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Implementation of Lower Limb Robotic Exoskeleton in Gait Rehabilitation by Subacute Stroke Patients: A Literature Review

Diploma Thesis

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Prague, April 2025

Declarations

I, Karolína Valterová hereby declare that I have completed this diploma thesis independently and that I have cited all sources of information and literature used. This thesis, or any substantial part of it, has not been submitted for the award of any other or the same academic degree.

Prague, April 2025 Karolína Valterová

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Abstrakt

Název

Implementace robotického exoskeletu dolních končetin při rehabilitaci chůze u pacientů v subakutní fázi cévní mozkové příhody: Literární rešerše

Cíle

Hlavním cílem této literární rešerše je zhodnotit účinnost použití robotických exoskeletů dolních končetin při zlepšování chůze u lidí po subakutní cévní mozkové příhodě. Hodnocení bude založeno na základě výstupních ukazatelů, jako je test šestiminutové chůze (6MWT), funkční kategorie chůze (FAC) a údaje o spokojenosti uživatelů získané z nedávných vědeckých publikací.

Metody

Tato práce je literární rešerše. Návrh studií zahrnutých do literární rešerše byly randomizované kontrolované studie, kontrolované klinické studie a experimentální studie napsané v angličtině, němčině nebo češtině, publikované v posledních 10 letech, tedy v období 2014–2024. Studie byly vyhledány v databázích PubMed, Cochrane, Science Direct, PEDro pomocí Booleovského vyhledávání zahrnujícího logické operátory a klíčová slova. Vyhledávání probíhalo mezi 2. 10. 2024 a 23. 10. 2024. Proces výběru a třídění článků probíhal podle protokolu PRISMA a byl dokončen v online softwaru Rayyan. Účastníci studií museli být ve subakutní fázi cévní mozkové příhody, muži i ženy ve věku 18–90 let a studie musely obsahovat FAC nebo 6MWT jako primární či sekundární výstupní ukazatel.

Výsledky

Po dokončení výběrového procesu bylo pro literární rešerši způsobilých celkem 6 studií. Všechny zahrnuté studie byly publikovány v letech 2019 až 2023 a intervence trvaly 2 až 4 týdny. Analýza těchto studií naznačila, že existují významný rozdíly mezi vstupním a výstupním měřením jak ve skupině s konvenčním tréninkem chůze, tak ve skupině s roboticky asistovaným tréninkem chůze. Roboticky asistovaný trénink chůze však obecně vykazoval větší zlepšení v ušlé vzdálenosti (měřené v metrech) v rámci testu 6MWT ve srovnání s konvenčním tréninkem chůze, stejně jako dosažení vyšší úrovně samostatnosti dle FAC.

Závěry

Zjištění celkově ukazují pozitivní efektivitu robotických exoskeletů dolních končetin a podporují jejich použití jako vhodné intervence ve srovnání s konvenčním tréninkem chůze pro zlepšení chůze z hlediska vytrvalosti a funkční schopnosti chůze u jedinců v subakutní fázi cévní mozkové příhody. Ačkoliv ne všechny studie prokázaly lepší výsledky u roboticky asistovaného tréninku chůze, většina ano, což posiluje jeho efektivitu. Nicméně heterogenita uvnitř i mezi studiemi omezuje váhu a zobecnitelnost závěrů.

Klíčová slova

Robotický exoskelet dolních končetin, Subakutní fáze cévní mozkové příhody, Rehabilitace chůze, Roboticky asistovaný trénink chůze, Šestiminutový test chůze, Funkční kategorie chůze, Uživatelská zkušenost.

Abstract

Title

Implementation of Lower Limb Robotic Exoskeleton in Gait Rehabilitation by Subacute Stroke Patients: A Literature Review

Objectives

The primary objective of the literature review is to evaluate the effectiveness of using lower limb robotic exoskeletons in improving gait by people after subacute stroke. This will be assessed using outcome measures such as the 6-Minute Walk Test, Functional Ambulation Category and user satisfaction data retrieved from recent scientific publications.

Methods

The thesis is a literature review. The study design of the retrieved studies were randomized controlled trials, controlled clinicals trials and experimental studies written in English, German or Czech language, published in the last 10 years from 2014-2024. The studies were retrieved from PubMed, Cochrane, Science Direct, PEDro using a Boolean search consisting of logical operators in addition to keywords. The search took place between 02.10.2024 and 23.10.2024. Selection process and screening of articles followed the PRISMA protocol and was completed in Rayyan. Participants of the study had to have subacute stroke at the time of testing, both male and female gender aged 18-90 and studies had to feature Functional Ambulation Category or the 6MWT as a primary or secondary outcome measure.

Results

After the screening process a total of 6 articles were eligible for the literature review. All included articles were published between 2019 and 2023 with interventions ranging from 2 to 4 weeks. The analysis of the reviewed articles suggested that there was a significant difference between baseline and final assessments in both the conventional gait training and the robot assisted gait training group. Nevertheless, robot assisted gait training generally showed greater improvements in walking distance in participants measured in meters within the 6MWT compared to conventional gait training as well as reaching higher ambulation in the FAC.

Conclusions

The findings demonstrate an overall positive indication of effectiveness of lower limb robotic exoskeletons and support the use of lower limb robotic exoskeletons as a favorable intervention compared to conventional gait training for improving gait in terms of walking endurance and functional ambulation in individuals after subacute stroke. While not all studies demonstrated superior outcomes of robot assisted gait training, the majority did, reinforcing its effectiveness. Yet the heterogeneity found within and between studies limit the strength and generalizability of the conclusions.

Keywords

Lower limb robotic exoskeleton, Subacute stroke, Gait rehabilitation, Robot assisted gait training, 6-Minute Walk Test, Functional Ambulation Category, User experience.

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List of Abbreviations

Abbreviation	Full term
6MWT	Six-Minute Walk Test
10MWT	Ten Minute Walk Test
FIM	Functional Independence Measure
MAS	Motor Assessment Scale
FAC	Functional Ambulation Category
RE	Robotic Exoskeleton

1. INTRODUCTION

Stroke is one of the main causes of disability and death worldwide and due to an ageing population, the prevalence is on a rise (Saleh et at., 2023). Globally, 101 million people that are currently alive have experienced a stroke (World Stroke Organization, 2022). Affecting millions of people yearly, stroke poses a great burden on the quality of life of the patient and their family (Katan & Luft, 2018).

One of the most serious consequences of stroke is the loss of motor function, which affects 80% of patients. Most commonly patients present with unilateral paresis also known as hemiparesis presenting itself as weakness of one entire side of the body or hemiplegia presenting itself as unilateral paralysis (Li et al., 2018). Both hemiparesis and hemiplegia significantly limit movement and ability of independent gait. Hemiplegic gait often manifests itself in stroke patients as a consequence of muscle weakness, abnormal synergistic activation, their interactions and spasticity (Rodríguez-Fernández et al., 2021).

Effective rehabilitation focusing on restoring motor function and improving mobility is crucial for gaining independence and increasing the quality of life of the patient. Gait training plays a fundamental role in stroke rehabilitation from restoring symmetrical gait patterns, enhancing walking speed, stride length, cadence and balance to promoting neuroplasticity and motor recovery in patients (Saleh et at., 2023). Traditional gait rehabilitation approaches can be divided into neurophysiological approaches where patients play a passive role and motor learning techniques which stress active patient involvement. Neurophysiological approaches consist of the Bobath approach, Brunnström method, Proprioceptive neuromuscular facilitation, Vojta method, Rood technique and The Johnstone method. Motor learning techniques on the other hand consist of The Perfetti method, Carr and Shepherd motor relearning method, Peto method, The Affolter method and lastly the Sensory integration or Ayres method (Belda-Lois et al., 2011). The effectiveness of the various gait training methods depends on the stage of stroke recovery, the patient's functional abilities, and the techniques utilized (Peurala et al., 2014).

Traditional therapies often face limitations due to time constraints and the physical capacities of both the therapist and the patient (Yang et al., 2024). Limited training time is associated with poorer recovery outcomes, as repetitive, high-intensity practice, crucial for motor learning and neuroplasticity (Montero-Almagro et al., 2024), particularly important during the subacute phase of stroke, when patients are most responsive to interventions (Li et al., 2024).

Conventional gait rehabilitation is often labor intensive (Zhu et al., 2021) requiring significant manual assistance of multiple therapists for manual guidance and in order to ensure a safe environment for the patient at all times. This imposes a rising healthcare burden (Teodoro et al., 2024), creating bottlenecks in care delivery and leading to delays or reduced access for other patients (Nair & Taly, 2002). Moreover, traditional therapies often follow standardized protocols often resulting in limited patient adherence due to lack of personalization, lack of feedback, limiting room for autonomy and patient engagement (Gilbertsen, 2024).

Vast developments in technology, specifically progress in sensor technology, machine learning techniques and in robotics have had a huge impact in reshaping the current healthcare system and landscape of rehabilitation medicine (Licardo et al., 2024). Originally developed for industrial and military purposes to amplify wearers strength for example, robotic exoskeletons have gained popularity in healthcare as well due to their wide range of applications in assisting and augmenting human mobility (Vukobratovic, 2007). Presently we are witnessing rapid development in exoskeleton mechanical complexity and their capabilities are coming close to those of humans (Tiboni et al., 2022).

A lower limb robotic exoskeleton is an external, wearable, mechanized device which has powered joints operating through sensor systems and control algorithms. They were first developed in 1969, serving paraplegics and similarly disabled people (Luo et al., 2023) but only in recently have been introduced for gait assistance rehabilitation in patients with motor disorders (Rodríguez-Fernández et al., 2021). Lower limb robotic exoskeletons are capable of providing trajectory guidance and joint- specific support to assist, resist, or enhance muscle torque (Karunakaran et al., 2023) as well as deliver high-dose, regular, and symmetrical bilateral loading profile during walking, crucial for effective neuroplasticity (Karunakaran et al., 2020). Furthermore, they have the capacity to adapt to patient's unique gait patterns, facilitate task specific movements and provide real time feedback to the patient essential for recovery. Lastly compared to conventional therapies they enable longer training times and more precisely controlled forces delivery (Zhu et al., 2021).

Lower limb robotic exoskeletons play a crucial role in supporting the neuroplasticity-driven objectives of subacute stroke rehabilitation (Calabrò et al., 2018). The subacute phase, which is divided into the early (1–3 weeks) and late subacute stages (3 weeks to 6 months post-stroke), represents a critical window for recovery (Gaillard, 2019). At this stage the brain is most primed for recovery, making it an ideal time frame for targeted interventions (Moore et al., 2022). Given their ability to deliver consistent, intensive, and task-specific training, lower limb robotic exoskeletons are particularly well-suited for use in this population, maximizing recovery potential and functional outcomes (Zhu et al., 2021).

Despite existing evidence, robotic assisted gait training is still a relatively new approach and has had a slower adaptation in stroke care than conventional therapies (Belda-Lois et al., 2011). Definitive functional effectiveness needs to be addressed as well as a strong need of making a comprehensive framework which summarizes lower limb exoskeletons, their effectiveness and patient experience on how it has been adapted by them. The work will provide health care professionals with a structured analysis of the usage of the above-mentioned technological innovation in regards to implementation and effectiveness and aid in decision making process when deciding on whether to incorporate it, thereby increasing its utilization making treatment sessions more variant, motivating patient and increasing adherence to therapy. Increased implementation and adoption of lower limb robotic exoskeletons in gait rehabilitation could yield better functional outcomes, have potential to address current challenges in healthcare systems such as reducing the burden (Postol et al., 2023) on overextended healthcare systems, which are struggling to meet the demands of increased stroke cases.

Therefor the research question arises: What is the effectiveness of using lower limb robotic exoskeleton in improving gait by people after subacute stroke?

Sub questions:

1. How is the lower limb robotic exoskeleton adopted by people after subacute stroke in terms of acceptability?

2. THEORETICAL BACKGROUND

Cerebrovascular accident, commonly referred to as stroke, is an acute medical condition that occurs when blood flow to the brain is restricted or sudden bleeding into the brain takes place (Coupland et al.,2017). Stroke is the second leading cause of death in the world (Katan & Duft, 2018). Due to the debilitating nature of the disease, it poses a global burden on the medical, social and economic infrastructure.

2.1 Stroke

Stroke has been under the attention of medical professionals from the 5th century B.C, references to the condition appearing in Hippocratic writings (Storey & Pols, 2010). Within the Hippocratic corpus the condition was described as apoplexy characterized as a sudden loss of consciousness as well as lack of movement and included several pathologies within (Coupland et al.,2017). Although a no longer used medical term, stroke remained to be referred to as apoplexy until 1820. It wasn't until the early 20th century when growing understanding, awareness and acceptance of vascular theories took place and recognition of the consequences of sudden disruption of vascular supply to the brain are that an alternative term cerebrovascular accident started being used. Despite that in today's understanding of stroke the term accident is discouraged (Storey & Pols, 2010).

According to the statement of the World health organization published in 1971, stroke is “rapidly developed clinical signs of focal (or global) disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin” (World Health Organization, 2006). Stroke occurs as a result of ischemia to a part of the entire brain or hemorrhaging into the subarachnoid space of brain tissue (Kolář, 2020), and therefore we classify stroke into ischemic stroke and hemorrhagic stroke.

2.2 Epidemiology

According to the global stroke fact sheet published by the World Stroke Organization (WSO) from the year 2022 featuring values that have been extracted from the Global Burden of Disease Stroke Statistics Worldwide for year 2019 the incidence of stroke accounts for 12.2 million new cases each year. It has been concluded that globally one in four people over the age of 25 will have a stroke in their lifetime. There is a minor difference between incidence in men and women, each year 47% of strokes occur in men and 53% occur in women. In terms of prevalence, globally, 101 million people currently alive have experienced a stroke. Differentiating ischemic and hemorrhagic stroke, yearly there are 7.6 million ischemic strokes, 3.4 million intracerebral hemorrhages and 1.2 million new subarachnoid hemorrhages. Globally, 77 million currently living people have experienced ischemic stroke, 21 million people intracerebral hemorrhage and 8.4 million people subarachnoid hemorrhage (World Stroke Organization, 2022). Incidence rate of stroke is highest in Asia. There is a significant variation in stroke case fatality between low income countries and high income countries (Pandian et al., 2023; Thayabaranathan et al., 2022) .

2.3 Physiology of vascular supply to the brain

2.3.1 Major arteries supplying the brain

Vertebral arteries originate from the subclavian arteries and run through the transverse foramina of the cervical vertebrae. As they ascend, they branch into posterior inferior cerebellar arteries which further branch into posterior spinal arteries (Purves,1970). Occlusion of the posterior inferior cerebellar artery leads to loss/reduction of cerebellar function, the patient will be experiencing poor coordination, altered balance and poor muscle tone (Murphy, 2018). Cranially from the posterior inferior cerebellar arteries at the level of medulla oblongata the vertebral arteries branch off and fuse into anterior spinal artery which descends all the way down the spinal cord supplying the pyramidal tracts (Purves,1970). Occlusion of the anterior spinal artery can result in ipsilateral cranial nerve 12 palsy affecting tongue movements, swallowing and dysarthria, contralateral hemiplegia and contralateral loss of pressure, touch and vibration (Murphy, 2018). Above the anterior spinal artery at the level of the pons, the vertebral arteries fuse and form a vessel called the basilar artery. Occlusion of the basilar artery damages the corticospinal tracts bilaterally resulting in quadriplegia.

Branching at the base of the basilar artery is referred to as anterior inferior cerebellar artery. The anterior inferior cerebellar artery supplies the medial portions of frontal lobes and superior medial parietal lobes (Purves,1970). Occlusion of the anterior inferior cerebellar artery results in paralysis of facial muscles, vertigo, nystagmus and possibly deafness, loss of tone of muscles, ataxia and balance on the ipsilateral side to the localization of the occlusion and contralateral loss of pain and temperature sensation (Murphy, 2018). Cranially there is further branching of the basilar artery into labyrinthine arteries and Pontine branches. Lastly above the Pontine branches, the basilar artery branches into the superior cerebellar artery.

The internal carotid artery is found most superiorly. The internal carotid artery branches into the ophthalmic artery. Further down the carotid artery branches into the middle cerebral artery (Purves,1970).

