The Effects of Incorporated Exoskeletal-Assisted Walking in SCI Acute Inpatient Rehabilitation
PI: Ann M. Spungen EdD
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Summary of Changes from Previous Version:

Affected Section(s)	Summary of Revisions Made	Rationale

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STATEMENT OF COMPLIANCE

Provide a statement that the trial will be conducted in compliance with the protocol, International Council on Harmonisation Good Clinical Practice (ICH GCP) and applicable state, local and federal regulatory requirements. Each engaged institution must have a current Federal-Wide Assurance (FWA) issued by the Office for Human Research Protections (OHRP) and must provide this protocol and the associated informed consent documents and recruitment materials for review and approval by an appropriate Institutional Review Board (IRB) or Ethics Committee (EC) registered with OHRP. Any amendments to the protocol or consent materials must also be approved before implementation. Select one of the two statements below. If the study is an ***intramural*** *NIH study, use the second statement below:*

1. The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

    - United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

    National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.
    OR
2. The trial will be conducted in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP), applicable United States (US) Code of Federal Regulations (CFR), and the [specify NIH Institute or Center (IC) [Terms and Conditions of Award. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the funding agency and documented approval from the Institutional Review Board (IRB), and the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor, if applicable, except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection and ICH GCP Training.
    For either option above, the following paragraph would be included:
    The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	The Effects of Incorporated Exoskeletal-Assisted Walking in SCI Acute Inpatient Rehabilitation	
Study Description:	A randomized controlled trial	
Objectives:	Primary Objective:	Primary Objectives: To determine the effects of acute inpatient rehabilitation (AIR) with exoskeletal-assisted walking (EAW) compared with AIR without EAW (same total therapy time) on the changes from admission to discharge in the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) upper and lower extremity motor scores, Functional Independence Measure (FIM) scores, and Spinal Cord Independence Measure (SCIM) scores as classified by clinicians. Primary hypothesis: At discharge, compared to the baseline data (collected at admission), the AIR with EAW group will have significantly greater changes in ISNCSCI, FIM, and SCIM scores compared to the AIR without EAW group.
	Secondary Objectives:	To determine the effects of AIR with EAW compared to AIR without EAW on reducing pain using the International Spinal Cord Injury Basic Pain Data Set 2.0 (ISCIBPDS 2.0) measures where type of pain is classified with the Spinal Cord Injury Pain Instrument (SCIPI). Secondary hypothesis: At discharge, compared with baseline, the AIR with EAW group will report significantly more reduction in the average intensity of the participant's worst pain over the preceding 7 days than the AIR without EAW group.
	Tertiary Objectives:	To determine the effects of AIR with EAW compared with AIR without EAW on reducing a specific systemic inflammatory mediator (C reactive protein, CRP). Tertiary hypothesis: At discharge, as compared with baseline, the AIR with EAW group will have greater reductions in measured values for CRP than the AIR without EAW group.
Endpoints:	Primary Endpoint:	The changes from admission to discharge in the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI)

		upper and lower extremity motor scores, Functional Independence Measure (FIM) scores, and Spinal Cord Independence Measure (SCIM) scores
	Secondary Endpoints:	Pain evaluation using the International Spinal Cord Injury Basic Pain Data Set 2.0 (ISCIBPDS 2.0) measures where the type of pain is classified with the Spinal Cord Injury Pain Instrument (SCIPI).
	Tertiary Endpoints:	systemic inflammatory mediator (C reactive protein, CRP)
Study Population:	Individuals with SCI who stay in the SCI acute inpatient rehabilitation	
Phase:	NA	
Description of Sites/Facilities Enrolling Participants:	Icahn School of Medicine at Mount Sinai	
Description of Study Intervention:	In the intervention group, participants will receive locomotor training provided with an Ekso™ powered exoskeleton. The EAW training will be incorporated into the designated therapy times (3 hours of physical therapy (PT) and/or occupational therapy (OT)).	
Study Duration:	3 years	
Participant Duration:	Twenty to thirty minute per session, one session a day, equal or more than 3 sessions/days per week, from enrollment in the study to discharge from the acute inpatient rehabilitation. Different participants have different duration of participation based on their length of inpatient stay.	

