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Invited Review

Robot-assisted gait training in stroke

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ABSTRACT

Stroke is the second most common cause of mortality and disability worldwide. Most of the patients cannot regain their walking ability after a stroke. Impaired gait and mobility negatively affect the activities of daily living and quality of life of stroke survivors. Restoring gait and mobility are the most important targets of the rehabilitation approaches. Advances in computers and engineering have enabled robotics to be used in many areas of rehabilitation medicine. One of them is gait training. High-intensity, repetitive task training is crucial for neural plasticity and motor learning. Robot-assisted gait training may be a promising method leading to functional recovery in patients with stroke. In this review, the efficacy of robot-assisted gait training in stroke rehabilitation is discussed in light of current literature.

Keywords: End-effectors, exoskeletons, gait, robot assisted gait training, stroke.

Stroke is the second most common cause of mortality and disability all over the world.[1] The prevalence of stroke is estimated at 3.3%, and this rate increases with age.[2] Hemiparesis or hemiplegia, muscle weakness, sensory impairment, abnormal muscle tonus, and abnormal muscle synergies are major consequences of stroke and are leading causes of dysfunction of mobility and gait. Although a decrease in mortality rates after stroke onset has been reported, approximately half of the patients cannot regain their walking ability, and 10% need assistance while walking.[3] Asymmetric walking patterns with decreased speed, increased stride width, and double support phase are the main characteristics of hemiparetic gait in stroke patients. These gait, balance, and mobility disorders negatively affect the activities of daily living and impair the quality of life of stroke survivors. Additionally, there is a high risk of falling after a stroke due to impaired balance control and gait. Within the first year after stroke onset, 73% of stroke patients experience a fall due to loss of balance while walking.[4] Furthermore, fear of falling is a common problem in stroke patients, leading to decreased physical activity, socialization within the community, and consequently loss of independence. Thus, ensuring mobility and improving gait with respect to safety should be the main objectives of stroke rehabilitation.

An early, multidisciplinary rehabilitation program is crucial for motor recovery after stroke. It is known that neuroplasticity is the basis of motor recovery, and it is accepted that high-intensity, repetitive training has significant contributions to brain plasticity and motor learning. Exercise promotes neuroplasticity by improving interhemispheric connections, strengthening the formation of new neural pathways, improving myelination, increasing the reorganization and regeneration of neurons, and regulating neurotrophins and synaptic activity.[5] Therefore, repetitive practice of high-intensity training, particularly task-specific training, may favor additional motor learning and functional recovery. Robot-assisted gait training (RAGT) can be a promising rehabilitation option for these patients. Providing highly intensive and repetitive task-specific training, ability to adapt to the patient's functional status and needs, maintaining controlled training, recording the data to monitor the effectiveness of

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the treatment, and providing feedback with games or virtual reality to support patients' compliance with rehabilitation are main advantages of RAGT. Improvements in cardiopulmonary functions, balance recovery, decrease in spasticity, and increase in muscle strength are additional benefits of RAGT.

Conventional methods in gait rehabilitation may be limited due to excessive need for human resources, equipment, and time. Robot-assisted gait training provides long-duration, intensive exercise and relieves the burden on physiotherapists during the rehabilitation process. Furthermore, during the early stage of stroke onset, which is defined as the critical window, where neuroplasticity and functional recovery are greatest, early and intensive rehabilitation is accepted to be associated with better functional outcomes.[6] At this point, RAGT could be a good option for gait training for acute stroke patients who require maximum assistance by reducing required labor and time.

In recent years, advances in computers and engineering have enabled robotics to be used in many areas of rehabilitation medicine. Although various robotic devices that assist walking have been developed and research into their use in stroke rehabilitation is growing rapidly, there are conflicting results and limited information about which type, at which stage, and with what intensity they should be used. Moreover, it is also unclear whether RAGT can replace traditional gait rehabilitation. Herein, this review aimed to provide an overview of the effectiveness of RAGT on improving gait and mobility in stroke rehabilitation in light of the literature in recent years.