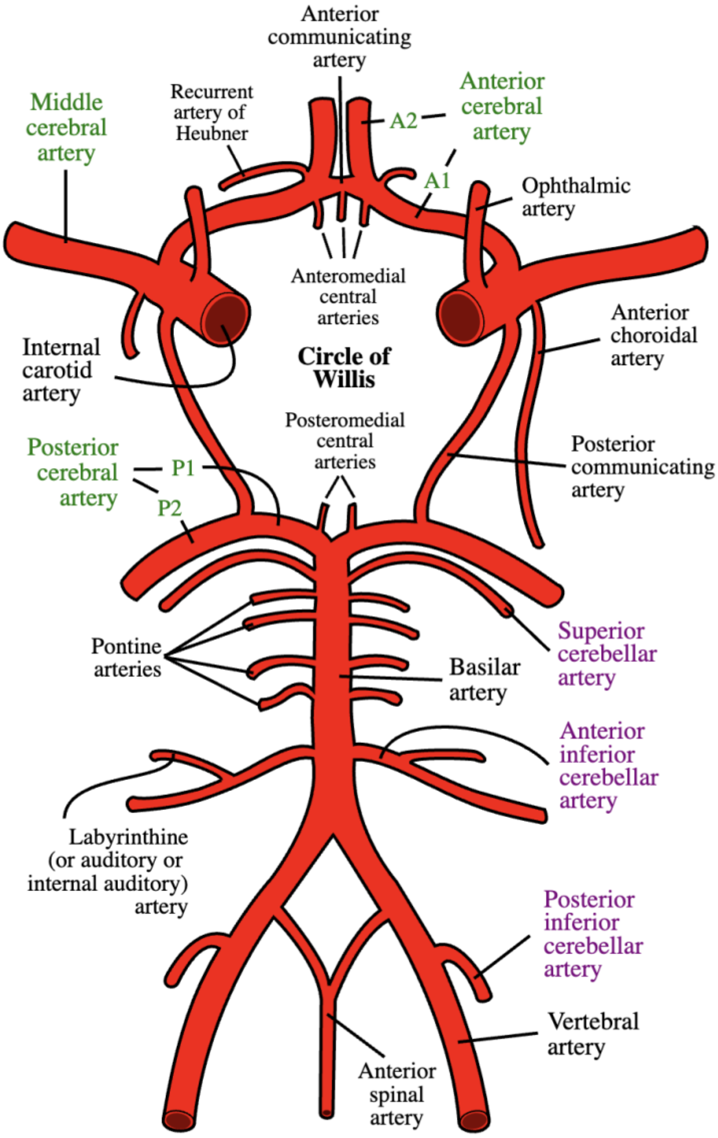


Figure 1: Arterial supply to the brain (Dumitrescu et al.,2021)

2.3.2 Major branches and their supply areas

At the level of the midbrain the basilar artery joins and feeds in into the posterior part of the Circle of Willis (Konan, 2023). In the posterior part of the Circle of Willis branching of the basilar artery takes place into the posterior cerebral artery. The first segment of the posterior cerebral artery further ascends into the posterior communicating arteries. The posterior cerebral artery supplies blood to the occipital lobe, inferior section of the temporal lobe and deep structures such as the thalamus. If a person suffers from occlusion of the posterior cerebral artery they will lose temporal as well as nasal visual field (Murphy, 2018).

The middle cerebral artery is located midway through the Circle of Willis. Significant branches arise from the middle cerebral artery. The first branch is the anterior coroital artery followed by lenticulostriate arteries. The middle cerebral artery supplies the lateral surface of the brain including frontal, parietal and temporal lobes. Occlusion of the middle cerebral artery leads to contralateral loss of sensation and motor control to the upper extremity and the face. Furthermore, occlusion of the middle cerebral artery can damage Broca's area and lead to Broca’s aphasia defined as the inability to produce speech (Murphy, 2018).

Cranially from the middle cerebral artery the anterior cerebral artery arises. The anterior cerebral artery supplies medial portions of the frontal lobes and superior medial parietal lobes. Anterior cerebral artery supplies the medial portion of the primary motor cortex and the primary somatosensory cortex, occlusion of this artery results in loss of sensation and motor control on the contralateral side of the body specifically in the lower extremity (Murphy, 2018).

2.3.3 Circle of Willis

Blood supply to the brain can be divided into anterior and posterior circulation. Anterior circulation derives blood from the internal carotid artery and the vertebral artery, supplying blood to the majority of cerebral hemispheres, frontal, parietal, lateral temporal lobes as well as the anterior part of deep cerebral hemispheres. Posterior circulation is mediated by the vertebro-basilar system, more specifically the bilateral vertebral arteries supplying blood to the cerebellum, brain stem, occipital as well as medial temporal lobes, posterior part of deep hemispheres more concretely the thalamus (Symonds, 1955). Circle of Willis is an anatomical structure composed of a ring of vessels linking anterior and posterior circulations, providing collateral blood flow, protecting against ischemia due to vessel damage in one or more areas of the brain. Twenty percent of the total blood supply to the circle of Willis is from the verterbro-basilar system, and the remaining eighty percent is from the internal carotid artery (DeVault et al., 2008).

2.3.4 Venous drainage

Venous drainage is responsible for removing deoxygenated blood as well as metabolic waste products from the brain, making it an essential component of the cerebral circulatory system. This process is managed by a network of veins and dural sinuses that eventually drain into internal jugular veins. The veins can be divided into superficial veins which are located on the surface of the brain and drain outer portions of cerebral hemispheres, deep veins which are responsible for draining internal structures of the brain such as white matter, basal ganglia and the diencephalon. The last structure responsible for venous drainage are channels located between the layers of the dura mater called dural venous sinuses, draining blood from the brain into internal jugular veins (Castle & Gaillard, 2008). Venous blood from the brain flows into the internal jugular veins which will afterwards transport it back to the heart. Venous drainage is crucial for maintaining ones homeostasis and ensuring removal of metabolic waste takes place (Pittman, 1970).

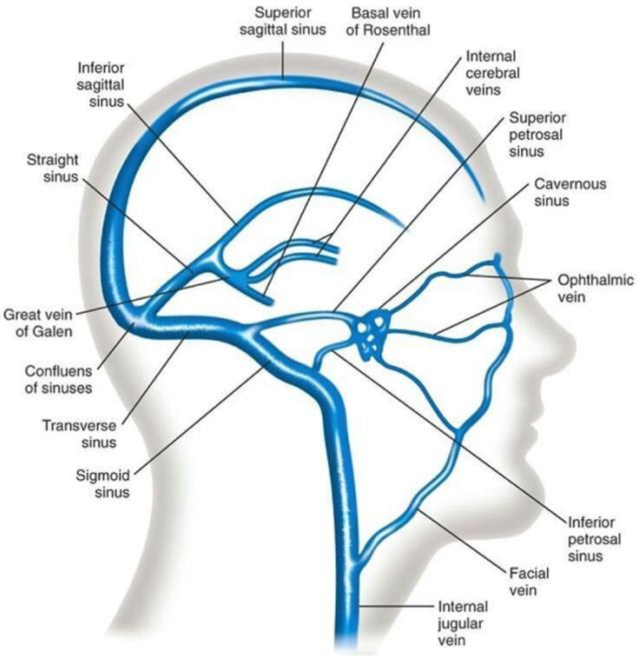


Figure 2: Venous drainage of the brain (Gupta, 2017)

2.3.5 Autoregulation

Cerebral blood flow regulation refers to the brain's capacity to maintain stable and constant blood flow despite changes in perfusion pressure (Markus, 2004). In a healthy adult, cerebral blood flow is sustained at approximately 50 mL per 100 g of brain tissue per minute and cerebral perfusion pressure at ~60 to 160 mmHg (Cipolla, 2009). When perfusion pressure falls outside the autoregulatory range, the brain loses its ability to self regulate, and the cerebral blood flow is dependent on mean arterial pressure. If cerebral perfusion pressure drops below the lower threshold, cerebral ischemia arises. The significant role of autoregulation in normal brain function is highlighted by the occurrence of severe brain injury when these autoregulatory mechanisms are compromised or lost (Hlatký et al., 2002).

2.4 Hierarchical control of movement

2.4.1 Forebrain and initiation of movement

The prefrontal cortex, premotor cortex as well as the primary motor cortex located in the frontal lobes of the brain contribute to movement vastly and have a specific sequence of activation to initiate movement. Firstly, the global sensory integration center also referred to as the posterior parietal cortex ensures that motor planning is adapted to current environmental conditions. Then the prefrontal cortex plans and makes decisions of executing a certain action. Afterwards the premotor cortex receives information from the prefrontal cortex, constructing necessary motor sequences, selecting most appropriate patterns for the specific task. The information about the specific motor sequence to be performed is received by the primary motor cortex which produces the required movement through muscle contraction and relaxation (Berni, 2023).

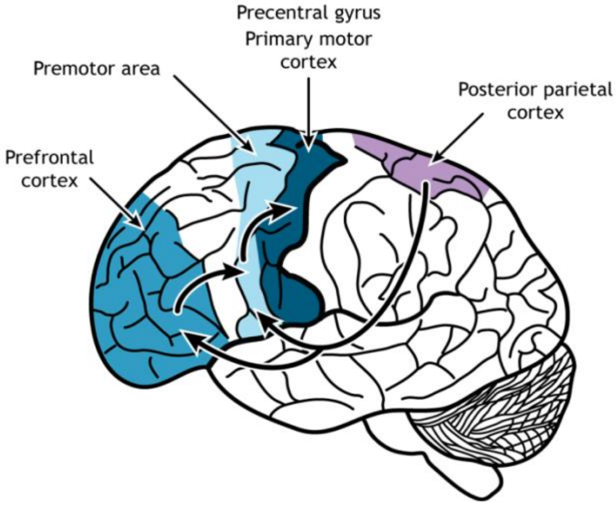


Figure 3: Sequential activation of cortical regions that initiate movement (Berni, 2023)

2.4.2 Corticospinal tract and motor neurons

The corticospinal tract is the main afferent route from primary motor cortex to the brainstem and the spinal cord that provides voluntary motor function enabling movement of distal extremities. The corticospinal tract descends through the brainstem, fibers crossing over to the opposite side within the medulla after which it continues down the spinal cord innervating distal extremities and muscle groups. This structure continues to develop postnatally, maturation occurring during puberty due to increasing androgen levels. Preservation as well as recovery of the corticospinal tract is necessary for recovery when there is an impaired motor function following brain injury (Natali et al., 2020). Research has proven that the severity of motor impairment during acute ischemic stroke is determined by the extent to which the corticospinal tract is affected by the lesion. Motor paralysis is one of the debilitating consequences of stroke, and rehabilitation has been found to be the most effective treatment. Patients that demonstrate the greatest improvement after stroke tend to have a better corticospinal integrity compared to those who show less improvement during rehabilitation (Huang et al.,2023).

2.5 Biomechanics of Gait

Gait is characterized as the pattern of movement between the upper and the lower extremities in order to create forward progression. It requires coordination of both musculoskeletal and the nervous system to ensure balance, stability, posture and forward motion. The human gait is typically divided into two phases: stance phase and the swing phase. Stance phase alludes to when the reference foot is in contact with the floor and makes up 62% of the normal gait cycle. The swing phase, when the reference foot is not in contact with the floor, makes up only 38 % of the normal gait cycle. The full gait cycle starts with the contact of one foot on the ground and concludes when the same foot makes contact with the ground again (Chan & Rudins, 1994).

The stance phase is made up of initial contact, loading response, midstance, terminal stance, pre-swing and toe off. Initial contact refers to the moment where the foot touches the ground, also known as heel strike. The hip is at 20 degrees, knee and ankle at 0 degrees. From initial contact to loading response there is minimal activity in the hip flexors, whereas there is an eccentric contraction in the knee extensors and ankle dorsiflexors. Initial contact is followed by a loading response. Loading response refers to when the weight is transferred onto one limb. The hip is in 20 degrees of flexion, knee is in 20 degrees of flexion and ankle is in 10 degrees of plantarflexion. From loading response to mid stance there is concentric activity of the hip extensors, concentric activity of the knee extensors and concentric activity of ankle dorsiflexors. In mid stance the body progresses directly over a single limb. During midstance the hip is at 0 degree of flexion, knee at 0 degrees of flexion and the ankle at 5 degrees of dorsiflexion. From mid stance to terminal stance there is minimal activity in the hips, minimal activity in the knee and eccentric activity of the ankle plantar flexors. In terminal stance progression advances moving the body forward of the limb and weight is transferred to the forefoot. The hip is in 20 degrees of extension, knee at 0 degrees and the ankle is at 10 degrees of dorsiflexion. From terminal stance to pre swing the hip, knee and ankle produce minimal muscle activity. During the pre-swing phase, the limb undergoes rapid unloading as the body weight is transferred to the contralateral lower extremity. The hip is in 0 degrees, knee in 40 degrees of flexion and ankle in 20 degrees of plantarflexion. From pre swing to initial swing primary muscle activity occurs in the hip flexors through concentric contraction, concentric contraction of the knee flexors occurs and concentric contraction of the ankle dorsiflexors occurs. Lastly the toe off phase takes place, single moment in time that signifies the end of the stance and the beginning of swing (Walters, 2021).

The swing phase comprises of initial swing, mid swing and terminal swing. During initial swing the foot comes off the floor and the femur begins to advance forward. During initial swing our hip is in 10 degrees of flexion, knee in 60 degrees of flexion and ankle in 5 degrees of plantar flexion. From initial swing to mid swing primary muscle activity occurs in the hip flexors through concentric contraction, knee extensors through concentric contraction and ankle dorsiflexors through concentric contraction. During mid swing the knee begins to extend, and the foot clears the ground as the femur continues to advance. The hip is in 20 degrees of flexion, knee is in 30 degrees of flexion and ankle is at 0 degrees. From mid swing to terminal swing primary muscle activity occurs through eccentric contraction of the hip extensors, concentric contraction of the knee extensors and isometric contraction of ankle dorsiflexors. In the terminal swing the knee is fully extended as the lower extremity prepares to contact the ground. During terminal swing the hip is in 20 degrees of flexion, knee and ankle is at 0 degrees (Walters, 2021).

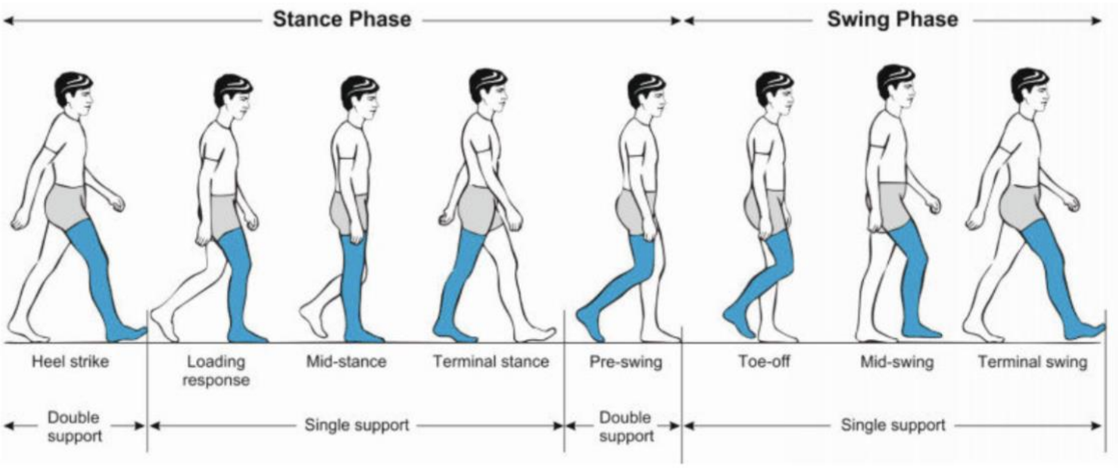


Figure 4: Phases of normal gait cycle (Pirker & Katzenschlager, 2016)

2.6 Classification of stroke types

Ischemic stroke is the most common subtype of stroke, comprising 85% of the total amount of strokes. In a healthy adult the brain oxygen requirement accounts for 20% of the total for the whole body although its relative size is only 2% ranging from 50-60ml/100g of brain tissue (Kim, 2017). Reduction of blood flow under 20ml/100g results in reduction of function of neurons and signs of ischemic lesion occur. Structural changes occur in the hypoxic brain tissue leading to brain infarction (Salaudeen et al., 2024). There are several different mechanisms of vascular occlusion. Embolism is the most common mechanism leading to ischemic stroke, in an embolic event debris from other locations within the body affects the blood flow within the vessel (Hui et al., 2022). Common cardiac disorders leading up to stroke are atrial fibrillation, valvular heart disease and cardiomyopathy. Another underlying cause is large vessel disease, more specifically large vessel atherosclerotic disease (Feske, 2021). In a thrombotic event a thrombus obstructs the blood flow to the brain within a blood vessel. Thrombus may arise secondary to atherosclerotic disease, arterial dissection, fibromuscular dysplasia or inflammatory conditions. The brain region that is affected is referred to as the ischemic core. It is in the ischemic core where cells undergo irreversible death. The ischemic core is surrounded by a region of salvageable cells called the ischemic penumbra (Sutherland, 2023) which is targeted during therapeutic interventions (Salaudeen et al., 2024).