2 INTRODUCTION

2.1 STUDY RATIONALE

The purpose of this fellowship is to conduct a prospective, randomized controlled trial (RCT) in two groups to determine if exoskeletal-assisted walking (EAW) training, incorporated in acute inpatient rehabilitation (AIR), is a feasible, safe and efficacious approach to facilitating functional independence and reducing pain and inflammatory response in those with a spinal cord injury (SCI) who are candidates for locomotor training during AIR.

2.2 BACKGROUND

Paralysis from traumatic SCI results in an abrupt reduction in the level of daily physical activity. Depending on the neurological level and completeness of SCI, those with more severe SCI may lose neuromuscular control of the upper extremities, trunk, and/or lower extremities which can result in a loss of the ability to sit, stand and walk and to perform activities of daily living (ADLs). For people with SCI, the ability to walk consistently rank at the top of their priority list for recovery [1, 2]. Most feel that their quality of life is lower than it could be without SCI due to difficulties in independently performing daily activities, finding a job or vocation, and challenges in participating in all that a community may offer [3]. Reductions in physical activity and other physical changes also promote pain in individuals with SCI, including the two main subtypes of neuropathic and nociceptive musculoskeletal pain [4]. Approximately 80% of people with SCI experience ongoing pain [5], and about 20% of people with SCI indicate that this pain interferes with work and daily activities [6]. Furthermore, immobilization and paralysis after SCI often leads to a sedentary life style resulting in loss of muscle mass and gain of adiposity [7]. This change in ratio of muscle to fat mass predisposes to insulin resistance and the development of type II diabetes mellitus as well as to obesity [7-10]. A compromised immune system has also been reported to occur after SCI with evidence of increased markers of systemic inflammation, including elevated CRP [11-15]. Changes in cholesterol and triglyceride levels as well as immunosuppression, such as reduced natural killer, T-cell, and lymphocyte functions, have also been reported [11-16]. The inflammatory response may also play an important role in the modulation of pain after SCI [17, 18]. Clinical data shows that elevated inflammatory mediators are present in persons with acute or chronic SCI, including factors that mediate pain in preclinical models [14, 19-21]. Reductions of functional activity and increased pain and
inflammatory response all worsen each other, negatively impacting an individuals' quality of life.

Locomotor training for people with SCI using body weight supported treadmill training (BWSTT) has been reported to increase muscle mass [22, 23], improve cardiovascular function [24], decrease spasticity [25], decrease pain [26], and preserve bone density [23, 27]. Although walking is considered a light intensity physical activity, a number of studies have shown clinically meaningful health benefits

from a consistent regimen of walking, in diverse populations including those who are overweight or obese [28, 29], postmenopausal [30], and elderly [31, 32]. In people with chronic obstructive pulmonary disease and peripheral artery disease, walking impairment has been associated with higher levels of systemic inflammatory cytokines [33, 34]. In persons with SCI, consistent exercise has been associated with a reduction in inflammatory mediators, e.g. CRP, as is seen in able-bodied people [35]. These data support the view that even light physical activity in persons with SCI could have clinically meaningful therapeutic effects resulting potentially in a reduction of systemic inflammation.

In theory, adding locomotor training to AIR may have the potential to improve motor recovery and functional independence through neuroplasticity. A study has shown that in an animal model locomotor training in the acute stage could improve the connectivity of the spinal neurons after SCI, resulting in reflex excitability and reduced spasticity [36]. People with SCI who participated in intensive locomotor training (five days per week for 8 weeks) using BWSTT within 6 months after SCI had a greater rate of improvement in lower-extremity motor scores than those who received this intervention in the chronic stage of SCI [37]. Patients also report the desire to begin physical training as soon as possible after acute SCI and to continue the inpatient training longer than conventionally available [38].

