versus physical therapy on subacute stroke patients: a follow-up study. *J Bodyw Mov Ther* 2020;24:194–8.
 66. Straudi S, Baroni A, Mele S, Craighero L, Manfredini F, Lamberti N, et al. Effects of a robot-assisted arm training plus hand functional electrical stimulation on recovery after stroke: a randomized clinical trial. *Arch Phys Med Rehabil* 2020;101:309–16.
 67. Pennati GV, Da Re C, Messineo I, Bonaiuti D. How could robotic training and botulinum toxin be combined in chronic post stroke upper limb spasticity? A pilot study. *Eur J Phys Rehabil Med* 2015;51: 381–7.
 68. Hung JW, Chen YW, Chen YJ, Pong YP, Wu WC, Chang KC, et al. The effects of distributed vs. condensed schedule for robot-assisted training with botulinum toxin A injection for spastic upper limbs in chronic post-stroke subjects. *Toxins* 2021;13:539.
 69. Calabrò RS, Naro A, Russo M, Milardi D, Leo A, Filoni S, et al. Is two better than one? Muscle vibration plus robotic rehabilitation to improve upper limb spasticity and function: a pilot randomized controlled trial. *PLoS One* 2017;12:e0185936.
 70. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. *Scand J Rehabil Med* 1975;7:13–31.
 71. van Wijck FMJ, Pandyan AD, Johnson GR, Barnes MP. Assessing motor deficits in neurological rehabilitation: patterns of instrument usage. *Neurorehabilitation Neural Repair* 2001;15:23–30.
 72. Singer B, Garcia-Vega J. The Fugl-Meyer upper extremity scale. *J Physiother* 2017;63:53.
 73. Hung JW, Yen CL, Chang KC, Chiang WC, Chuang IC, Pong YP, et al. A pilot randomized controlled trial of botulinum toxin treatment combined with robot-assisted therapy, mirror therapy, or active control treatment in patients with spasticity following stroke. *Toxins* 2022;14:415.
 74. Takebayashi T, Takahashi K, Amano S, Goshō M, Sakai M, Hashimoto K, et al. Robot-assisted training as self-training for upper-limb hemiplegia in chronic stroke: a randomized controlled trial. *Stroke* 2022;53:2182–91.
 75. Chen YW, Chiang WC, Chang CL, Lo SM, Wu CY. Comparative effects of EMG-driven robot-assisted therapy versus task-oriented training on motor and daily function in patients with stroke: a randomized cross-over trial. *J NeuroEng Rehabil* 2022;19:6.
 76. Kiper P, Szczudlik A, Agostini M, Opara J, Nowobilski R, Ventura L, et al. Virtual reality for upper limb rehabilitation in subacute and chronic stroke: a randomized controlled trial. *Arch Phys Med Rehabil* 2018;99: 834–42.e4.
 77. Norouzi-Gheidari N, Archambault PS, Monte-Silva K, Kairy D, Sveistrup H, Trivino M, et al. Feasibility and preliminary efficacy of a combined virtual reality, robotics and electrical stimulation intervention in upper extremity stroke rehabilitation. *J NeuroEng Rehabil* 2021;18:61.
 78. Schrader M, Sterr A, Kettlitz R, Wohlmeiner A, Buschfort R, Dohle C, et al. The effect of mirror therapy can be improved by simultaneous robotic assistance. *Restor Neurol Neurosci* 2022;40:185–94.
 79. Hung CS, Hsieh YW, Wu CY, Lin YT, Lin KC, Chen CL. The effects of combination of robot-assisted therapy with task-specific or impairment-oriented training on motor function and quality of life in chronic stroke. *PM R* 2016;8:721–9.

80. Wolf SL, Catlin PA, Ellis M, Archer AL, Morgan B, Piacentino A. Assessing wolf motor function test as outcome measure for research in patients after stroke. *Stroke* 2001;32:1635–9.
81. Wolf SL, Lecraw DE, Barton LA, Jann BB. Forced use of hemiplegic upper extremities to reverse the effect of learned nonuse among chronic stroke and head-injured patients. *Exp Neurol* 1989;104:125–32.
82. Prochaska E, Ammenwerth E. A digital box and block test for hand dexterity measurement: instrument validation study. *JMIR Rehabil Assist Technol* 2023;10:e50474.
83. Hsieh YW, Wang CH, Wu SC, Chen PC, Sheu CF, Hsieh CL. Establishing the minimal clinically important difference of the Barthel Index in stroke patients. *Neurorehabil Neural Repair* 2007;21:233–8.
84. Ohura T, Hase K, Nakajima Y, Nakayama T. Validity and reliability of a performance evaluation tool based on the modified Barthel Index for stroke patients. *BMC Med Res Methodol* 2017;17:131.