Hemorrhagic stroke occurs when there is bleeding into the brain's parenchyma due to rupture of a blood vessel. Although forming only 15% of all stroke cases, hemorrhagic stroke has an increased mortality rate compared to ischemic stroke. Hemorrhagic stroke can be lacunar (typical) or global (atypical). Lacunar bleeding occurs due to a rupture in the blood vessel wall as a result of chronic arterial hypertension. Often bleeding into thalamus, basal ganglia and internal capsule occurs resulting in a poor prognosis. Global bleeding occurs due to a blood vessel anomaly, affecting subcortical region prognosis being more favorable (Kolář, 2012). The etiology of the stroke affects both the prognosis and the outcome by the patient (Hui et al., 2022).

2.7 Classification of stroke phases

In initial evaluation of suspected stroke, a non-contrast brain CT will be done. A non-contrast brain CT is useful in expediting diagnosis and treatment options for the patient. Through CT perfusion of the brain, aging of ischemic strokes can be evaluated and help determine when the stroke occurred. Based on the readings, stroke can be divided into three main phases denoting time from onset (since initial stroke event) and two subphases. Hyperacute stroke is defined as one where time from onset is less than 24 hours (Grefkes & Fink, 2020) representing cytotoxic edema with subtle but significant ischemic changes. There is a loss of gray and white matter differentiation, where lentiform nucleus changes can be seen as early as 1 hour after occlusion and in ¾ of patients at 3 hours and effacement of cortical sulci. It is also referred to as the time period in which the decision to employ thrombolytics is made (Gaillard, 2019). In the acute phase occurring between 24 hours to approximately 1 week after stroke (Grefkes & Fink, 2020) a thrombus in the proximal middle cerebral artery can be detected, appearing as hyper attenuation. The subacute phase of stroke refers to the period following the acute phase when the body begins to recover and stabilize from the stroke event. This phase is marked by processes like vasogenic edema, hypoattenuation, and the development of well-defined lesion margins on imaging, particularly in its earlier stages (Gaillard, 2019).

The subacute phase of stroke can be divided into early subacute phase spanning from 1 week to 3 months and late subacute phase which spans from 3 months to 6 months (Grefkes & Fink, 2020). Lastly, the chronic phase of stroke starts 6 months after the initial event and can last indefinitely. During this stage loss of brain tissue and hypoattenuating occurs (Gaillard, 2019). Stroke phase understanding is crucial in tailoring appropriate medical interventions and supporting each stage of stroke recovery. The key difference between the three stages is that in acute stroke there is an immediate onset, and it is a critical period for medical interventions. The subacute stroke phase is known as the early recovery and stabilization phases where main focus is preventing complications and initiation of rehabilitation. Brain is most primed for recovery at this stage. Chronic stroke phase is the long-term phase where ongoing recovery and adaptation to residual deficits takes place (BrainQteam, 2023).

2.8 Risk factors and prevention

2.8.1 Risk factors for ischemic stroke

Risk factors vary according to the stroke subtype the patient presents with. According to Global burden of disease estimates from 2019, attributable risk factors to 71% of stroke burden were metabolic factors; high blood pressure, high body mass index, high fasting of plasma glucose, low glomerular filtration rate and high total cholesterol. Behavioral factors that are attributable to increased risk of ischemic stroke are smoking, poor diet and low physical activity accounting for 47% of total stroke burden. Environmental factors that have been linked with higher risk of ischemic stroke is air pollution and lead exposure. Furthermore, after the age of 55 ischemic stroke risk doubles due to atherosclerosis increasing with age. Non modifiable risk factors for ischemic stroke are age, sex and ethnicity. Non modifiable risk factors by ischemic stroke on the other hand vary to the ones of hemorrhagic stroke. Non modifiable risk factors for ischemic stroke consist of hypertension, current smoking, waist to hip ratio, diet, physical inactivity, hyperlipidemia, diabetes, alcohol consumption, cardiac causes and Apolipoprotein B to A1. Globally the highest single risk factor for ischemic stroke is high systolic blood pressure (Boehme et al., 2017).

2.8.2 Risk factors of hemorrhagic stroke

Modifiable risk factors of hemorrhagic stroke are age, sex, family history and ethnicity. Studies show that incidence of hemorrhagic stroke has been higher in Western countries attributed to racial and genetic factors as well as difference in risk factor burden. Hypertension is the most common cause of hemorrhagic stroke, therefor being the biggest risk factor. Furthermore, cigarette smoking, moderate to heavy alcohol consumption as well as chronic alcoholism and use of sympathomimetics are ranked as high risk factors. If an individual presents with decreased low-density lipoprotein cholesterol and low triglycerides, chronic liver disease they are at an increased risk of suffering from hemorrhagic stroke (Unnithan et al., 2023).

2.8.3 Prevention of stroke and risk factor management

Most risk factors for stroke are modifiable, meaning they can be reduced or controlled with altered behavior of the individual. Treatment of hypertension, diabetes mellitus and high cholesterol with medications as well as lifestyle modifications belong to the secondary stroke prevention strategies. Lifestyle modifications consist of adherence to medication, limiting alcohol intake, smoking cessation, adhering to balanced, healthy diet, maintaining normal weight and performing regular physical activity (Prabhakaran & Chong, 2014).

2.9 Clinical presentation of onset of stroke

Signs and symptoms of stroke can have a quick onset but can also develop over hours or days. Symptoms presented depend on the location and type of stroke the patient presents with. The most common symptoms are sudden numbness or weakness predominantly on one side of the body, sudden severe headache with no apparent cause, sudden problems with eyesight such as blurred vision, patient may experience trouble walking, dizziness, loss of balance and coordination (National Heart, Lung and Blood Institute, 2022).Furthermore, a person may be confused, have trouble speaking and understanding speech (Baye et al., 2020).Upon arrival to the hospital, patient suspected to stroke will often present with elevated systolic blood pressure as well as elevated respiratory rate regardless of the stroke subtype.

2.10 Diagnostics

During intake if a patient presents with acute onset of focal neurological deficit they need to undergo a rapid, focused history taking and examination after which they need to proceed immediately to urgent brain imaging which is done with a non-contrast head computed tomography (Birenbaum et al., 2011). Early signs of infarction will be visualized as loss of gray-white differentiation due to decreased density in gray matter structures (Feske, 2021).

2.11 Initial Therapy

Initial therapy by an ischemic stroke comprises intravenous thrombolysis or Endovascular therapy. Intravenous thrombolysis is the most common acute stroke treatment dissolving dangerous blood clots (Oliveira-Filho & Samuels, 2023).

Thrombectomy, mechanical clot removal is done in cases when there is a visible occlusion of a vessel (Mathews & De Jesus,2020), can be performed up to 6h from the onset of symptoms (Bernheisel et al., 2011).

Initial therapy by a hemorrhagic stroke is anticoagulant reversal, management of increased intracranial pressure (National Heart, Lung and Blood Institute, 2022) or performing invasive surgical intervention in order to remove intracerebral hemorrhage (Unnithan et al., 2023).

2.12 Clinical picture of stroke

By ischemic stroke the patient often presents with contralateral deficit in mobility, which is more evident in the upper extremity acral region as well as in the mimic muscles. Furthermore, contralateral deficit of sensation and visual field is common (homonymous hemianopsia). One can observe deviation of eye to the side of deficit and paresis on the opposite side. When the dominant hemisphere is affected, the cortical functions are often diminished whereas when the non-dominant hemisphere is affected the patient may not realize disability/ deficit that he has, referred to as neglect syndrome. When observing a patient post ischemic stroke Wernicke- Mann posture with spastic pattern is often present followed by depression, adduction and internal rotation of shoulder, flexion in the elbow joint, pronation of the wrist and flexion of hand and fingers. On the lower extremity one can notice internal rotation of the lower extremity and extension in the hip and knee, inversion and plantar flexion of the foot (Kolář, 2012).

The clinical picture by hemorrhagic stroke patients overlaps significantly with those of ischemic stroke patients. Nevertheless, hemorrhagic stroke patients are more likely to experience nausea or vomiting, seizures or even loss of consciousness by larger bleeds (Ko et al., 2012). Lastly, neck stiffness may be present in patients after subarachnoid hemorrhage (Backes et al., 2015).

2.13 Gait deviations

Gait dysfunction is at high prevalence in stroke survivors due to damage in neural control mechanisms such as in motor cortices and the descending corticospinal tracts (Beyaert et al., 2015). Brainstem, descending pathways and the intraspinal motor network become disinhibited and turn hyperexcitable (Li et al., 2018). Studies report that stroke survivors adopt simplified walking patterns that consist of altered walking speed, speed modulation, step length asymmetry and propulsive asymmetry meaning they walk more slowly and display gait asymmetry. These gait adaptations reflect the central nervous systems compensatory response to muscle weakness and lack of voluntary muscle control on affected side (Kline et al., 2007; Finley et al., 2008). Furthermore, stroke survivors often present with abnormal muscle synergies and spastic synergistic activation patterns. Hemiplegic gait is a mechanical consequence of muscle weakness, abnormal synergistic activation, their interactions and spasticity. It is often characterized with decreased stance phase and prolonged swing phase on the paretic side along with decreased walking speed and shorter stride length. Recovery of walking ability is one of the main aims in stroke rehabilitation as it poses difficulties in performing activities of daily living and mobility for the person (Rodríguez-Fernández et al., 2021).

Mulroy et al., 2003 classified hemiplegic gait into four categories; fast walker, moderate walker, slow-extended walker also referred to as circumduction gait and slow flexed walker. Fast walker gait pattern presents with lack of heel rise in the terminal stance phase due to plantar flexor weakness and is at 44% of normal walking speed. Due to lack of heel rise in the terminal phase, knee hyperextension can be observed as a compensatory mechanism so that the body can roll forward on the forefoot and step length is reduced due to the lack of momentum transfer from the unaffected limb. Moderate walker gait is at 21% of normal walking speed and presents with weakness in gluteus maximus, quadriceps and spastic characteristic is apparent in the plantar flexors of the foot. Due to extensor weakness, excessive hip and knee flexion occur in the mid stance phase and there is inadequate ankle plantar flexion, knee flexion and heel off movement due to lack of pre swing forward progression. In the moderate walker gait, neutral foot position in the mid swing phase can still be achieved. In the circumduction gait, by a slow extended walker which is classified at 11% of normal walking speed the quadriceps are weakened and cannot support the knee during stance phase. Although muscles in the lower extremity are weakened, the gluteus maximus is still able to retract the femur into knee hyperextension and support the body. During swing phase persistent gluteus maximus and ankle plantar flexor spasticity occurs. Hip hiking and leg circumduction occur for foot clearance. Slow flexed walkers are characterized at 10% of normal walking speed. In this category the gluteus maximus is weak to the point where it cannot retract the femur and stabilize the knee. We can observe trunk forward leaning, excessive hip and knee flexion and ankle dorsiflexion. Step length is reduced due to lack of transition of momentum from the unaffected leg (Kaushik, 2020).

2.14 Rehabilitation by stroke

Rehabilitation by a stroke patient should be designed according to all the neurological symptoms that the patient presents with, and a complex rehabilitation plan should target them. Often patients who have suffered a stroke will have sensory deviations, problems with cognitive function, mobility of the extremities, disability of the head nerves, problems with superficial and deep sensation, and lastly vestibular and cerebral problems. The examination consists of assessing postural muscle tonus, postural and movement patterns, functional examination while taking into account the phase of stroke. In the acute phase of stroke the patient will present with muscle hypotone, in the subacute phase spasticity dominates which is followed by apparent improvement in condition until plateau is reached and chronic phase is initiated (Kolář, 2012).

Early intensive training in the acute phase, therefore in the first 24h of the stroke may be counterproductive due to risk of additional damage to tissue close to lesion (Stephan & Pérennou, 2021) It has been recommended to start rehabilitation 48h after stroke, 2-3 times a day, less than 3 hours every day (Selves et al., 2020).

The thesis area of scope is on subacute stroke, rehabilitation in the mentioned stage focuses on practice of active mobility which is followed by verticalization. The verticalization phase can be divided into multiple phases. Firstly, the patient learns to sit on the hospital bed, with the patient's back supported, core and head in upright position preventing thoracic kyphosis. In order to progress to the following phases of rehabilitation, the patient must regain stability in a seated position, which is trained on the hospital bed. Only once the patient is able to go into side lying position, has learned transfers into sitting and has regained stability in seated position can they be verticalized further.

Patient will often present with a spastic pattern typically affecting upper extremity flexors and lower extremity extensors, for which gradually progressive exercises are targeted. To control spasticity, exercises for both upper and the lower extremity are introduced combining upper and lower extremity exercises supine following by mobilizations of the shoulder girdle. Progression into exercises in prone, with forearm support, kneeling with forearm support, quadruped, tall sitting, concluding with walking on knees which mimics correct movement pattern for the re-introduction of gait. Patient learns to make transfers from sitting into standing, further training stability in sitting targeting lateral stability. Exercises focus on knee stability and isolated dorsiflexion of foot (Kolář, 2012).

2.15 Gait rehabilitation post stroke

In order to re-establish gait, in the subacute phase of stroke intensive gait rehabilitation should be performed. Gait rehabilitation should be task oriented, repetitive, intensive and individualized according to patient's initial gait analysis (Belda-Lois et al., 2011). Development of theories of motor control have directed and changed the focus in rehabilitation strategies following neurological disease or injury. The Dynamic Systems Theory in particular has helped understand underlying mechanisms in CNS and altered movement patterns post stroke through the concepts of "movement variability", "nonlinearity", "self-organization of a dynamic system" and "degrees of freedom". Motor skills training which goes by the phrase "use it and improve it" drives restorative neural plasticity concerning neuromotor processes of motor function in relation to action. Repetitive task gait training is also often incorporated in post stroke gait training short term improvements in lower limb functions especially in speed and distance covered during gait, however evidence is lacking in the long-term improvements (Beyaert et al., 2015).

Traditional therapies in gait training post stroke consist of original Bobath, Brunnstorm, Proprioceptive Neuromuscular Facilitation targeting muscular dysfunction such as flexor and extensor synergies, abnormal muscle tone, muscle weakness which in consequence form a dysfunctional movement pattern. According to studies performed the above-mentioned approaches have not shown a better effect on motor performance after stroke than other treatment methods, moreover permanent improvements in walking performance were also lacking (Beyaert et al., 2015).

Functional electrical stimulation, therapeutic intervention where predetermined frequencies and amplitude of electrical current are applied to nerves or myoneural junctions have displayed augmented muscle force production (Bogey & Hornby, 2007), yet with the byproduct of fatigue and insufficient data to formulate recommendations regarding this method for clinicians (Peterson & Martin, 2010).

Reduced muscle strength is among the initial deficits experienced after stroke, in relation to both muscle strength and endurance (Bohannon, 2007). As there is a strong relationship between muscle strength and function there has been a substantial drive to direct research into addressing the optimal model of strength training in post stroke rehabilitation. Study by Clark and Patten which compared the use of eccentric and concentric exercises in terms of neuromuscular activation and power in affected leg concluded that the greatest gains both in neuromuscular activation and power were apparent in the group practicing eccentric training (Clark & Patten, 2013).

Another technique used in gait rehabilitation is task-oriented focus which combines theories of motor learning and motor control aiming to prevent impairments and promote task specific strategies, adapting goal-oriented tasks to changing environmental circumstances. This technique is a form of repetitive task gait training (Beyaert et al., 2015).