Powered exoskeletons are a technology that can offer overground locomotion for people with SCI who would ordinarily be unable to walk and have been suggested as a way to promote increased function and quality of life [39]. In studies pioneered by Dr. Spungen (co-mentor), exoskeletons have been studied in the chronic (>6 months post) SCI population for about seven years with preliminary reports showing benefits in mobility, health and quality of life (QOL) outcomes [40, 41]. While walking in an exoskeleton, people with SCI stand upright with full weight bearing through the feet [41] and walk while activating trunk and lower limb muscles. This activation may facilitate improvements in neuroconnectivity [39]. EAW has several benefits over BWSTT. It provides ground gait training experience that offers the potential benefits of standing and gait training with just one trainer and requires less of a constant equipment space allotment in an inpatient rehabilitation setting. EAW also possesses the unique potential for use after inpatient discharge to continue training and allow functional use in home, work, and community settings.
Previous studies show that EAW can elicit moderate-intensity activity for people with SCI, and participants can learn to walk without hands-on physical assistance by another person [40, 42-44]. Subjective reports from inpatients who were given the opportunity to use an exoskeleton during AIR in Mount Sinai Hospital had comments such as: "it was really great to have the legs moving again", "walking helped with regaining trunk support" and resulted in "good sensations in the legs and feet".

Despite the potential functional and health benefits of using EAW training in persons in SCI AIR, there are few studies published that have used, or are using an EAW intervention in early inpatient rehabilitation for patients with acute/sub-acute SCI. As such, there is a critical gap in knowledge that limits the use of EAW across the clinical care spectrum in SCI: we don't know if the EAW can be

effectively incorporated in clinical practice and if adding EAW into AIR program is better than traditional AIR without EAW. We expect this prospective randomized control trial (RCT) to determine if EAW training during AIR is a feasible, safe and efficacious approach to facilitate functional independence and to reduce post-SCI pain, as well as inflammation.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

There are several potential risks associated with the EAW and the testing procedures.

1) EAW training has the potential risks of hypotension, falls resulting in bone fracture, muscle soreness, joint damage, or other musculoskeletal injury, and/or autonomic dysreflexia (AD).

2) Persons using the Ekso may also be at risk for bruising, skin abrasion, pressure sores, soft tissue injury, or adverse tissue reaction from direct contact of the body with the device. Notable contact points exist between the sacrum and back pack, hip pads and greater trochanters, shin pads and shins, and with the straps for the thighs and legs.

3) Other possible risks to exoskeleton use include discomfort, triggered spasms, reflex bowel or bladder activity, diastolic hypertension and changes in blood pressure and heart rate, or autonomic instability during use of the device.

4) The person operating the controller could initiate a use error by incorrectly inputting individual participant specifications which could affect the participant's ability to move correctly with the device thus increasing risk to the participant.

5) Lastly, the device itself could malfunction due to premature battery failure, interference with other electrical equipment or devices, electrical shock, or unanticipated operation (stoppage or unintended movement).

6) Psychological risks could include anxiety (e.g., when you begin walking training), altered mood when you complete the questionnaires, and depression (e.g., when you end the study).

7) Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

2.3.2 KNOWN POTENTIAL BENEFITS

There is no expected benefit to subjects. However, possible benefits may be improving subjects' activities of daily living or reducing their pain or systemic inflammation from early intervention of walking training using EAW, although it is not guaranteed. These benefits may not continue after subjects discharge from the hospital and stop the walking training.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS
Primary	
To determine the effects of AIR with EAW compared with AIR without EAW (same total therapy time) on the changes from admission to discharge in the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) upper and lower extremity motor scores, Functional Independence Measure (FIM) scores, and Spinal Cord Independence Measure (SCIM) scores as classified by clinicians.	ISNCSCI examination results FIM scores SCIM scores
Secondary	
To determine the effects of AIR with EAW compared to AIR without EAW on reducing pain using the International Spinal Cord Injury Basic Pain Data Set 2.0 (ISCIBPDS 2.0) measures where type of pain is classified with the Spinal Cord Injury Pain Instrument (SCIPI).	Intensity of pain
Tertiary/Exploratory	
To determine the effects of AIR with EAW compared with AIR without EAW on reducing a specific systemic inflammatory mediator (C reactive protein, CRP).	CRP results