85. Iwamoto Y, Imura T, Suzukawa T, Fukuyama H, Ishii T, Taki S, et al. Combination of exoskeletal upper limb robot and occupational therapy improve activities of daily living function in acute stroke patients. *J Stroke Cerebrovasc Dis* 2019;28:2018–25.
86. McLean DE. Medical complications experienced by a cohort of stroke survivors during inpatient, tertiary-level stroke rehabilitation. *Arch Phys Med Rehabil* 2004;85:466–9.
87. Roosink M, Renzenbrink GJ, Geurts AC, Ijzerman MJ. Towards a mechanism-based view on post-stroke shoulder pain: theoretical considerations and clinical implications. *NeuroRehabilitation* 2012;30:153–65.
88. Serrezuela RR, Quezada MT, Zayas MH, Pedrón AM, Hermosilla DM, Zamora RS. Robotic therapy for the hemiplegic shoulder pain: a pilot study. *J NeuroEng Rehabil* 2020;17:54.
89. Kim MS, Kim SH, Noh SE, Bang HJ, Lee KM. Robotic-assisted shoulder rehabilitation therapy effectively improved poststroke hemiplegic shoulder pain: a randomized controlled trial. *Arch Phys Med Rehabil* 2019;100:1015–22.
90. Aprile I, Germanotta M, Cruciani A, Pecchioli C, Loreti S, Papadopoulou D, et al. Poststroke shoulder pain in subacute patients and its correlation with upper limb recovery after robotic or conventional treatment: a secondary analysis of a multicenter randomized controlled trial. *Int J Stroke* 2021;16:396–405.
91. Zhang X, Yue Z, Wang J. Robotics in lower-limb rehabilitation after stroke. *Behav Neurol* 2017;2017:3731802.
92. Bergmann J, Krewer C, Bauer P, Koenig A, Riener R, Müller F. Virtual reality to augment robot-assisted gait training in non-ambulatory patients with a subacute stroke: a pilot randomized controlled trial. *Eur J Phys Rehabil Med* 2018;54:397–407.
93. Li D-X, Zha F-B, Long J-J, Liu F, Cao J, Wang Y-L. Effect of robot assisted gait training on motor and walking function in patients with subacute stroke: a random controlled study. *J Stroke Cerebrovasc Dis* 2021;30:105807.
94. Lin YN, Huang SW, Kuan YC, Chen HC, Jian WS, Lin LF. Hybrid robot-assisted gait training for motor function in subacute stroke: a single-blind randomized controlled trial. *J NeuroEng Rehabil* 2022;19:99.
95. Mayr A, Quirbach E, Picelli A, Kofler M, Smania N, Saltuari L. Early robot-assisted gait retraining in non-ambulatory patients with stroke: a single blind randomized controlled trial. *Eur J Phys Rehabil Med* 2018;54:819–26.
96. Mizukami M, Yoshikawa K, Kawamoto H, Sano A, Koseki K, Asakwa Y, et al. Gait training of subacute stroke patients using a hybrid assistive limb: a pilot study. *Disabil Rehabil Assist Technol* 2017;12:197–204.
97. Miyagawa D, Matsushima A, Maruyama Y, Mizukami N, Tetsuya M, Hashimoto M, et al. Gait training with a wearable powered robot during stroke rehabilitation: a randomized parallel-group trial. *J NeuroEng Rehabil* 2023;20:54.
98. Ogino T, Kanata Y, Uegaki R, Yamaguchi T, Morisaki K, Nakano S, et al. Effects of gait exercise assist robot (GEAR) on subjects with chronic stroke: a randomized controlled pilot trial. *J Stroke Cerebrovasc Dis* 2020;29:104886.
99. Ogino T, Kanata Y, Uegaki R, Yamaguchi T, Morisaki K, Nakano S, et al. Improving abnormal gait patterns by using a gait exercise assist robot (GEAR) in chronic stroke subjects: a randomized, controlled, pilot trial. *Gait Posture* 2020;82:45–51.
100. Yu D, Yang Z, Lei L, Chaoming N, Ming W. Robot-assisted gait training plan for patients in poststroke recovery period: a single blind randomized controlled trial. *BioMed Res Int* 2021;2021:5820304.
101. Hesse S, Tomelleri C, Bardeleben A, Werner C, Waldner A. Robot-assisted practice of gait and stair climbing in nonambulatory stroke patients. *J Rehabil Res Dev* 2012;49:613–22.
102. Alfieri FM, Dias CDS, Dos Santos ACA, Battistella LR. Acute effect of robotic therapy (G-EO System™) on the lower limb temperature distribution of a patient with stroke sequelae. *Case Rep Neurol Med* 2019;2019:8408492.