Overground physical therapy gait training using simple aids such as parallel bars is the most common intervention in clinical practice, the patient needs to be able to hold their body against gravity in order to complete tasks. There is insufficient evidence addressing the effect of the intervention, yet single measures of gait performance showed small and short term statistically significant improvements. On the other hand, treadmill training is an intervention where body weight is supported by a harness and the patient can practice coordinated stepping while increasing postural control, controlling gait speed, stimulating normal walking pattern. Studies have shown improvement in gait parameters, yet the above-mentioned intervention is not likely to improve ability to walk independently when patient has body weight support (Beyaert et al., 2015). According to the KNGF guidelines, treadmill training has shown to be more effective than conventional therapy in regard to increasing walking speed and stride, when a patient does not have body weight support (Royal Dutch Society for Physical Therapy, 2014).

Ankle foot orthoses are used in gait rehabilitation as an intervention to control spasticity, excessive plantar flexion and improve patient’s balance. Both solid and dynamic models are in use confirming positive effects on ankle kinematics, knee kinematics during stance, energy cost and weight transfer on affected leg (Beyaert et al., 2015).

In recent years there has been a rising interest in investigation and use of virtual reality and robot assisted gait training. Virtual reality offers the patient an enriched environment and high dosage of training, yet studies have shown that the effect on gait speed and global motor function post stroke without significant improvement. Robot assisted gait training enables extended training duration, reduced need for physical input lowering demand on health care professionals as well as collecting and recording joint kinetic and kinematic data simultaneously with walking tracking progress over time. Due to inconclusive results on the effect of the above-mentioned therapy, further research is required to draw reliable conclusions (Beyaert et al., 2015).

2.16 Spatiotemporal gait outcome measures

Outcome measures are important tools when it comes to integrating evidence-based practice into the physiotherapy profession (Renteria & Berg, 2019) as they assess the effectiveness of the given treatments, are able to indicate prognosis and provide a justification to the value of the given interventions (Jette et al., 20090). Initially, prior to guiding treatment decisions, improving care or helping patients recognize their own improvement (Nordal, 2012), an outcome measure supplies baseline data. When analyzing gait, clinicians and researchers use both qualitative and quantitative parameters. The most relevant outcome measures when analyzing gait are the spatiotemporal gait outcome measures which can be further divided into 3 categories. The categories are as follows; distance variables, temporal variables and other variables (Roberts et al.,2017) .

Distance-related metrics encompass step length, step width and stride length (König et al., 2017). Step length is categorized into the left foot's step length and the right foot's step length. The step length of the left foot refers to the distance between the previous heel strike of the right foot and the subsequent heel strike of the left foot (Aggarwal et al., 2018). On average, a normal step length is approximately 70 cm (Hazari et al., 2021). Step width refers to the mediolateral distance between the two feet, measured as the space between the right and left heels during walking (Hazari et al., 2021). The average normal step width typically ranges from 8 to 10 cm. Stride length is the distance measured between consecutive heel strikes of the same foot, such as from one heel strike of the right foot to the next (Aggarwal et al., 2018).

Temporal variables encompass step time and stride time. Step time is the duration between the initial contact of one foot and the initial contact of the contralateral foot (Hazari et al., 2021). Whereas stride time is the duration between successive initial contacts of the same foot (Hazari et al., 2021)

The last category are the other variables and encompass cadence and gait velocity. Cadence, also referred to as step frequency, is the number of steps taken per minute (Mohamed & Appling 2019) Gait velocity or gait speed, refers to the time it takes for an individual to cover a specified distance. The term "velocity" encompasses both the speed of travel and the direction of travel (Mohamed & Appling 2019)

2.17 Predictive factors for gait recovery & progress assessment

Studies as well as guidelines such as the KNGF guideline have identified factors that when present within the first two weeks after stroke can predict better walking outcome. These factors include younger age, absence of hemianopia, less lower limb motor impairment, less sensory loss, better trunk control and sitting balance (Royal Dutch Society for Physical Therapy, 2014).

It is of great interest when it comes to managing patient and family expectations to be able to predict whether and when the patient is going to be able to walk and therefore outcome measures have been designed to evaluate, keep track of and predict patient extent of recovery (Shariat et al., 2023). A systematic review by Mudge &Stott published in 2007 evaluating existing outcome measures to assess walking ability after stroke concluded that most frequently used outcome measure was self-paced gait speed over a short distance, followed by fast or maximal pace. Furthermore, the use of an outcome measure depended on the chronicity of the stroke (Mudge & Stott, 2007). In studies where the subjects were acute or subacute patients 64% used the Functional Ambulation Category, 63% used Barthel index and Rivermead Mobility index in 52% of the studies. By chronic patients on the other hand 6-Minute Walk Test, kinetics and kinematics was most commonly used.

2.18 Functional mobility and performance assessment measures

In the subacute stroke patient population group the Functional Ambulation Category, Barthel index, Rivermead Mobility index and the 6-Minute Walk Test are most frequently used as outcome measures. The Functional Ambulation Category (FAC) is designed to evaluate ambulation ability through a functional walking assessment. It is a 6-point scale measuring the level of human assistance required for walking, irrespective of whether the individual uses a personal assistive device (Marvin, 2011).

The Barthel index is a functional assessment scale evaluating patient performance across ten domains of daily living. The domains are as follows: bowel control, bladder control, toileting, grooming, dressing, bathing, feeding, chair transfer, ambulation and stair climbing. This scale combines assessments of physical function and mobility while accounting for frailty, classifying levels of dependence based on both observed and reported abilities. It is particularly valuable in assessing progression of frailty over time and linking frailty to disability and functional capacity but does not differentiate between causes of functional decline (Chokshi,2023).

The Rivermead Mobility index is a hierarchical mobility scale that is utilized in neurological rehabilitation and primarily assesses functional mobility such as gait, balance and transfers following a stroke. The Rivermead Mobility index is displayed in questionnaire format consisting of 14 self-reported items and 1 direct observation. The items with the questionnaire are score 0 if the patient is unable to complete the task and 1 when they are able to complete the task. Scores are added together, maximum score is 15, higher scores portraying better functional mobility (Williams, 2011)

The 6-Minute Walk Test (6MWT) is a 1 item objective measure of functional exercise capacity. It assesses submaximal/aerobic functional walking capacity, walking endurance and predictor of morbidity in cardiac patients. The test itself does not require complex equipment or technical expertise of researcher. During the test the patient is asked to walk as far as possible along a 30m marked corridor for the duration of 6 minutes. The primary outcome of the test is the 6 minutes walk distance that is measured in meters (Agarwala & Salzman, 2019).

2.19 Lower limb robotic exoskeleton

A promising intervention in gait rehabilitation in recent years has been robotic assisted therapy. The wearable robots are strapped to the legs of the user, have electrically operated motors that control joint motion in order to automate overground walking. Originally rehabilitation exoskeletons were designed to serve as an assistive device for people with spinal cord injury to walk. Nevertheless, as the device allows users to walk without overhead bodyweight support or treadmill they have become increasingly popular as an alternative intervention in gait rehabilitation where there is a need for repetitive gait training to improve walking function (Louie & Eng, 2016).

Rehabilitation exoskeleton robots are intended for use by patients with disabilities that can be recovered through rehabilitation and training primarily used in rehabilitation of elderly and patient with lower limb motor dysfunctions. They connect with the human body in a wearable way and have the ability to control movement of all joints in the training process (Lee et al., 2020). The earliest research on lower limb robotic rehabilitation exoskeletons dates back to 1960s, initially the early robots failed to reach expected targets, but were used as foundation for follow up studies. In recent years, also thanks to digitalization, lower limb robotic exoskeletons have become a significant research topic. It is a comprehensive technology that combines sensing, control, information, and computer science to create wearable mechanical devices. The lower limb exoskeletons can be divided into two subtypes, treadmill based and overground application. Treadmill based robotic exoskeletons combine the use of the lower limb robotic exoskeleton that provides assistance for leg movements and a body weight support system reducing gravitational force, maintaining balance and ensuring increased safety of the user. Examples of treadmill based robotic exoskeletons include ALEX, Lokomat and LOPES. Overground robotic exoskeletons aid patients in regaining overground gait (Shi et al., 2019). They have a rigid structure at the joints also referred to as links. Depending on the type of exoskeleton they may provide back support ensuring upright position of the user. Upright posture is an important aspect in gait training to provide quality repetitions. Lower limb robotic exoskeletons are capable of early mobilization, assisting user with severe gait and balance deficits and providing the user with consistent and repetitive physical therapy. Furthermore, many post stroke patients develop compensatory mechanisms to be able to ambulate more efficiently and effectively including circumduction, hip hiking, toe walking, steppage gait, resulting in slower walking speed, asymmetry, shorter step length, reduced gait and balance adaptability as well as increased risk of falls. Lower limb robotic exoskeletons are capable of correcting these pathological deviations and retraining users to achieve a more efficient physiologically appropriate overground ambulation (Karunakaran et al., 2023). Examples of overground robotic exoskeletons include eLEGS, Indigo, Rewalk, MINDWALKER, HAL (Shi et al., 2019).

2.20 Principle of use

Typically, a lower limb robotic exoskeleton is made up of a frame, sensors, actuators and control system that imitate human locomotion. They are powered by batteries or other energy sources and controlled by either person's actions, software-based controller or both. Actuators on the lower limb robotic exoskeleton can be located on hip, knee, ankle joints assisting in different movements produced by the anatomical joint. Hip exoskeletons are single joint lower limb exoskeletons assisting users in performing flexion, extension, adduction, abduction, medial and lateral rotation of the hip. Actuators are placed on the user's hips, reducing stress on hip and ankle muscles. Knee exoskeletons typically allow movement in one degree of freedom allowing the patient to perform flexion and extension of the knee. The actuator in the knee exoskeletons is commonly a soft inflatable cushion that is placed behind the user's knee, to reduce weight of the exoskeleton. The soft inflatable cushion is inflated during the swing phase of the gait cycle and deflated when walking. Similarly to the knee exoskeletons, the ankle exoskeletons also operate in one degree of freedom into plantar and dorsiflexion (Coser et al., 2024). Latest lower limb exoskeletons have advanced to multiple joint structures assisting at least two joints assisting the entire limb for maximum effect. Study by Franks et al., 2021 proved that two joint assistance reduced metabolic cost of walking by 33-42% and three joint assistance by 50%, metabolic cost being an important determinant to take into consideration during stroke rehabilitation as often therapy compliance is low due to post stroke fatigue.

2.21 Available lower limb exoskeletons

Study conducted by Rodríguez-Fernández et al., 2021 concluded that the majority of lower limb robotic exoskeletons assist two or more joints (hip and knee or hip, knee and ankle joint). Most commonly joints within the exoskeletons are active joints, meaning that the joints are actuated enabling control over the position of limbs. Passive joints on the other hand are connection points between bones and precise position of the joint cannot be controlled. Optionally by passive joints, non-actuated parts such as springs might be attached (2.3.1 Types of joints, 2023). The number of degrees of freedom in lower limb robotic exoskeletons in the sagittal plane ranges from 1 to 3. The majority of the available lower limb exoskeletons operate on electric motors instead of hydraulic or pneumatic actuators with battery life lasting 6 hours, and 2-4 hours when in continuous use.

2.22 Neuroplasticity and motor learning in exoskeleton assisted gait training

"Neuroplasticity is the ability of the nervous system to change its activity response to intrinsic and extrinsic stimuli by reorganizing its structure, functions and connections" (Puderbaugh & Emmady, 2025). A study by Calabro et al., 2018 assessed whether there are specific neurophysiological mechanisms (among those related to sensorimotor plasticity, frontoparietal effective connectivity and transcallosal inhibition) by which Ekso™ improves functional ambulation capacity in the chronic post-stroke phase. They found out that exoskeleton gait training induced greater reshaping of corticospinal and interhemispheric connectivity alongside improved frontoparietal effective connectivity and rebalanced sensory motor integration between the affected and unaffected hemispheres. Neuroplasticity was leveraged during the exoskeleton assisted gait training through repetitive and task-oriented training, sensory motor integration, multisensory stimulation, reduction of compensatory mechanisms, long term neural adaptations, corticospinal excitability, restoring interhemispheric balance, frontoparietal effective connectivity, activation of both proximal and distal muscle groups and lastly supporting engagement in active participation.

Repetitive and Task-Oriented Training resulted in improvement in motor control, gait function, walking independence, and quality of life in stroke patients specifically in the subacute patient group (French et al., 2016). Researchers observed improved movement synergies, reflexes, and isolated motor actions. An increased step length, cadence and gait symmetry was noted by the participants. Higher walking independence measured using the Functional Ambulation Category, static and dynamic balance measured using the Berg Balance Scale and walking velocity was measured. No significant improvements were observed in walking endurance measured using 6-Minute Walk Test. (Yang et al., 2024)

Sensory motor integration can be described as the brain's ability to combine sensory inputs and motor outputs for effective movement control. Studies have shown that embodiment of robotic exoskeleton devices improves the functionality of these devices. By using perturbation or stimuli, the user is able to react in their typical behaviour. The exoskeletons deliver real-time proprioceptive input, strengthening neural circuits that link sensory and motor pathways, thereby enhancing the brain's ability to perceive limb position and movement (Hybart & Ferris, 2024).

Lower limb robotic exoskeletons achieve multisensory stimulation through maximizing sensory inputs which are needed for motor recovery. Lower limb robotic exoskeletons combine visual feedback, auditory feedback from the physiotherapists or the device itself, and proprioceptive feedback. High sensory input increases brain stimulation improving brain plasticity through the engagement of numerous cortical and subcortical areas (Yang et al., 2024). Moreover, through their ability to facilitate repetitive, symmetrical movements, the lower limb robotic exoskeletons aid in normalizing communication between the hemispheres, reducing overactive inhibition exerted from the unaffected side (Siviy et al., 2022).

Lower limb robotic exoskeletons discourage compensatory patterns that patients will often take up post stroke such as circumduction or vaulting gait by encouraging symmetric gait patterns. Symmetric gait patterns are achieved through rhythmic muscle activation (Longatelli et al., 2021) that the exoskeleton’s promote, proprioceptive feedback and control strategies (Warutkar et al., 2022). Furthermore, a study by Karunakaran et al., 2020 showed improved linearity and slope during loading phase of the gait cycle using the lower limb robotic exoskeleton (Karunakaran et al., 2020).

3. METHODOLOGY

3.1 Objectives and research methods

The literature review investigates the effectiveness of using lower limb robotic exoskeletons in improving gait by people after subacute stroke using randomized controlled trials and controlled clinical trials.

3.2 Goal of thesis

The goal of the thesis is to explore the effectiveness and role lower limb robotic exoskeletons play in gait rehabilitation by subacute stroke patients using the 6-Minute Walk Test and Functional Ambulation Category as outcome measures, provide a structured analysis of the usage of the above mentioned technological innovation aiding in decision making process when deciding on whether to incorporate it, thereby potentially increasing its utilization making treatment sessions more variant, motivating patient, increasing adherence to therapy yielding to better functional outcomes and addressing current challenges in healthcare.

3.3 Research Question

What is the effectiveness of using lower limb robotic exoskeleton in improving gait by people after subacute stroke?

3.4 Criteria for research

3.4.1 Types of studies

Randomized controlled trials and controlled clinicals trials were included in the literature review to ensure high quality evidence (randomization, control group, blinding, causal interference). Due to rapid technological advancement studies published between 2014 to 2024 were included.

3.4.2 Languages

Studies in English, German and Czech language were amongst the inclusion criteria of the study.

3.4.3 Types of participants

The participants included in the literature review were individuals, both male and female, over the age of 18 till 90 years of age.

3.4.4 Types of pathologies

Patients with subacute stroke, with disregard to the type of subacute stroke; whether it is ischemic or hemorrhagic.

3.4.5 Types of interventions

Gait rehabilitation with the lower limb robotic exoskeleton.

3.5 Outcome measures

3.5.1 6-Minute Walk Test (6MWT)

The 6-Minute Walk Test is a functional walking assessment particularly valuable in evaluating functional mobility, walking endurance and overall gait performance. The walking course should be performed indoors on a 30m straight corridor/ walking surface with turnaround points at each end which are marked with tape or cones. Every 3 meters of the 30m course should be marked with tape for easy distance measurement.