4 STUDY DESIGN

4.1 OVERALL DESIGN

A two-group, single-blinded (raters are not part of intervention) and randomized clinical trial (RCT) with stratification for traumatic or non-traumatic injury will be performed. The stratification will help to ensure balanced groups prior to randomization.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

1. Age 18 years or greater
2. Height between 5'2" and 6'2" (1.6 meters to 1.9 meters)
3. Weight less than 220 pounds (100 kilograms)
4. Near Normal range of motion (ROM), as follows: 1) Hip: more than 5 degrees of extension and 110 degrees of flexion; 2) Knee: Full extension to 110 degrees of flexion; 3) Ankle: at least 0 degree of dorsiflexion to 25 degrees of plantarflexion
5. Are eligible for locomotor training as part of inpatient rehabilitation
6. Independent with static sitting balance
7. Sufficient function upper extremity strength to manage walking aid (front-wheeled walker, platform walker, or crutches)
8. Able to follow directions

5.2 EXCLUSION CRITERIA

1. Uncontrolled cardiovascular conditions (i.e. heart failure, angina, hypertension)
2. Inability to sit upright due to orthostatic hypotension
3. Any form of progressive SCI as defined by the physician, such as cancers
4. Upper leg length discrepancy > 0.5" or lower leg discrepancy >0.75"
5. Skin integrity issues in areas that would contact the device or that would likely be made worse by device use
6. Pregnancy, colostomy, mechanical ventilation
7. Any other medical issue in the judgment of his/her clinicians that might prevent safe standing or walking
8. Non-English Speaking
9. Cognitive and/or communicative disability (e.g. due to brain injury). Participants must be able to follow directions
well and demonstrate learning capability.

5.3 STRATEGIES FOR RECRUITMENT AND RETENTION

Prospective subjects will be recruited following admission to the AIR unit at Mount Sinai Hospital. Attending physicians and rehabilitation clinicians will identify patients admitted to the unit who may be eligible for the study. The informed consent process will be provided to interested and prospective

participants. Once the consent form is signed, a research team member and the study physician will begin the screening process for the inclusion/exclusion criteria.

6 STUDY INTERVENTION

6.1 STUDY INTERVENTION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

Intervention (N=20): In the intervention group, participants will receive locomotor training provided with an Ekso™ powered exoskeleton according to the standard of care of AIR at Mount Sinai Hospital with the exception that the EAW training will be incorporated into the designated therapy times (3 hours of physical therapy (PT) and/or occupational therapy (OT)) which will be provided as determined by the clinical team from the earliest time they are identified to be able to safely stand, through discharge. The goal of EAW intervention is to complete three or more sessions of EAW training a week during the AIR period (after enrolling into the study until discharge). One EAW session is defined to have at least 20 minutes of uptime in the device (based on data output from EksoTM, device, not including donning and doffing time). EAW sessions will include device fitting, instruction for sit-to-stand and stand-to-sit maneuvers; balance and fall protection training; and walking on smooth indoor surfaces with total or variable device assistance. The clinical team will determine the frequency, duration, and intensity of each EAW session based on the participant's response to the previous session.

Control (N=10): In the control group, participants will receive standard of care AIR which includes three hours of PT and/or OT per day until they are discharged. This standard of care AIR may include bed mobility, balance, strength, gait, transfers, and wheelchair mobility training to improve participants' independence in activities of daily living, such as bathing, eating, dressing, grooming, and wheelchair use but does not include EAW. The two groups (control and intervention) will have the same total amount of therapy time.