CLASSIFICATION OF ROBOTS IN GAIT REHABILITATION

The robotic systems used in gait rehabilitation can be classified into two groups according to their mechanical structure: exoskeletons (stationary or overground) and end-effector devices. These tools may have a body weight support device, treadmill, or an overground walking system. Robotic devices also provide support when the patient needs it (assist as needed), allowing the patient to actively participate in the training.

Exoskeleton devices provide direct joint control via axes aligned to the patient's anatomical axes, enabling independent and simultaneous movement. Both stationary and overground exoskeletons are wearable devices. These devices are affixed to the patient's limbs and produce different mechanic forces or torques, resulting in a reduction in abnormal movement and posture, or providing assistance in walking, leading to normative gait patterns. The intensity and timing of the assistance are adjunct and controlled by a computer and given during the gait cycle.[7] Stationary exoskeletons allow patients to walk in a limited and fixed area (e.g., treadmill), while overground exoskeletons allow patients to walk free on the ground similar to daily activities.

Hybrid assistive limb (HAL) is a new wearable overground exoskeleton-type robotic technology. The assistance principle of HAL is different from other exoskeletons. Providing motion with the voluntary drive of the individual distinguishes HAL from other exoskeleton-type robotics. The movement is initiated and supported by muscle activation recorded through surface electrodes over the hip and knee muscles. This system allows for both voluntary and predefined autonomous control during walking. It can also be used in combination with body weight support and treadmill.[8,9]

End-effector robotic devices apply mechanic forces to the distal segments of the lower extremity for simulating normal gait phases. The patient's feet are placed on the footplane or a platform deriving stance and swing phases of gait. Some end-effector devices allow simulation of stair climbing up and down. Although easily set up and adapted to the patients and the opportunity to walk on different grounds are advantages of end-effector devices, these types of devices may cause abnormal posture and movement patterns since they do not provide any restriction of the proximal extremity and allow free movement of proximal joints. Thus, stroke patients with mild to moderate neurologic deficits may benefit more from these end-effector devices than those with more severe neurologic deficits.[7,10]

Many robotic devices can be used along with a harness and lift system allowing partial or full-body weight bearing, which supports trunk stabilization, avoids falls, and provides safety during gait training in nonambulatory stroke patients. Gait training by using body weight support compared to full weight is found to be more effective in improving balance and gait in patients with stroke.[11,12] In the initial stages of gait training, approximately 70% of the patient's weight is unloaded, and in the following periods, body weight support is gradually decreased according to the improvement of the patient's muscle strength.[7]

TABLE 1
Classification of robotic systems for gait training[10,12]

Type	BWS	Treadmill
Exoskeletons		
- Stationary exoskeletons	+	+
- Overground exoskeletons	–	–
- HAL	+	–
End-effectors		
- Foot-plane based	+	N/A
- Platform-based	+	N/A
Powered ankle-foot orthosis	–	–
Powered walking frames	–	–
Soft wearable robots	–	–

BWS: Body weight support; HAL: Hybrid assistive limb; N/A: Not available.

Classification of robotic systems for gait training is given in Table 1.[10,12]

Robot devices combined with virtual reality-based biofeedback

Virtual reality is a computer-aided, three-dimensional simulation system that allows the patient to interact with the virtual environment through visual, auditory, or haptic feedback, encouraging patients to correctly execute movements during rehabilitation. These systems consist of applications or games that provide functional and multidimensional virtual environments. Patients can experience live interactions through a gaming environment that can increase the patient's compliance, motivation, engagement, and performance. A recent meta-analysis reported significant improvements in balance and gait with RAGT combined with virtual reality in patients with stroke.[13] The authors also concluded that the improvements were associated not only with increased patient participation and compliance but also with increased hip and knee strength and improved support phase of the hemiparetic side. It has also been reported that adding virtual reality systems to RAGT provides an additional contribution to the improvements in motor functions and cognitive functions in patients with stroke. The combination of robotic walking and virtual reality systems appears to be an ideal option to provide the intensive, repetitive tasks and multisensory inputs needed for neuroplasticity and motor relearning.[14] Although some studies reported adverse events such as nausea, dizziness, and headaches due to intense visual stimulation, it was concluded that these side effects were very mild. However, they should be kept in mind.[15]