The test measures the distance the patient can walk on a flat, hard surface in the period of 6 minutes (Crapo et al., 2002).

3.5.2 Functional Ambulation Category (FAC)

The Functional Ambulation Category is designed to evaluate ambulation ability through a functional walking assessment. It is a 6-point scale measuring the level of human assistance required for walking, irrespective of whether the individual uses a personal assistive device. (Marvin, 2011). The FAC does not evaluate endurance, the participant is asked to walk only 3 meters, where the assessor asks the participant various questions and observes their walking ability. The rating is a score from 0 to 5. The number 0 indicates the participant in a non- functional ambulator and 5 that the participant is a independent ambulator who can walk freely on any surface (Holden et al., 1986).

3.6 Research design

The most suitable research design for the research question that has been posed "What is the effectiveness of using lower limb robotic exoskeleton in improving gait by people after subacute stroke?" is a literature review. The purpose of the literature review is to scope a body of literature, gain understanding of already existing research, identify gaps in knowledge and where future research might be best directed (Reviewing the literature, n.d.)

Furthermore, it showcases relationships between previous studies. A literature review is the appropriate research design when addressing the mentioned question as while there has been an increased amount of studies on using robotic exoskeletons in gait rehabilitation due to its promising future and vast benefits there is a strong need of making a comprehensive framework which summarizes lower limb exoskeletons, their effectiveness through comparison using outcome measures and patient experience on how it has been adapted by them. A literature review summarizes the current state of knowledge, provides space for identification of current research gaps allowing researchers to visualize where further research in regard to the implementation of exoskeletons needs to be focused at to increase its use.

In order to present a clear and structured literature review, the methodology that this research paper will follow is the Arksey and O'Malley framework (Arksey & O'Malley, 2005) consisting of 6 steps:

1. Specify the research question
2. Identify relevant literature
3. Study selection
4. Mapping out the data
5. Summarize, synthesize and report results
6. Include expert consultation (optional)

3.7 Search Strategy

The databases that were used to conduct the research were PubMed, Cochrane, Science Direct, PEDro. PubMed was chosen as the primary search engine because it offers a broad selection of freely accessible articles in the medical field, providing a comprehensive overview of available evidence. The search took place between 02.10.2024 and 23.10.2024.

3.8 Search String

The search string has been made up of 3 key terms that have been extracted from the research question and are as follows “lower limb robotic exoskeleton”, “gait rehabilitation” and “stroke”. Synonyms for the above stated terms were retrieved from database searches as well as existing literature and presented in table 1.

Table 1: Synonyms of key terms

Lower limb robotic exoskeleton		**Gait rehabilitation**		**Stroke**	
lower extremity-powered exoskeleton	TiAb	locomotor training	TiAb	cerebrovascular accident	TiAb
lower limb exoskeleton	TiAb	gait therapy	TiAb	subacute stroke	TiAb
lower-limb exoskeleton		gait training	TiAb	apoplexy	TiAb
Exoskeleton robots for lower limb assistance	TiAb	locomotion therapy	TiAb	cerebral accident	TiAb
lower-limb powered robotic systems	TiAb	walking training	TiAb	cerebral infarction	TiAb
powered exoskeleton	TiAb	walking therapy	TiAb	CVA	TiAb
		locomotion rehabilitation	TiAb	ischemic stroke	TiAb
				hemorrhagic stroke	TiAb

Synonyms listed in the same column of the table, reflecting a common theme, were linked using "OR" in PubMed's advanced search query. Each group of words within the column was then connected to the other two grouped words using "AND." To ensure precise search results, the Title/Abstract or MeSH field was specified for each term. The search string was adjusted as needed to account for variations in advanced search features across different databases (see attachments).

3.9 Eligibility criteria

3.9.1 Inclusion criteria

Firstly, filters regarding the publication year of the study have been applied to the search string due to technology advancing at an unprecedented pace. The aim of the literature review is to provide the reader with the currently available lower limb exoskeletons with most recent evidence-based findings on their effectiveness, therefore the filter applied marks 10 years. The second filter applied ensured that all studies used are in full text version. Furthermore, featured articles can be written in English, Czech or German only. The population of the literature review focuses on patients with subacute stroke, with disregard to the type, whether it is ischemic or hemorrhagic due to the limited amount of search results. Furthermore, gender of participants is extended to both males and females aged 18-90. Regarding study design, pilot studies have been included, providing preliminary data about the potential lower limb robotic exoskeletons on the market. Another inclusion criteria that has to be met is regarding the outcome measures, where the primary or the secondary outcome measure has to be Functional Ambulation Category or the 6MWT to allow comparison to take place.

3.9.2 Exclusion criteria

All the articles that have not met the inclusion criteria will be rejected. Further elaborating on the population specifications, when the population in question has acute stroke or chronic stroke the study will be rejected. Furthermore, the study design of the selected studies cannot be any type of literature review i.e. scoping review, systematic review, meta-analysis. Studies had to be purely lower limb robotic exoskeletons without upper limb robotic exoskeleton as well.

Table 2: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Studies available in full text	Participants of study having acute or chronic stroke
Studies in English, Czech or German language	Literature review as publication type
Studies published in the last 10 years	Upper limb robotic exoskeleton included
Participant of the study have subacute stroke at the time of testing	
Participants of both male and female gender aged 18-90	
Primary or the secondary outcome measure has to be Functional Ambulation Category or the 6MWT	

3.10 Selection process

The studies analyzed within the master thesis were initially searched within the chosen databases according to the keywords. The keywords were added to the advanced search option in each of the databases to scope all available literature regarding the desired topic. The complete list of search results was selected, extracted and uploaded into "Rayyan" an online software which aids researchers in the selection process within literature review. The duplicates were removed using the software as well as manually by the researcher. Next screening of the title followed by the abstract and lastly full text took place. Screening of title, abstract and full texts has been done using the predetermined inclusion and exclusion criteria. Selection process including figures has been further visualized through the PRISMA diagram (PRISMA-ScR)(Tricco et al.,2018).

A total of 768 articles were identified among PubMed, ScienceDirect, Cochrane and PEDro and were exported into Rayyan - Intelligent Systematic Review, an online software aiding in the selection process. A total of 21 duplicates were found manually and using the software and were eliminated reducing total number of articles to 747. Screening of the title followed, where relevant keywords were searched within title further excluding 680 articles. 67 articles were screened by abstract out of which 48 were excluded. Leaving 19 articles which were screened by full text. 12 articles were excluded when screening the articles by full text. Reasons for exclusion consisted of 2 articles not specifying the type of stroke, 2 articles featuring the wrong population and 1 article not specifying further on the type of stroke the participants suffered, 2 articles were of inappropriate study design: trial registry records, 1 article couldn't be retrieved, 1 article did not display the full text version and lastly 4 articles featured outcome measures that did not match the inclusion criteria. Finally, 6 articles met the inclusion criteria and were selected for the literature review.

Figure 5: PRISMA Flow Diagram

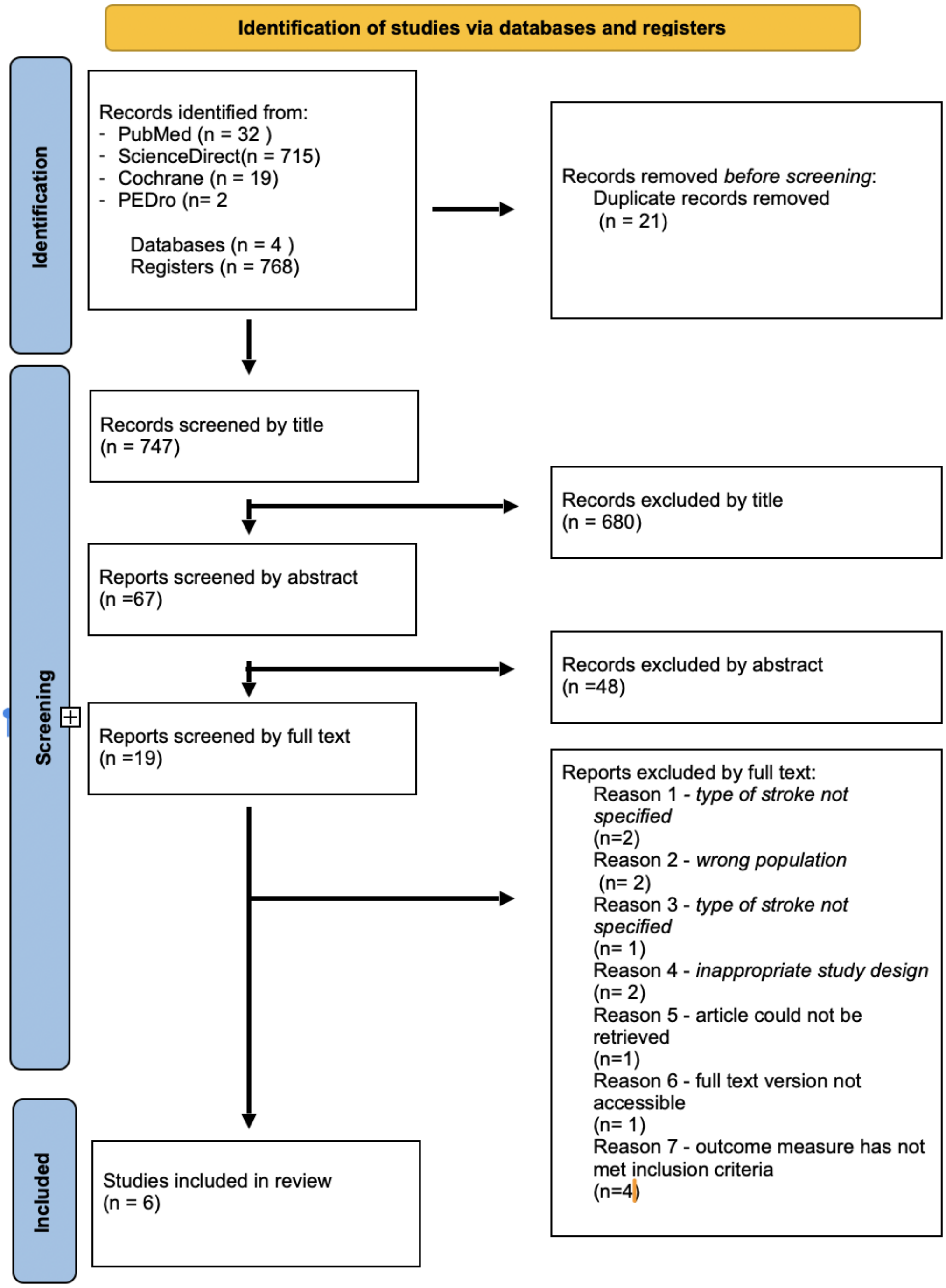


Figure 5:Prisma Flow Diagram (Tricco et al.,2018)

3.11 Data extraction and analysis

In order to analyze the effectiveness of using lower limb robotic exoskeletons in improving gait for people after subacute stroke the data that was chosen to be extracted consisted of 6-Minute Walk Test readings. The 6-Minute Walk Test has been chosen to be the comparable outcome measure as five out of the six studies feature the 6-Minute Walk Test either as their primary or secondary outcome measure allowing comparison to take place between included studies and the variety of lower limb robotic devices. The 6-Minute Walk Test readings were the test results of the Experimental Group - Robotic Exoskeleton and Control Group at baseline and final assessments. The second group of data chosen to be extracted were the Functional Ambulation Category readings. The Functional Ambulation Category readings were the test results of the experimental group - Robotic Exoskeleton and Control Group at baseline and final assessments.

Thirdly, to answer how the lower limb robotic exoskeleton has been adopted by people after subacute stroke in terms of acceptability, data relating to population characteristics, usability as well as acceptance will be extracted.

3.12 Evaluation of Methodological Quality and Data Extraction

All eligible articles were evaluated for methodological quality using the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA), commonly represented through the PRISMA flow diagram. The PRISMA flow diagram provides the reader with a visual summary of the screening process, ensuring transparency in the screening process by visualizing the decision process along the different stages and clearly specifying reasons for exclusion in the later stages of the screening process (Tricco et al.,2018).

The screening process was completed in Rayyan, an online software which ensures a structured, organized and simplified review process. The eligible articles were categorized into included, excluded and undecided through the title, abstract and full text screening process.

Data extraction took place through systematically collecting relevant information into a data extraction table template which ensured a standardized process for the chosen studies. Key components of the extraction tables included author, year of publication, study design, objective/aim, intervention, specifications of sessions, primary and secondary outcome measures and device name. A second extraction table was created to clearly visualize and distinguish 6-Minute Walk Test outcomes and Functional Ambulation measure outcomes. A detailed summary of the extracted data can be found in the tables 2, 4 and 5.

The Downs and Black Checklist for Clinical Trial Quality assessment has been used to evaluate the quality of the randomized controlled trials (see table 3). The Downs and Black Checklist for Clinical Trial Quality assessment consists of 27 questions, the first 10 questions focused on reporting, question 11 to 13 on external validity, question 14 to 20 on internal validity and lastly question 21 to 27 on internal validity more specifically confounding variables and selection bias (Downs & Black, 1998).

The TREND Statement (Transparent Reporting of Evaluations with Nonrandomized Designs) has been used to evaluate the quality of the non-randomized experimental studies (see table 3). The 22-item checklist evaluates the theoretical framework of the study, participant eligibility and recruitment, intervention details, bias control measures and lastly outcomes and statistical methods (Des Jarlais et al., 2004). The checklist is divided in the following order: the first question is regarding the title and the abstract, second question regarding the introduction, question 3 to 11 is on the methods where participants, interventions, objectives, outcomes, sample size, assignment method, blinding, unit of analysis and statistical methods are taken into account. Question 12 to 19 are based on the results evaluating interpretation, generalizability and overall evidence.

Table 3: Evaluation of Methodological Quality and Data Extraction Results per study

Author/year	**Study design**	**Quality Assessment**	**Score**
Goffredo et al. (2019)	Prospective, pilot pre-post, open label, non-randomized experimental study	TREND Statement (Transparent Reporting of Evaluations with Nonrandomized Designs)	39/59
Li et al. (2021)	RCT	Downs and Black Checklist for Clinical Trial Quality assessment	20/27
Molteni et al. (2021)	Multicenter RCT	Downs and Black Checklist for Clinical Trial Quality assessment	22/27
Pournajaf et al. (2023)	Multicenter Controlled Clinical Trial	Downs and Black Checklist for Clinical Trial Quality assessment	23/27
Xie et al. (2023)	RCT pilot	Downs and Black Checklist for Clinical Trial Quality assessment	24/27
Yoo et al. (2023)	RCT pilot	Downs and Black Checklist for Clinical Trial Quality assessment	23/27

*Full evaluation of Methodological Quality and Data Extraction Results per study can be found in the attachments.

4. RESULTS

In the following chapter the studies were rigorously analyzed, data retrieved and organized into extraction tables. Extraction tables have been created to provide a reader friendly overview and allow for easy comparison of studies. The first table provides an overview of the study characteristics of the six included studies to have a clear overview of study designs, intervention, duration of study, primary and secondary outcome measures and the name of the lower limb robotic exoskeleton used. Furthermore, it aids in future analysis of research finding accuracy, reliability, and applicability to the questions at hand. The chapter concludes with a comprehensive summary that details the study parameters, findings, and conclusion.