103. Hesse S, Waldner A, Tomelleri C. Innovative gait robot for the repetitive practice of floor walking and stair climbing up and down in stroke patients. *J NeuroEng Rehabil* 2010;7:30.
104. van Dellen F, Aurich-Schuler T, Labrüyère R. Within- and between-therapist agreement on personalized parameters for robot-assisted gait therapy: the challenge of adjusting robotic assistance. *J NeuroEng Rehabil* 2023;20:81.
105. Choi W. Effects of robot-assisted gait training with body weight support on gait and balance in stroke patients. *Int J Environ Res Public Health* 2022;19. <https://doi.org/10.3390/ijerph19105814>.
106. Yoo D, Son Y, Kim DH, Seo KH, Lee BC. Technology-assisted ankle rehabilitation improves balance and gait performance in stroke survivors: a randomized controlled study with 1-month follow-up. *IEEE Trans Neural Syst Rehabil Eng* 2018;26:2315–23.
107. Yeung LF, Ockenfeld C, Pang MK, Wai HW, Soo OY, Li SW, et al. Randomized controlled trial of robot-assisted gait training with dorsiflexion assistance on chronic stroke patients wearing ankle-foot-orthosis. *J NeuroEng Rehabil* 2018;15:51.
108. Flansbjerg UB, Miller M, Downham D, Lexell J. Progressive resistance training after stroke: effects on muscle strength, muscle tone, gait performance and perceived participation. *J Rehabil Med* 2008;40:42–8.
109. Tamburella F, Moreno JC, Herrera Valenzuela DS, Pisotta I, Iosa M, Cincotti F, et al. Influences of the biofeedback content on robotic post-stroke gait rehabilitation: electromyographic vs joint torque biofeedback. *J NeuroEng Rehabil* 2019;16:95.
110. Park C, Oh-Park M, Bialek A, Friel K, Edwards D, You JSH. Abnormal synergistic gait mitigation in acute stroke using an innovative ankle-knee-hip interlimb humanoid robot: a preliminary randomized controlled trial. *Sci Rep* 2021;11:22823.
111. Duncan Millar J, van Wijck F, Pollock A, Ali M. Outcome measures in post-stroke arm rehabilitation trials: do existing measures capture outcomes that are important to stroke survivors, carers, and clinicians? *Clin Rehabil* 2019;33:737–49.
112. Kwakkel G, Lannin NA, Borschmann K, English C, Ali M, Churilov L, et al. Standardized measurement of sensorimotor recovery in stroke trials: consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable. *Int J Stroke* 2017;12:451–61.

113. Kamper SJ, Maher CG, Mackay G. Global rating of change scales: a review of strengths and weaknesses and considerations for design. *J Man Manip Ther* 2009;17:163–70.
114. Ochi M, Wada F, Saeki S, Hachisuka K. Gait training in subacute non-ambulatory stroke patients using a full weight-bearing gait-assistance robot: a prospective, randomized, open, blinded-endpoint trial. *J Neurol Sci* 2015;353:130–6.
115. Zhang H, Li X, Gong Y, Wu J, Chen J, Chen W, et al. Three-dimensional gait analysis and sEMG measures for robotic-assisted gait training in subacute stroke: a randomized controlled trial. *BioMed Res Int* 2023; 2023:7563802.
116. Aprile I, Guardati G, Cipollini V, Papadopoulou D, Mastrorosa A, Castelli L, et al. Robotic rehabilitation: an opportunity to improve cognitive functions in subjects with stroke. An explorative study. *Front Neurol* 2020;11:588285.
117. Bergqvist M, Möller MC, Björklund M, Borg J, Palmcrantz S. The impact of visuospatial and executive function on activity performance and outcome after robotic or conventional gait training, long-term after stroke-as part of a randomized controlled trial. *PLoS One* 2023;18:e0281212.
118. De Luca R, Calabrò RS, Gervasi G, De Salvo S, Bonanno L, Corallo F, et al. Is computer-assisted training effective in improving rehabilitative outcomes after brain injury? A case-control hospital-based study. *Disabil Health J* 2014;7:356–60.
119. De Luca R, Leonardi S, Spadaro L, Russo M, Aragona B, Torrisi M, et al. Improving cognitive function in patients with stroke: can computerized training be the future? *J Stroke Cerebrovasc Dis* 2018;27:1055–60.
120. Adomavičienė A, Daunoravičienė K, Kubilius R, Varžaitytė L, Raistenskis J. Influence of new technologies on post-stroke rehabilitation: a comparison of armeo spring to the kinect system. *Medicina* 2019;55:98.