CLINICAL AND RESEARCH RESULTS

As engineering and technology advances, interest in robotic systems in neurorehabilitation is growing, and their use in the rehabilitation field is increasing. Currently, evidence-based recommendations are conflicting in terms of RAGT in patients with stroke. According to the Royal Dutch Society for Physical Therapy guidelines, RAGT is recommended for stroke patients who cannot walk independently because it increases walking speed, distance, and balance compared to traditional therapy (Level 1 evidence), while according to the American Heart Association/American Stroke Association guidelines, it can only be considered in combination with conventional rehabilitation (Class IIa, Level A evidence).[16,17] A Cochrane review published in 2020 also found that adding RAGT to physiotherapy improved walking independence in patients with stroke.[18] According to the results of a systemic review of 10 guidelines for robotic lower limb rehabilitation after stroke published between 2010 and 2020, adding RAGT to conventional physical therapy improved gait in stroke patients.[10] According to all these guidelines reviewed, exercise should be started as early as possible for better gait recovery. Additionally, more impaired stroke patients appear to benefit more from RAGT. It was also stated in the systematic review that the guidelines were inadequate regarding the type of robotic device recommended; however, the results of end-effector-type devices were better.[10] There was no evidence for wearable devices. In a more recent review, 27 studies were included regardless of the stage of stroke onset, robotic device type, application method, and period.[19] Combining RAGT with conventional rehabilitation was found to be effective in enhancing gait and balance.

Robot-assisted gait training in patients with acute stroke

There's a lack of evidence on the effectiveness of RAGT in the early stage of stroke. However, its implementation in the early stages of stroke has been shown to increase the potential for long-term functional recovery by providing the opportunity for high-intensity repeated task training. A meta-analysis of 15 randomized controlled trials (RCTs) concluded that end-effector devices were more effective and that more affected patients benefited more.[20] However, the included studies had a small sample size. Mayr et al.[21] reported no superiority of RAGT over conventional gait training in terms of ambulation in acute stroke patients. On the other hand, in a study investigating the effectiveness of exoskeleton-type robotic devices in the early period of stroke rehabilitation, a greater increase in motor Functional Independence Measure scores was reported in the group where exoskeleton-type RAGT was combined with conventional therapy compared to conventional therapy alone. Nilsson et al.[22] investigated the safety and effectiveness of gait training with HAL integrated inpatient rehabilitation in patients with acute stroke, and they reported that it was safe to use in patients with severely impaired gait function in early stages of stroke. They also reported improvements in walking ability assessed by a 10-m walk test and Functional Ambulation Category. However, there was no control group in this study, and the sample size was relatively small. Adding RAGT to conventional therapy allows patients to perform higher doses of task-specific exercise during the same treatment period, thus contributing to early recovery onset by stimulating the neural plasticity crucial in the early phase of the rehabilitation period.[23] Talaty and Esquenazi[24] compared exoskeleton-type RAGT and conventional therapy with therapist-assisted gait training in patients with acute stroke, and the authors concluded that exoskeleton-type RAGT was a more effective tool for gait training and lead to an optimal therapy dose. Meng et al.[25] investigated the effectiveness of exoskeleton type RAGT, intensity-matched enhanced lower limb therapy, and conventional rehabilitation therapy started within 48 h of stroke onset. After four weeks of treatment, RAGT was found to be better in motor function, balance, and quality of life than the other two groups. A recent Cochrane review revealed that RAGT is more beneficial, particularly for patients in the first three months of stroke and those who are unable to walk, but the role of the robotic device type is unknown.[18]