Table 4: Extraction table with study characteristics

Author/year	**Study design**	**Objective/aim**	**Intervention**	**Specifications of sessions**	**Primary outcome measure**	**Secondary outcome measure**	**Device**
Goffredo et al. (2019)	Prospective, pilot pre-post, open label, non-randomized experimental study	Assess feasibility of using an overground wearable powered exoskeleton with subacute stroke patients and examine the clinical effects with regard to improving motor and functional ambulation outcomes	Participants, in addition to conventional therapy, performed walking rehabilitation training using an overground wearable powered exoskeleton	*No. of sessions:* 15 ± 2 *Length of session:* 60min *Frequency per week:* 3-5x No. of weeks: N/a	6MWT	10MWT	Ekso
Li et al. (2021)	RCT	Investigate whether exoskeleton assisted gait training is a more effective way for improving motor and walking ability than traditional training in	Experimental group received BEAR-H1 assisted gait training, and the control group received conventional training	*No. of sessions:* 20 *Length of session:* 30min *Frequency per week:* 5x	6MWT	• Fugl-Meyer Assessment for lower extremity • MAS • FAC	BEAR-H1

		subacute stroke patients		*No. of weeks:* 4			
Molteni et al. (2021)	Multicenter RCT	Assess the efficacy of employing an overground exoskeleton for gait training in subacute stroke subjects as well as investigating the clinical effects compared to conventional gait training.	All subjects conducted daily conventional rehabilitation. Experimental group conducted gait training with overground wearable powered exoskeleton, control group underwent conventional gait training.	*No. of sessions:* 15 *Length of session:* 60min *Frequency per week:* 5x *No. of weeks:* 3 weeks	6MWT	- MAS for lower extremity - Motricity Index of the Affected lower Limb - Trunk Control Test - 10MWT - Modified Barthel Index - Walking Handicap Scale	Ekso
Pournajaf et al. (2023)	Multicenter Controlled Clinical Trial	Evaluate the effects in terms of gait speed of robot-assisted gait training compared with overground gait training in subacute stroke patients	Both experimental and control group received standard daily therapy. In terms of gait training experimental group received robot-assisted gait training , and the control group received overground gait training.	*No. of sessions:* 20 *Length of session:* 30min *Frequency per week:* 3-5x *No. of weeks:* N/a	10MWT	- Timed up and go test - 6MWT - Motricity Index of the Affected lower Limb - Modified Ashworth scale of affected lower limb - FAC	Lokomat Pro

Xie et al. (2023)	RCT pilot	Evaluate the effects of soft robotic exoskeleton for gait training on clinical and biomechanical gait outcomes in patients with subacute stroke	Experimental group received conventional rehabilitation training combined with robotic exoskeleton overground walking training, control group received conventional rehabilitation training only	*No. of sessions:* 10 *Length of session:* 30min *Frequency per week:* 5x *No. of weeks:* 2 weeks	• 6MWT • 10MWT	• FAC, • Fugl-Meyer Assessment for Lower Extremity • Berg balance Scale	Yrobot Relink
Yoo et al. (2023)	RCT pilot	Investigate the efficacy and usefulness of overground RAGT in patients with subacute stroke	All participants received conventional stroke neurorehabilitation program. The intervention group received overground robot-assisted gait training in addition, while the control group received conventional gait training	*No. of sessions:* 12 *Length of session:* 30 min *Frequency per week:* 3x *No. of weeks:* 4 weeks	FAC	• Pulmonary function test • 10MWT • Berg Balance Scale • Timed-up-and-go test • Fugl–Meyer assessment of lower extremity • Korean version of the modified Barthel index • Euro quality of life 5-dimensions	Exo Atlet Medy

4.1 Description of results

4.1.1 Study Characteristics

The following chapter refers to Table 4 which presents the extraction table with study characteristics.

Goffredo et al. (2019) in their prospective, pilot pre-post, open label, non-randomized experimental study assessed and evaluated the feasibility of using an overground Ekso wearable powered exoskeleton in subacute stroke patient as well as examined the clinical effects with regard to improving motor and functional ambulation outcomes. In order to assess the feasibility and examine clinical effects, participants in addition to conventional therapy performed walking rehabilitation training using the Ekso overground wearable powered exoskeleton. Participants would undergo 3 to 5 sessions per week, which averaged to 15 plus or minus 2 sessions overall. Sessions spanned over 60 minutes.

Li et al. (2021) in their randomized control trial investigated whether exoskeleton assisted gait training is a more effective way for improving motor and walking ability than traditional training in subacute stroke patients. To assess this the experimental group received BEAR-H1 assisted gait training, and the control group received conventional training. The experimental group would receive 30 minutes of the BEAR-H1 assisted gait training while the control group received 30 minutes of conventional therapy 5 times a week for 4 weeks. Number of sessions totaled to 20 by the end of the 4 weeks.

Molteni et al. (2021) in their multicenter randomized controlled trial assessed the efficacy of employing an overground exoskeleton for gait training in subacute stroke subjects alongside with investigating the clinical effects compared to conventional gait training. To do so the control group underwent the conventional gait training only whereas the experimental group underwent both the conventional gait training and overground exoskeleton gait training. Both the groups conducted daily conventional rehabilitation. The exoskeleton group underwent 15 sessions, 5 days per week for 3 weeks with the Ekso lower limb exoskeleton. Each session lasted 60 minutes. Within gait rehabilitation the participants would also practice the following motor tasks: sit-to-stand re-learning, re-adaptation to verticalization and awareness of the position, training of proprioception, balance, and load shifting while standing and during the gait, stepping and relearning of the correct gait pattern and progressing to gradual adaptation to speed and resistance during walking. The control group had the same parameters during the conventional gait training 15 sessions, 5 times a week for 3 weeks with sessions lasting 60 minutes. The conventional gait training consisted of tasks such as lower limb stretching, lower limb muscle strengthening, static and dynamic balance exercises, proprioception, trunk control exercises, gait training at parallel bars or in clinical open spaces both with and without assistive devices and lastly training of climbing up and down stairs.

Pournajaf et al. (2023) in their multicenter controlled clinical trial evaluated the effects in terms of gait speed of robot-assisted gait training compared with overground gait training in subacute stroke patients. Similarly to the study by Molteni et al., 2021 both the experimental and the control group received standard daily therapy but in terms of gait training the experimental group received robot assisted gait training using the Lokomat Pro lower limb robotic exoskeleton and the control group received overground gait training. The length of the intervention was not classified but participants received 20 sessions spanning over 30 minutes, 3 to 5 times a week.

Xie et al. (2023) in their randomized controlled trial pilot study evaluated the effects of a soft robotic exoskeleton called Yrobot Relink for gait training on clinical and biomechanical gait outcomes in patients with subacute stroke. To do so the experimental group received conventional rehabilitation training combined with robotic exoskeleton overground walking training while the control group received conventional rehabilitation training only. They all received 10 sessions over 30 minutes 5 times a week over 2 weeks.

Yoo et al. (2023) in their randomized controlled trial pilot study investigated the efficacy and usefulness of overground robot assisted gait training using the Exo Atlet Medy exoskeleton in patients with subacute stroke. To do so the intervention group received overground robot-assisted gait training in addition to conventional stroke neurorehabilitation program, while the control group received conventional gait training in addition to conventional stroke neurorehabilitation program. Total number of sessions added up to 12, 30-minute sessions over the span of 4 weeks.

4.1.2 Population Characteristics

A summary of the participant characteristics can be found in Table 5. All of the participants included in the study were diagnosed with subacute stroke. The studies included in this review comprised a total of 289 participants, with sample sizes ranging from 17 to 89 participants. In 4 out of the 6 studies the number of participants was evenly distributed ±2 into the experimental group and the control group. The study by Goffredo et al. (2019) did not incorporate a control group and in the study by Pournajaf et al. (2023) there were 33 more people in the experimental group than in the control group.

The average age of participants varied across studies, with a mean age ranging from 50,13 years to 68,24 years. Gender distribution was reported in all 6 studies, with a higher percentage of males participating in both the experimental group and the control group. The average age range presented, reflects the population accurately with stroke as according to the 'Global Stroke Fact Sheet 2022' published by the World Stroke organization, each year over 62% of all strokes occur in people under 70 years of age, providing a relevant sample for investigating.

To promote greater comparability of population characteristics between studies table 5 provides an overview of the number of participants in each study, number of participants in both the intervention group and the control group along with gender of participants and age range of participants in each study group.

Table 5: Study Participant Characteristics

Author/ year	**No. of participants in study**	**No. of participants in RE group**	**No. of people in CTR group**	**Gender of participants in RE group**	**Gender of participants in CTR group**	**RE group age range (years)**	**RE group mean age**	**CTR groupage range (years)**	**CTR group mean age**
Goffredo et al. (2019)	46	46	no CTR group	M=27 F=19	no CTR group	42,55-71,13	56,84	N/a	63
Li et al. (2021)	32	17	15	M=15 F= 2	M=14 F= 1	38,27-62,79	50,53	40,64-59,62	50,13
Molteni et al. (2021)	75	38	37	M=21 F=17	M=21 F=19	53,38-70,88	62,13	59,66-76,82	68,24
Pournajaf et al. (2023)	89	61	28	M=36 F=35	M=18 F=10	44-74	59	50,54-76,24	63.39
Xie et al. (2023)	30	15	15	M=12 F= 3	M=9 F=6	50,87-67,13	59	56,43-70,17	63.30
Yoo et al. (2023)	17	9	8	M=4 F=5	M=5 F=3	42-85	61	43-87	65

4.1.3 Visualization of 6 Meter Walk test Results

Table 6: 6-Minute Walk Test results of the Experimental Group - Robotic Exoskeleton (RE) and Control Group (CTR) at baseline (T0) and final (T1) assessments

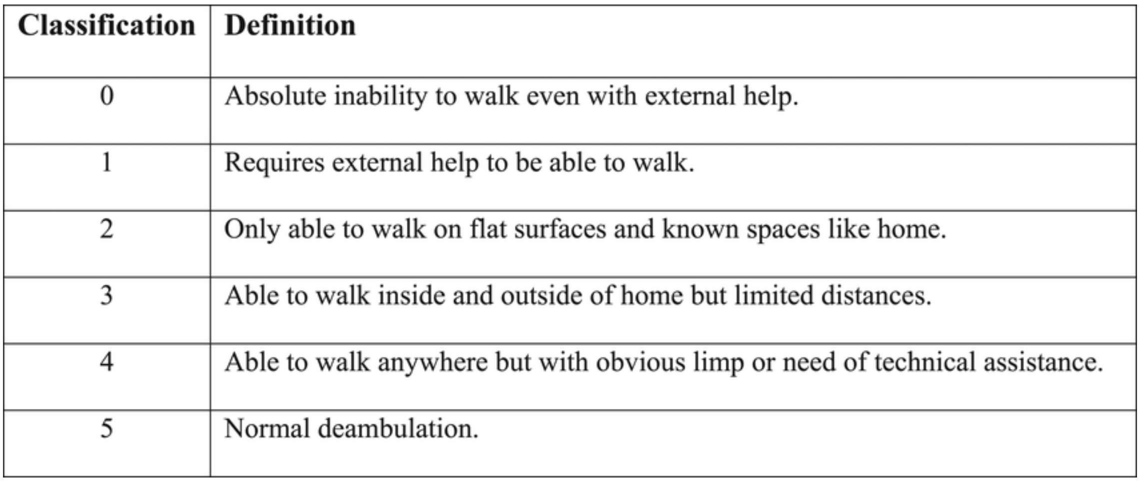
	RE group			**CTR group**		
Author/year	**T0 (m)**	**T1 (m)**	**Difference T1-T0 (m)**	**T0 (m)**	**T1 (m)**	**Difference T1-T0 (m)**
Goffredo et al. (2019)	Ambulant patients: 69,53 Non ambulant patients: 0,00	Ambulant patients: 130,41 Non ambulant patients: 76,13	Ambulant patients: 60,88 Non ambulant patients: 76,13	No CTR group	No CTR group	N/a
Li et al. (2021)	107,88	197,24	89,36	137,80	179,80	42
Molteni et al. (2021)	48,60	139,24	90,64	44,29	149,43	105,14
Pournajaf et al. (2023)	102	194	92	122	172	50
Xie et al. (2023)	155,02	190,7	35,68	160,36	184,62	24,26
Yoo et al. (2023)	N/a	N/a	N/a	N/a	N/a	N/a

4.1.4 Visualization of Functional Ambulation Category Results

Table 7: Functional Ambulation Category results of the Experimental Group - Robotic Exoskeleton (RE) and Control Group (CTR) at baseline (T0) and final (T1) assessments

	RE group			**CTR group**		
Author/year	**T0**	**T1**	**Difference T1-T0**	**T0**	**T1**	**Difference T1-T0**
Goffredo et al. (2019)	N/a	N/a	N/a	N/a	N/a	N/a
Li et al. (2021)	2,65	3,76	1,11	2,93	3,67	0,71
Molteni et al. (2021)	1,08	2,71	1,63	0,656	2,69	2,034
Pournajaf et al. (2023)	1,5	3,5	2	2	3	1
Xie et al. (2023)	3,47	3,8	0,33	3,40	3,67	0,27
Yoo et al. (2023)	0-1= 7 2-4= 2	0-1= 2 2-4=7	N/a	0-1=7 2-4= 1	0-1= 6 2-4= 2	N/a

Table 8: Functional Ambulation Category Units Description (Mehrholz et al., 2007)



Classification	**Definition**
0	Absolute inability to walk even with external help.
1	Requires external help to be able to walk.
2	Only able to walk on flat surfaces and known spaces like home.
3	Able to walk inside and outside of home but limited distances.
4	Able to walk anywhere but with obvious limp or need of technical assistance.
5	Normal deambulation.

4.2 Summarization of results

Table 9: Difference between mean baseline (T0) and mean final (T1) assessment results of the Experimental Group - Robotic Exoskeleton (RE) and Control Group (CTR) in 6MWT and total difference in the mean improvement over the distance reached between the experimental and control group

Author/year	**T1 - T0 (m)**	**T1 - T0 (m)**	**Total difference between the mean improvement over the distance reached between experimental and control group (m)**
	RE group	**CTR group**	
Goffredo et al. (2019)	Ambulant patients: 60,88 Non ambulant patients: 76,13	N/a	N/a
Li et al. (2021)	89,36	42	47,36
Molteni et al. (2021)	90,64	105,14	14,5
Pournajaf et al. (2023)	92	50	42
Xie et al. (2023)	35,68	24,26	11,42
Yoo et al. (2023)	N/a	N/a	N/a

Table Legend

Color - improvement over distance reached between the baseline and final assessment greater in the RE group

Color - improvement over distance reached between the baseline and final assessment greater in the Control group

4.2.1 Summarization of 6-Minute Walk Test results

The following chapter refers to Table 6 which presents the experimental group and the control group 6-Minute Walk Test results at baseline and at final assessments as well as Table 9 which presents the difference between baseline and final assessment results in experimental group and the control group and the mean improvement over the distance reached.

The 6-Minute Walk Test results in the **Goffredo et al. (2019)** study visualize that the study did not include a control group, whereas the experimental group was divided into ambulant and non-ambulant patients. Participants underwent baseline assessments as well as final assessments. The difference between the final assessment result by the ambulant patients was 60,88m and for non-ambulant patients 76,13m showing significant statistical improvement with the lower limb robotic exoskeleton.

In the study by **Li et al. (2021)** the 6-Minute Walk Test, where the researchers were looking at the total distance covered, presents results of the robotic exoskeleton and control group at baseline and final assessments. In the robotic exoskeleton group the difference between the final assessment and the baseline assessment was 89,36m whereas in the control group the difference was 42m, marking a 47,36m difference overall between the improvement reached by the experimental group compared to the control group.

In the study by **Molteni et al. (2021)** the 6-Minute Walk Test presents results of the robotic exoskeleton and control group at baseline and final assessments. In the intervention group which received robotic exoskeleton gait training in addition to conventional therapy the difference between the final assessment and the baseline assessment was 90,64m whereas in the control group the difference in distance was 105,14m showing statistically significant results both in the experimental and the control group but the improvement was 14,5m greater in the control group.

In the study by **Pournajaf et al. (2023)** results from the 6-Minute Walk Test of the experimental group and the control group were evaluated at baseline and through final assessment after the intervention. The difference between the mean final assessment and the mean baseline assessment readings for the intervention group was 92m whereas for the control group the difference was 50m, marking a 42m difference in improvement between the control group and the intervention group marking a significant improvement in the experimental group.

The 6-Minute Walk Test results in the study by **Xie et al. (2023)** display that the difference between the mean final assessment and the mean baseline assessment readings for the intervention group was 35,68m whereas for the control group the difference was 24,26m, marking a 11,42m difference in improvement between the control group and the intervention group.

The study by **Yoo et al. (2023)** have not chosen 6-Minute Walk Test as a primary or secondary outcome measure, therefore the results display N/a.