6.2 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

Eligible participants will be randomized into either the intervention group or the control group. In order to provide more opportunities for participants to accept EAW training, the intervention group will have 20 participants, and the control group will have 10 participants.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

Subjects may be withdrawn without their consent if it is found that they do not meet eligibility criteria for the study, or if during an exoskeleton instruction session, research staff or clinicians have concerns about the participant's performance or safety and feel that discontinuing involvement would be in the best interest of the participant.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

If subjects decide to stop being in the research study, they can contact the Principal Investigator or the research staff. There are no early withdrawal procedures that will be required of participants. Participants may also withdraw their permission for the use and disclosure of any of their protected information for research, but they must do so in writing to the Principal Investigator at the address on the first page. Even if they withdraw their permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Their health information may still be used or shared after their withdraw their authorization if they have an adverse event from participating in the research study.

If they decide they don't want their samples and/or data to be used for research anymore, they can contact the researcher and ask to have their samples and/or data removed from future use. If any samples or data have already been shared without their identity, it won't be possible to retrieve them because no one will know who they are.

Samples and data that have already been used will not be affected by their decision. Any samples and/or data that are still linked to their identity by a code the researcher has will be withdrawn so that no future sharing of their samples and/or data will take place. If their samples have already been deposited in an external repository, the study team will request that their samples be removed.

7.3 LOST TO FOLLOW-UP

N/A

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 EFFICACY ASSESSMENTS

Demographic data:

1. Age: age of patient in years
2. Sex: male (M) or female (F)
3. Race: race of patient
4. Diagnosis: primary diagnosis of the patient from medical chart (include level of injury from the International Standard for Neurological Classification of Spinal Cord Injury (ISNCSCI) examination and the completeness of injury from American Spinal Injury Association Impairment Scale (AIS)) at admission and discharge.
5. Date (or year) of injury: the date of getting the diagnosis
6. Admission date: the date that the patient starts acute inpatient rehabilitation
7. Discharge date: the date that the patient discharged

Pain scale: 1) International Spinal Cord Injury Basic Pain Data Set (ISCIBPDS) to identify pain locations, average intensity (over the past three days), and influence on daily activities. 2) Spinal Cord Injury Pain Instrument (SCIPI) to classify patients' neuropathic or nociceptive pain. ISCIBPDS and SCIPI will be performed on the enrollment and discharge dates. 3) Participants' current level of pain before and after walking training will be recorded in the walking
session data form.

Walking session results include session date, total up time, total walk time, and total steps. If subjects can walk independently 10-meter walking test and Walking Index for Spinal Cord Injury II (WISCI II) will be tested. In the 10 MWT, the participant will be asked to walk 10 meters (without the exoskeleton) at their fastest, comfortable pace. The time to cover this distance will be timed with a stopwatch. The 20-item WISCI-II provides a rank-order rating of the ability of a person with SCI to walk 10 meters in relation to the severity of impairment. Ratings consider the amount of assistance and the types of assistive devices (e.g., leg braces) required to walk. Both the 10 MWT and WISCI II will be evaluated after enrollment (within 1-2 days) and before discharge from AIR (±2 days).

The presence and degree of systemic inflammation will be determined by measuring the concentration of serum C-reactive protein (CRP). CRP is an acute-phase protein that rises in response to inflammation. It is not specific to inflammation caused by SCI. Six ml of blood will be drawn in a red top tube, two times (after enrolling into the study and before discharge) for a total of 12 ml of blood over the course of the full study for analyses of the inflammatory markers. CRP is routinely measured from patients clinically when it is important to assess the degree of inflammation is present. The analysis will compare changes in levels of CRP pre- and post-intervention, in both the EAW with AIR or AIR groups.

8.2 SAFETY AND OTHER ASSESSMENTS

Once the study attending physicians (Drs. Bryce, Escalon, and Huang) and rehabilitation clinicians identify potential subjects for the study, they will introduce the study to them and ask their permission for referring them to the study team. If they express interest, the study team will approach subjects and provide more detailed information about the study to them. If participants agree, the informed consent process will be proceeded.