Robot-assisted gait training in patients with subacute stroke

A systematic review of 14 RCTs in the last 14 years conducted in 2021 assessed the efficacy of exoskeleton-type RAGT for gait recovery in patients with subacute stroke (duration of stroke shorter than six months), and it was concluded that RAGT with conventional therapy was effective in gait recovery but not superior to conventional therapy alone.[26] The findings of a recent pilot RCT with a small sample size also support the results of this meta-analysis.[27] On the other hand, two RCTs failed to identify significant differences between exoskeleton RAGT and conventional treatment in terms of improvement in walking independence, gait speed, endurance, balance, cognitive function, and quality of life posttreatment and after six months.[28,29] The results of the studies investigating the effectiveness of gait training with HAL in patients with subacute stroke are contraversial. In a study conducted with a small number of patients and without a control group, HAL was reported to be effective and safe in walking, balance, and motor recovery in subacute stroke patients.[30] In another study, conventional training using HAL was compared with conventional training alone in terms of gait function, and it was concluded that combining HAL with conventional training did not provide any additional benefit.[31] Watanabe at al.[32] compared the effectiveness of HAL and conventional therapy in subacute stroke patients who received 20 sessions of gait training. The HAL group showed significant improvement in Functional Ambulation Category scores after treatment compared to conventional therapy. Bruni et al.[33] stated that gait training with both exoskeleton and end-effector robotic devices provided better results than conventional therapy in subacute stroke patients. A recent multicenter controlled clinical trial investigated the effectiveness of RAGT (exoskeleton or end-effector type) in comparison to conventional overground gait training in 89 subacute stroke patients.[34] After 20 training sessions, significant improvements in gait speed (10-m walk test), endurance (6-meter walk test), balance, and disability were observed in RAGT groups compared to conventional overground gait training. The increase in gait speed with end-effector-type RAGT was more significant than with exoskeleton-type RAGT. In this study, patients training with end-effector-type robotics had a shorter disease duration than patients training with exoskeleton-type robotics. Moreover, patients in the exoskeleton RAGT group had a lower functional ability. This nonhomogeneous distribution of the treatment groups may have affected the results of the study.

Combined with conventional therapy, RAGT appears to be beneficial, particularly in patients with subacute stroke.[35] It is widely accepted that spontaneous recovery occurs within the first three months after the onset of stroke. Considering all this, in clinical trials that include both acute and subacute stroke patients, it is difficult to estimate the effectiveness of RAGT application due to the spontaneous recovery process of stroke in early periods.

Robot-assisted gait training in patients with chronic stroke

The majority of research has focused on the effectiveness of RAGT in patients with acute-subacute stroke. There have been few trials on RAGT in chronic stages of stroke, with conflicting results. Most of them were conducted as pilot studies with small sample sizes.[36,37] Bruni et al.[33] published a meta-analysis that found no evidence that RAGT was more effective than conventional therapy in patients with chronic stroke. According to a systematic review of 10 high-quality and well-designed RCTs carried out until 2023, six RCTs found greater efficacy with exoskeleton-type RAGT compared to conventional therapy, but the others reported equal or insufficient effects of exoskeleton-type RAGT.[38] It was concluded that exoskeleton-type RAGT could be a useful intervention in gait and balance function during chronic stroke without any adverse events. The authors of this review suggested at least a 5-h total training time for better effect.[38] A very recent study reported that exoskeleton-type RAGT administered for eight weeks in addition to conventional rehabilitation was effective on functional independence, functional capacity, and quality of life in patients with chronic stroke.[39] There are few low-quality studies evaluating the effectiveness of HAL in chronic stroke patients.[40,41] Greater improvements in gait ability were reported using the HAL system for gait training in a longitudinal observational study.[40] Although this study did not have a control group, the fact that the gains were maintained for three months after treatment could be indicative of long-term results.

There is insufficient information regarding the effectiveness of end-effector-type robotics in chronic stroke patients. Similar improvements have been detected in gait function between end-effector type RAGT and conventional gait training in chronic stroke patients in a review investigating the efficacy of different types of robotic devices.[35] In a retrospective multicentric study by Mazzoleni et al.,[42] one hundred patients with chronic stroke were included, and robot-assisted end-effector-based gait training was applied as the only rehabilitation treatment. Significant improvements were observed in gait endurance, balance, coordination, strength of lower limbs, and spasticity. However, no control group was included in the study.

In conclusion, RAGT appears to complement conventional rehabilitation methods rather than act as a replacement for them. It should be initiated as soon as possible to provide multisensory stimulation leading to neural plasticity. Additionally, RAGT appears to be a more beneficial option in stroke patients with severe impairment. However, there is an increasing need for high-quality studies in different stages and with different functional levels of stroke patients comparing different types of robotic devices with each other or conventional methods to determine their long-term effects, timing, optimal exercise duration, frequency, and cost analysis.

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