Table 10: Difference between mean baseline (T0) and mean final (T1) assessment results of the Experimental Group - Robotic Exoskeleton (RE) and Control Group (CTR) in FAC classification reached and total difference in the mean improvement in FAC classification reached between the experimental and control group

Author/year	**T1 - T0**	**T1 - T0**	**Total difference in the mean improvement of FAC classification between experimental and control group**
	RE group	**CTR group**	
Goffredo et al. (2019)	N/a	N/a	N/a
Li et al. (2021)	1,11	0,71	0,4
Molteni et al. (2021)	1,63	2,034	0,404
Pournajaf et al. (2023)	2	1	1
Xie et al. (2023)	0,33	0,27	0,06
Yoo et al. (2023)	N/a	N/a	N/a

Table Legend

Color - improvement over classification reached within the FAC between the baseline and final assessment greater in the RE group

Color - improvement over classification reached within the FAC between the baseline and final assessment greater in the Control group

4.2.2 Summarization of Functional Ambulation Category results

The following chapter refers to Table 8 which presents the experimental group and the control group Functional Ambulation Category results at baseline and at final assessments as well as Table 10 which presents the difference between baseline and final assessment results and the total difference in the mean improvement of FAC classification between experimental and control group.

The study by **Goffredo et al. (2019)** did not present with FAC as a primary or secondary outcome measure, therefor presenting with N/a in the Functional Ambulation Category results.

In **Li et al. (2021)** the Functional Ambulation Category presented results of the robotic exoskeleton and control Group at baseline and final assessments. In the robotic exoskeleton group the difference between the final results and the baseline results regarding classification reached in the 5-point FAC scale was 1,11. In the control group on the other hand the difference was at 0,71. The 0,4 difference between the control and the experimental group shows a greater independence and mobility in walking improvement in the RE group.

The study by **Molteni et al. (2021)** also assessed Functional Ambulation Category at baseline and after intervention in both the control group and the experimental group. In the robotic exoskeleton group the difference between the final results and the baseline results in FAC classification reached was 1,63. In the control group the difference was at 2,034. The 0,404 difference between the control and the experimental group shows a greater independence and mobility in walking improvement in the control group.

The study by **Pournajaf et al. (2023)** presented with a difference of 2 between the final and the initial results for the experimental group and a difference of 1 for the control group. The total difference in the mean improvement of FAC classification between experimental and control group was 1 presenting a greater independence and mobility in walking improvement in the experimental group.

The FAC in the study by **Xie et al. (2023)** displays a difference of 0,33 between the final and the initial results for the experimental group and a difference of 0,27 for the control group. The total difference in the mean improvement of FAC classification between experimental and control group of 0,06 shows a slightly greater overall improvement in FAC classification in the experimental group.

The FAC readings in study by **Yoo et al. (2023)** were presented differently than in previous studies. Overall, the results emphasize greater independence and mobility in walking improvement in the experimental group as more participants reached higher FAC classification when compared to the control group.

4.2.3 Summarization of Users experience and acceptability of lower limb robotic exoskeleton

Table 11: Users experience and acceptability of lower limb robotic exoskeleton

Author/year	**Reporting of user experience**	**Method of evaluating use experience**	**User experience**
Goffredo et al. (2019)	Yes	TAM (Technology Acceptance Model) questionnaire	Positive
Li et al. (2021)	Yes	No direct assessment	Positive
Molteni et al. (2021)	Yes	Usability and acceptance questionnaire	Positive
Pournajaf et al. (2023)	No	-	-
Xie et al. (2023)	No	-	-
Yoo et al. (2023)	Yes	Korean version of the Quebec User Evaluation of Satisfaction with Assistive Technology (K-QUEST 2.0)	Positive

Out of the 6 studies included in the literature review 4 reported on user experiences. The 4 studies that reported on user experiences were the study by Goffredo et al. (2019), Li et al. (2021), Molteni et al. (2021) and Yoo et al. (2023). The study by Pournajaf et al. (2023) and the study by Xie et al. (2023) had no direct discussion of patient experience.

In the study **by Goffredo et al. (2019)** patient acceptance of the lower limb robotic exoskeleton was measured using the TAM (Technology Acceptance Model) questionnaire. The questionnaire has 5 domains; Perceived Usefulness, Perceived Ease of Use, Attitude towards use, Behavioral intention to use and Actual use. According to the results in the study all participants perceived the Overground Exoskeleton Assisted Gait Training positively. The treatment was evaluated as enjoyable and comfortable, with a mean score of > 5 out 7 on the scale. The mean score of < 3 out of 7 in the next domain indicated the treatment was moderately painful and strenuous. Majority of the participants perceived the exoskeleton as useful, would recommend it and would use it in the future.

The study by **Li et al. (2021)** did not use any direct assessment in the form of a questionnaire or a survey. The study did state that there were no adverse effects reported both during and after use of the BEAR-H1 lower limb robotic exoskeleton and that the lower limb robotic exoskeleton was well tolerated.

The study by **Molteni et al. (2021)** assessed patient acceptance using a questionnaire. The name of the questionnaire was 'Usability and Acceptance Questionnaire' and the domains within the questionnaire were comfort, presence of fatigue, presence of pain, enjoyment, advantages, desire to continue and whether they would suggest it to someone further. The questionnaire was related to the perceived degree of these domains, each participant had to assign a score from 0 to 7 where 0 is strongly disagree and 7 is strongly agree. The results in the study demonstrate that the participants perceived the robotic treatment positively. The lower limb robotic exoskeleton was perceived comfortable by the participants with an average of 5.78 ± 1.81 and pleasant (5.91± 1.50). It was perceived as moderately painful with a mean score of 1.09 ± 2.09 and demanding (2.96 ± 2.10). The study participants perceived the lower limb robotic exoskeleton as useful (6.22 ± 1.13) and would like to do further robot assisted gait training in the future (5.57 ± 2.23). Lastly the participants would recommend this form or therapy to others (6.35 ± 1.07).

The study by **Yoo et al. (2023)** used the Korean version of the Quebec User Evaluation of Satisfaction with Assistive Technology (K-QUEST 2.0) to assess patient acceptance. The domains that were investigated were dimensions, weight, adjustments, safety, durability, simplicity of use, comfort and effectiveness. The items were rated on a 5-point Likert scale. The mean score ranges from 3.5 to 4.5 across the sections concluding that most participants positively perceived the exoskeleton. There were remarks regarding the weight, adjustments and durability, but more detail was not provided.

5. DISCUSSION

5.1 Discussion of the research question

In the literature review, evidence from 6 studies has been presented to evaluate the effectiveness of using lower limb robotic exoskeletons in gait rehabilitation by subacute stroke patients. In order to analyze the effectiveness of using lower limb robotic exoskeletons in improving gait by people after subacute stroke the 6-Minute Walk Test and the Functional Ambulation Category data was extracted from the studies included. As effectiveness is not just about clinical outcomes but also about patient adherence, acceptance and toleration to the intervention, user experience was also considered. The analysis of results provides a conclusion favoring the use of lower limb robotic exoskeletons in comparison to the control group which received conventional training. Although not all data demonstrated an advantage for robot-assisted gait training, most studies indicated its effectiveness, providing an overall positive indication of the effectiveness of lower limb robotic exoskeletons in improving gait by patients after subacute stroke. This statement is supported by the systematic review by Yang et al. (2023) which investigated the efficacy of exoskeleton robot assisted training on gait function by chronic stroke survivors. While the participants in the systematic review were exclusively individuals with chronic stroke, the findings nonetheless provide valuable support for the efficacy of exoskeleton robot-assisted gait training. Out of the 10 studies that were reviewed in Yang et al. (2023) study, 6 reported positive effects of robot assisted gait training on gait function, gait performance, physical endurance and balance function. Furthermore, the intervention group was significantly superior in terms of results compared to the control group receiving conventional therapy.

5.1.1 Discussion of the 6-Minute Walk Test results

All 6 studies featured in the literature review, showed an improvement in walking distance over baseline assessments. The data from the 6-Minute Walk Test also provided an insight into robot assisted gait training (intervention) compared to conventional gait training(control). The results suggest that robot assisted gait training generally showed greater improvements in walking distance measured in meters compared to conventional gait training and thereby having greater effectiveness in improving gait by people with subacute stroke. Out of the 4 studies that incorporated a control group and thereby allowing comparison to take place with the experimental group (robot assisted gait training), 75% of the studies showed greater improvement in walking distance in experimental group from baseline assessment to final assessment. The study by Li et al. (2021) marked a 47,36m difference between the mean improvement over the distance reached between experimental and control group, study by Pournajaf et al. (2023) a 42m greater improvement compared to control group and in the study by Xie et al. (2023) 11,42m greater improvement. Signifying that within the same time frame the patients with the intervention were able to improve walking endurance by at least 10m more than the control group would improve. Similar results were obtained in a study by Lee et al. (2023) where the extent of improvement was significantly greater in the robotic exoskeleton training group in terms of knee flexion torque, walking distance and quality of life.

Robotic exoskeletons used in robot assisted gait training generally improved walking endurance by patients, but their advantage over conventional gait training was not consistent across all studies**.**

While both the study by Li et al. (2021) and Pournajaf et al. (2023) presented an improvement of over 40m more in the intervention group compared to the control group, the study by Xie et al. (2023) showed only a small advantage in contrast with the control group of precisely 11,42m suggesting that the effectiveness of lower limb robotic exoskeletons varies.

One study by Molteni et al. (2021) on the other hand noted a 14,5m greater improvement in total walking distance in the control group compared to the intervention group. Both groups improved significantly over time, yet possible reason for greater improvement overall in the control group is a higher proportion of participants unable to walk at baseline assessment with a mean of 0,625 FAC whereas the intervention group had a mean of 1,08 FAC at baseline, potentially facilitating greater improvement in control group. This interpretation is supported by Reichl et al. (2020) which found out that participants having lower FAC score at baseline assessment experienced greater improvements during rehabilitation interventions compared to already ambulatory participants. Therefor conventional gait training alone might yield better results in some contexts.

Due to the limited number of studies and different lower limb robotic exoskeletons being tested, direct comparison could not be done. Based on the difference between the baseline assessment results and the final assessment results we can conclude that best results in terms of improvement in distance reached were by Lokomat Pro followed by Ekso lower limb robotic exoskeleton although presented with low sensitivity and specificity in terms of causal relationships. The length of the intervention and the number of sessions also needs to be considered. Length of intervention ranged from 2 weeks to 4 weeks and the number of sessions from 10-20 in total. In terms of comparability the study by Li et al. (2021) and Pournajaf et al. (2023) both provided their participants with 20 sessions and study by Goffredo et al. (2019) and Molteni et al. (2021) provided their participants with 15 sessions. Variability of intervention lengths limit comparability of outcomes across trials, making it hard to establish standard protocols or guidelines and making it unclear whether greater distance reached in one study with a particular robot is simply due to longer or greater intervention intensity. The dose-response effect has been studied in Clark et al. (2017) yet only proven theoretically and practically found no clear-dose-response relationship.

5.1.2 Discussion of the Functional Ambulation Category results

The FAC scores improved in both the control group and the intervention group in all studies from the initial to the final assessments. The study by Pournajaf et al. (2023) showed the biggest improvement in the RE group reaching a mean result of 2. On the contrary Molteni et al. (2021) presented greater improvement in the control group of 2,034, highlighting the continued effectiveness of conventional gait training by subacute stroke patients.

Similarly to the 6MWT only 4 studies out of 6 were comparable when addressing FAC as an outcome measure. The study by Yoo et al. (2023) used a different scaling system and study by Goffredo et al. (2019) didn’t feature FAC as an outcome affecting validity of the data presented. A total of 75% of the studies presented a greater improvement in FAC in the intervention group to the control group meaning they had a greater ability to walk independently with less need for physical support signifying greater effectiveness in improving gait by people after subacute stroke. The one study that used a different scaling system noted more participants reaching the FAC score 2-4 in the intervention group whereas most participants from the control group remained in FAC 0 to 1 requiring external help to be able to walk. It is evident that lower limb robotic exoskeletons contribute to functional gait improvements, but in some cases, conventional gait training remains equally or more effective**.** This claim is supported by a study by Wu et al. (2023) analyzing the effect of Lokomat robotic-orthosis system on lower extremity rehabilitation in patients with stroke which came to a conclusion that robot assisted gait training utilizing the Lokomat was not superior to conventional gait training in functional walking capacity. Another study by Tam et al. (2025) found out that exoskeleton assisted gait training significantly increased distance walked for those participants that were severely impaired scoring a 0-1 in FAC but not those who were mildly affected scoring FAC 2-3.

Similar conclusion can be drawn from the present study, where greater difference between the baseline and the final assessments was evident when the patients scored from 0 to 2 in the FAC classification than those who scored higher than 2 in the initial assessments in both the experimental and the control group. Lastly the Ekso lower limb robotic exoskeleton posed as the device that led patients to biggest improvement in FAC followed by the Lokomat Pro.

5.1.3 Discussion of population characteristics and user satisfaction

With a mean age range of 50,13 years to 68,24 years the participant demographics accurately represent the stroke population as according to the ‘Global Stroke Fact Sheet 2022’ published by the World Stroke organization, each year over 62% of all strokes occur in people under 70 years of age. Thus, the user experience data is relevant to the users which suffered a subacute stroke and makes it comparable to their needs at their age. Furthermore, the target population were patients with subacute stroke and the participant demographics reflected that as well. Participants included in the study were solely people with subacute stroke. It has been concluded in the study by Koldaş Doğan (2024) that people in the acute and subacute phases of stroke benefit more from robot assisted gait training then people more than 3 months after stroke. This highlights the importance of research within this patient demographic in terms of the use of lower limb robotic exoskeletons.

A positive user experience and acceptability was noted in the studies which reported on this outcome measure. The method of evaluation of user experience varied from questionnaire to evaluation limiting further evaluation of specific areas the user appreciated but the general feedback given from the participants in the intervention group was that the treatment was enjoyable, comfortable and useful with moderate levels of fatigue and discomfort and the majority would recommend it and use it in the future.

5.1.4 Discussion on the outcome measure choice

The 6-Minute Walk Test, Functional Ambulation Category and the user experience data have been retrieved from the included studies to evaluate the effectiveness of using lower limb robotic exoskeletons in improving gait by people after subacute stroke. Both the 6MWT and the FAC measure functional improvement, 6MWT providing a quantitative performance measure and FAC a functional independence score, together covering two key dimensions of gait recovery (Yoo et al., 2022).

The potential drawbacks of using the 6MWT test is that it is influenced by fatigue. Individuals after stroke present with greater fatigability than healthy adults which can influence their walking speed over the 6-minute test. A study by Stookey et al. (2021) confirmed that their participants which suffered from chronic stroke had slower walking speeds, worse dynamic balance and higher oxygen consumption during walking. Patients within this study who were severely impaired (FAC 0-1) may not have been able to complete the test meaningfully. Furthermore, it lacks to as quality of gait and symmetry. Additional assessments would be necessary to capture all dimensions in evaluating improvement of gait.

Since the FAC is an ordinal scale small but clinically significant improvements in ambulation ability may not have been detected limiting the sensitivity of the results. The intervention length within this study was at most 4 weeks therefor 6MWT was used alongside the FAC to provide more clinically meaningful evaluation. As concluded in study by Igarashi et al. (2023), high resolution measures would need to be used to detect small gait changes, otherwise missed when using the FAC due to its categorical nature.

5.1.5 Methodological quality of included studies and variability of scientific rigor

Based on the Downs and Black Checklist and the TREND Statement Checklist results we can conclude that the methodological quality of the included studies was generally good ranging from 20-24 out of 27. Five studies employed the randomized controlled designs which according to the hierarchy of evidence scores the second highest after systematic reviews. One study was a randomized experimental study ranking one level below randomized controlled trials on the hierarchy of evidence.

Variability in the scientific rigor of each study may have influenced the consistency of the results. Firstly, as discussed before length of intervention varied from study to study ranging from 2 to 4 weeks limiting comparability of improvement. The literature review discuses and provides an overview on the short-term effectiveness on the use of lower limb robotic exoskeletons in gait rehabilitation but long-term effectiveness is still unclear. Sample sizes ranged from 17 participants to 89 participants. Uneven sample sizes reduce comparability across studies, they hold an unequal weight in evidence synthesis as large samples have higher statistical power, greater representativeness and overall improve reliability and generalizability of study findings. This statement is supported by study by Biau et al. (2008) stating that larger sample sizes provide more precise estimates of treatment effects.

5.2 Strengths of the study

Articles featured in the literature review were of diverse nature consisting of randomized controlled trials, randomized pilot studies and controlled clinical trials. The literature review has been conducted according to methodological and scientific process to ensure reliability and validity, reproducibility as well as prevent bias. A total of 4 databases have been used each focusing on a different domain; PubMed – Biomedical and life sciences, ScienceDirect – Multidisciplinary, Scientific and Engineering, Cochrane library – evidence-based medicine and systematic reviews and lastly PEDro – Physiotherapy Evidence Database. The variety of databases used ensured that all the aspects of the research question were correctly addressed. The 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (PRISMA) was followed to report on the included studies optimizing the quality of reporting and ensuring a methodological selection process was applied. The study was conducted by a 5th year Applied

Physiotherapy student, with guidance of a thesis supervisor that provided multiple feedback moments during the writing process. With clear, extensive constructive feedback refinements to the literature review were done. A well-defined and structured plan over the 18-month timeframe facilitated a thorough completion of the introduction, theoretical background, methodology, results, discussion, strengths, limitations and the conclusion.

5.3 Limitations

5.3.1 Limitations of studies

Despite the valuable insights that the studies within the thesis provided, there are possible limitations that have to be considered.

The outcome measures that were evaluated in this study was the 6MWT and the FAC due to their ability to measure functional walking ability and endurance. Although these two outcome measures were inclusion criteria in selection process, the visualization of results or scoring system varied between studies limiting comparison to take place. In the study by Goffredo et al., 2019 there was no control group further hindering comparison. Similarly, the methods of evaluating user experience varied from study to study. In the future having one specific method for evaluating user experience in the inclusion criteria would allow more accurate comparison to take place between user experience and acceptability among the different lower limb robotic exoskeletons.

Only 6 studies met the selection criteria and therefore could be included in the study limiting the generalizability of the findings and although lower limb robotic exoskeleton's have been proven to be more effective than conventional therapy across all included outcome measures the evidence strength is low due to the small number of studies included in the literature review. Future research should focus on larger sample size, comparison of more outcome measures to improve quality and generalizability.

Despite generally the findings providing a positive indication of the effectiveness of lower limb robotic exoskeletons over conventional therapy it is unknown what is limiting its implementation in healthcare settings whether it is the financial aspect of high cost and limited funding or need of specialized training and supervision. A meta-analysis by Carpino et al. (2018) backs up the statement quoting that even though the lower limb robotic exoskeletons were more effective in achieving walking independence, they were 2-3 times more expensive than conventional therapy. It is up to the healthcare system in public or private domain to weight out the costs and conclude whether the investment is worth it.

5.3.2 Limitations of work

In addition to the limitations of the included studies, it is important to acknowledge possible constraints related to the research process.

The study has been conducted methodologically, and the interpretation of results has been done with a critical perspective, yet own potential bias in the selection of inclusion criteria cannot be excluded. A solution to minimize own potential bias in the future is to include a second researcher. A total of 6 synonyms were used in the advanced search string for the word “ lower limb robotic exoskeleton”, 7 for “ gait rehabilitation” and 8 for “stroke”. Extending the number of synonyms would have potentially led to more search results, thus more relevant articles across databases. As 4 different databases were used the search string had to be adapted, lack of expertise in the databases and how the search function (Boolean searching) works could have restricted the number of search results. Having an expert proof the search strings in each database outside of PubMed would have resulted in a clearer selection process. Likewise, a Peer review Electronic Search Strategies checklist could have been applied to evaluate the search strategies to ensure that the search strategy was precise, comprehensive and reproducible.

6. CONCLUSION

The aim of the literature review was to evaluate the effectiveness of using lower limb robotic exoskeletons in improving gait by people after subacute stroke. Effectiveness was assessed using outcome measures consisting of 6MWT, FAC and user satisfaction. The results of the literature review suggested an overall positive indication of effectiveness of lower limb robotic exoskeletons as well as favored the use of lower limb robotic exoskeletons in robot assisted gait training in comparison to conventional gait training.

Compared to baseline assessments improvement was statistically significant in both the experimental group receiving robot assisted gait training using lower limb robotic exoskeletons as well as the control group receiving conventional gait training in both walking endurance and ambulation ability. Yet, in the same time frame generally, the experimental group reached better results. The Ekso and Lokomat Pro device were the most effective devices in terms of improvement of gait metrics. Moreover, the user satisfaction was generally positive, with majority recommending it and willing to use it in the future supporting feasibility and acceptability of intervention.

However, the variability in results suggest that robot assisted gait training is not universally superior. In some cases, conventional gait training led to better outcomes, especially where the control group receiving conventional gait training started with lower functional baseline.

Despite studies being of high methodological quality, the heterogeneity across the studies limited the ability to come to strong, generalizable conclusions. Intervention durations were of different lengths and intensity, sample sizes varied, differences in control group composition and scaling systems were present limiting comparability. Small number of included studies limits the generalizability of results. The data retrieved presents short term effectiveness as the maximum length of study intervention was 4 weeks, yet long term effectiveness remains unclear.

Furthermore, the barriers to implementation remain unclear, whether it is due to financial constraints, specialized training or space the studies did not explore the potential restrictions in clinical integration. As technology continues to evolve rapidly, advancements in lower limb robotic exoskeletons are continuously being developed. Future research can specifically look into conducting larger, multicenter randomized controlled trials featuring standardized protocols and outcome measure to ensure greater comparability. Furthermore, it would be beneficial to investigate patient subgroups within the subacute stroke category such as severely impaired or mildly impaired to determine which subgroup is most likely to benefit from the given intervention. While certain correlations were made in terms of which participant subgroups responded most favorably to the intervention, large-scale studies are necessary to validate these trends and establish more generalizable conclusions. Lastly exploring long term effectiveness would aid healthcare setting with the decision process regarding integrating lower limb robotic exoskeletons in gait rehabilitation after stroke.

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8. ATTACHMENTS

Pubmed Search string:

((((((((lower limb robotic exoskeleton[Title/Abstract]) OR (lower extremity-powered exoskeleton[Title/Abstract])) OR (lower limb exoskeleton[Title/Abstract])) OR (lower-limb exoskeleton[Title/Abstract])) OR (Exoskeleton robots for lower limb assistance[Title/Abstract])) OR (lower-limb powered robotic systems[Title/Abstract])) OR (powered exoskeleton[Title/Abstract])) AND ((((((((Gait rehabilitation[Title/Abstract]) OR (locomotor training[Title/Abstract])) OR (gait therapy[Title/Abstract])) OR (gait training[Title/Abstract])) OR (locomotion therapy[Title/Abstract])) OR (walking training[Title/Abstract])) OR (walking therapy[Title/Abstract])) OR (locomotion rehabilitation[Title/Abstract]))) AND ((((((((((Stroke[Title/Abstract]) OR (cerebrovascular accident[Title/Abstract])) OR (sub-acute stroke[Title/Abstract])) OR (sub acute stroke[Title/Abstract])) OR (apoplexy[Title/Abstract])) OR (cerebral accident[Title/Abstract])) OR (cerebral infarction[Title/Abstract])) OR (CVA[Title/Abstract])) OR (ischemic stroke[Title/Abstract])) OR (hemorrhagic stroke[Title/Abstract]))

Cochrane search string:

(((((((("lower limb robotic exoskeleton":ti,ab) OR ("lower extremity-powered exoskeleton":ti,ab)) OR ("lower limb exoskeleton":ti,ab)) OR ("lower-limb exoskeleton":ti,ab)) OR ("Exoskeleton robots for lower limb assistance":ti,ab)) OR ("lower-limb powered robotic systems":ti,ab)) OR ("powered exoskeleton":ti,ab)) AND (((((((("Gait rehabilitation":ti,ab) OR ("locomotor training":ti,ab)) OR ("gait therapy":ti,ab)) OR ("gait training":ti,ab)) OR ("locomotion therapy":ti,ab)) OR ("walking training":ti,ab)) OR ("walking therapy":ti,ab)) OR ("locomotion rehabilitation":ti,ab))) AND ((((((((((Stroke:ti,ab) OR ("cerebrovascular accident":ti,ab)) OR ("sub-acute stroke":ti,ab)) OR ("sub acute stroke":ti,ab)) OR (apoplexy:ti,ab)) OR ("cerebral accident":ti,ab)) OR ("cerebral infarction":ti,ab)) OR (CVA:ti,ab)) OR ("ischemic stroke":ti,ab)) OR ("hemorrhagic stroke":ti,ab))"

TREND Statement Checklist (Des Jarlais et al., 2004) – Goffredo et al., 2019

Paper Section/Topic	Item No.	Descriptor	Reported?	
			✓	Pg #
TITLE and ABSTRACT				
Title and Abstract	1	• Information on how units were allocated to interventions	X	abstract
		• Structured abstract recommended	X	abstract
		• Information on target population or study sample	X	3
INTRODUCTION				
Background	2	• Scientific background and explanation of rationale	X	3 - 6
		• Theories used in designing behavioral interventions		N/A
METHODS				
Participants	3	• Eligibility criteria for participants, including criteria at different levels in recruitment/sampling plan (e.g., cities, clinics, subjects)	X	3
		• Method of recruitment (e.g., referral, self-selection), including the sampling method if a systematic sampling plan was implemented	X	3
		• Recruitment setting	X	3
		• Settings and locations where the data were collected	X	3
Interventions	4	• Details of the interventions intended for each study condition and how and when they were actually administered, specifically including:	X	4
		○ Content: what was given?	X	4
		○ Delivery method: how was the content given?	X	4
		○ Unit of delivery: how were subjects grouped during delivery?	X	4
		○ Deliverer: who delivered the intervention?	X	4
		○ Setting: where was the intervention delivered?	X	4
		○ Exposure quantity and duration: how many sessions or episodes or events were intended to be delivered? How long were they intended to last?	X	4
		○ Time span: how long was it intended to take to deliver the intervention to each unit?	X	4
		○ Activities to increase compliance or adherence (e.g., incentives)	X	4
Objectives	5	• Specific objectives and hypotheses	X	2
Outcomes	6	• Clearly defined primary and secondary outcome measures	X	4
		• Methods used to collect data and any methods used to enhance the quality of measurements	X	4-5
		• Information on validated instruments such as psychometric and biometric properties	X	4-5
Sample size	7	• How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules		N/A
Assignment method	8	• Unit of assignment (the unit being assigned to study condition, e.g., individual, group, community)	X	3
		• Method used to assign units to study conditions, including details of any restriction (e.g., blocking, stratification, minimization)		N/A
		• Inclusion of aspects employed to help minimize potential bias induced due to non-randomization (e.g., matching)		N/A
Blinding (masking)	9	• Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to study condition assignment; if so, statement regarding how the blinding was accomplished and how it was assessed	X	N/A
Unit of Analysis	10	• Description of the smallest unit that is being analysed to assess intervention effects (e.g., individual, group, or community)		N/A
		• If the unit of analysis differs from the unit of assignment, the analytical method used to account for this (e.g., adjusting the standard error estimates by the design effect or using multilevel		N/A

		analysis)		
Statistical methods	11	• Statistical methods used to compare study groups for primary methods outcome(s), including complex methods for correlated data	X	4-5
		• Statistical methods used for additional analyses, such as subgroup analyses and adjusted analysis		N/A
		• Methods for imputing missing data, if used		N/A
		• Statistical software or programs used	X	4-5
RESULTS				
Participant flow	12	• Flow of participants through each stage of the study: enrollment, assignment, allocation and intervention exposure, follow-up, analysis (a diagram is strongly recommended)		N/A
		○ Enrollment: the numbers of participants screened for eligibility, found to be eligible or not eligible, declined to be enrolled, and enrolled in the study	X	3
		○ Assignment: the numbers of participants assigned to a study condition	X	3
		○ Allocation and intervention exposure: the number of participants assigned to each study condition and the number of participants who received each intervention	X	3
		○ Follow-up: the number of participants who completed the follow-up or did not complete the follow-up (i.e., lost to follow-up), by study condition		N/A
		○ Analysis: the number of participants included in or excluded from the main analysis, by study condition	X	3
		• Description of protocol deviations from study as planned, along with reasons		N/A
Recruitment	13	• Dates defining the periods of recruitment and follow-up	X	3
Baseline data	14	• Baseline demographic and clinical characteristics of participants in each study condition	X	3
		• Baseline characteristics for each study condition relevant to specific disease prevention research		N/A
		• Baseline comparisons of those lost to follow-up and those retained, overall and by study condition		N/A
		• Comparison between study population at baseline and target population of interest		N/A
Baseline equivalence	15	• Data on study group equivalence at baseline and statistical methods used to control for baseline differences		N/A
Numbers analyzed	16	• Number of participants (denominator) included in each analysis for each study condition, particularly when the denominators change for different outcomes; statement of the results in absolute numbers when feasible	X	3
		• Indication of whether the analysis strategy was “intention to treat” or, if not, description of how non-compliers were treated in the analyses		N/A
Outcomes and estimation	17	• For each primary and secondary outcome, a summary of results for each estimation study condition, and the estimated effect size and a confidence interval to indicate the precision		N/A
		• Inclusion of null and negative findings	X	5-9
		• Inclusion of results from testing pre-specified causal pathways through which the intervention was intended to operate, if any		N/A
Ancillary analyses	18	• Summary of other analyses performed, including subgroup or restricted analyses, indicating which are pre-specified or exploratory		N/A
Adverse events	19	• Summary of all important adverse events or unintended effects in each study condition (including summary measures, effect size estimates, and confidence intervals)		N/A
DISCUSSION				
Interpretation	20	• Interpretation of the results, taking into account study hypotheses, sources of potential bias, imprecision of measures, multiplicative analyses, and other limitations or weaknesses of the study	X	9-11
		• Discussion of results taking into account the mechanism by which the intervention was intended to work (causal pathways) or	X	9-11

		alternative mechanisms or explanations		
		• Discussion of the success of and barriers to implementing the intervention, fidelity of implementation	X	9-11
		• Discussion of research, programmatic, or policy implications	X	9-11
Generalizability	21	• Generalizability (external validity) of the trial findings, taking into account the study population, the characteristics of the intervention, length of follow-up, incentives, compliance rates, specific sites/settings involved in the study, and other contextual issues	X	10-11
Overall evidence	22	• General interpretation of the results in the context of current evidence and current theory	X	9-11

Downs and Black Checklist for Quality Assessment (Downs & Black, 1998)

	Li et al., 2021	Molteni et al., 2021	Pournajaf et al., 2023	Xie et al., 2023	Yoo et al., 2023
REPORTING					
Q1 Hypothesis/ aim/ objective clearly described	1	1	1	1	1
Q2 Main outcomes in introduction and methods	1	1	1	1	1
Q3 Patient characteristics clearly described	1	1	1	1	1
Q4 Interventions of interest clearly described	1	1	1	1	1
Q5 Principal cofounders clearly described	0	1	1	1	1
Q6 Main findings clearly described	1	1	1	1	1
Q7 Estimates of random variability provided for main outcomes	1	1	1	1	1
Q8 All adverse events of intervention reported	1	1	1	1	1
Q9 Characterstics of patients lost to follow-up clearly described	0	0	0	1	1
Q10 Probability values reported for main outcomes	1	1	1	1	1
EXTERNAL VALIDITY					
Q11 Subjects asked to participate were representative of source population	1	1	1	1	1
Q12 Subjects prepared to participate were representative of source population	1	1	1	1	1
Q13 Location and delivery of study treatment was representative of source population	1	1	1	1	1
INTERNAL VALIDITY – BIAS & CONFOUNDING					
Q14 Study participants blinded to treatment	0	0	0	0	0
Q15 Blinded outcome assessment	1	1	1	1	1
Q16 Any data dredging clearly described	0	0	0	0	0
Q17 Analyses adjust for differing lengths of follow-up	1	1	1	1	1

Q18 Appropriate statistical tests performed	1	1	1	1	1
Q19 Compliance with interventions was reliable	1	1	1	1	1
Q20 Outcome measures were reliable and valid	1	1	1	1	1
Q21 All participants recruited from the same source population	1	1	1	1	1
Q22 All participants recruited over the same time period	1	1	1	1	1
Q23 Participants randomized to treatment(s)	1	1	1	1	1
Q24 Allocation of treatment concealed from investigators and participants	0	1	1	1	0
Q25 Adequate adjustment for confounding	1	1	1	1	1
Q26 Losses for follow-up taken into account	0	0	0	1	1
POWER					
Q27 Sufficient power to detect treatment effect at significance level of 0.05	0	0	1	0	0
TOTAL	20	22	23	24	23