Once the consent form is signed, research team members and the study physicians (Drs. Bryce, Escalon, and Huang) will begin the screening process using the study's inclusion/exclusion criteria. Medical record review will also be conducted to identify any other medical concerns that might increase the risks associated with participation.

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

There are several potential risks associated with the EAW and the testing procedures.
1) EAW training has the potential risks of falls resulting in bone fracture, muscle soreness, joint damage, or other musculoskeletal injury, and/or autonomic dysreflexia (AD).
2) Persons using the Ekso may also be at risk for bruising, skin abrasion, pressure sores, soft tissue injury, or adverse tissue reaction from direct contact of the body with the device. Notable contact points exist between the sacrum and back pack, hip pads and greater trochanters, shin pads and shins, and with the straps for the thighs and legs.
3) Lastly, the device itself could malfunction due to premature battery failure, interference with other electrical equipment or devices, electrical shock, or unanticipated operation (stoppage or unintended movement).

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

A Serious Adverse Event (SAE) is defined by the ICH for Clinical Safety Data Management and CSP Global SOP 3.6.2, as any untoward medical occurrence that: results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, a congenital anomaly/birth defect, or any other condition that, based upon medical judgment, may jeopardize the subject and require medical, surgical, behavioral, social or other intervention to prevent such an outcome.

8.3.3 ADVERSE EVENT REPORTING

In this study, all AEs will be collected by the Sponsor. The reporting period for AEs begins when the participant signs the informed consent form and continues until the participant's completion or early termination of participation or the end of the study.

8.3.4 SERIOUS ADVERSE EVENT REPORTING

All AEs and SAEs that occur throughout the study, whether study-related or non-related, will be documented and reported to the IRB, as per IRB regulations. AE/SAE report forms will be completed within 48 hours throughout the study for each participant. We will keep a running log of all AE/SAEs (anticipated and unanticipated) throughout the study. Any SAE will be reported to the IRB within 24 hours, and the study will be suspended until the study physician states that it is safe to resume the study.

9 STATISTICAL CONSIDERATIONS

9.1 SAMPLE SIZE DETERMINATION

All statistical tests will be 2-sided. The outcome measures will be tested at a 0.05 level of significance. SPSS will be used to conduct the statistical analyses. All participants who have EAW sessions will be included (regardless of the number of sessions they complete before discharge, but the number and reason of missing EAW sessions will be recorded). To test the three main hypotheses of the proposed study, the change score of each outcome between baseline and discharge will be calculated. The change score will be compared between the intervention and control groups using independent t-test analyses (if the outcomes are not normally distributed, Mann-Whitney tests will be used).
Since the primary aim of the study is to compare the improvement of FIM scores between the groups, the FIM score results from the preliminary data were used to perform the power analysis for this study. In the preliminary data, the mean change in FIM score from the intervention group was 35±12, and the control group was 22±13. The effect size of the FIM score change in our preliminary data was 1.07 (controlling for the different number of participants between the two groups). The power analysis showed that using the effect size (1.07) and 0.05 level of significance with two-sided analysis in independent t-test, a total of 30 participants will provide the study 80% power.
To account for an expected attrition rate of about 25%, 40 participants will be enrolled. It is expected that 30 participants will complete the study (the reasons and number of screening failures and dropouts will be recorded).

9.2 STATISTICAL ANALYSES

9.2.1 GENERAL APPROACH

All statistical tests will be 2-sided. The outcome measures will be tested at a 0.05 level of significance. SPSS will be used to conduct the statistical analyses. All participants who have EAW sessions will be included (regardless of the number of sessions they complete before discharge, but the number and reason of missing EAW sessions will be recorded). To test the three main hypotheses of the proposed study, the change score of each outcome between baseline and discharge will be calculated. The change score will be compared between the intervention and control groups using independent t-test analyses (if the outcomes are not normally distributed, Mann-Whitney tests will be used).

In addition to the primary analysis, several secondary analyses will be performed. 1) Each of the outcomes will be compared between pre- and post-EAW training using a paired t-test analysis (if the outcomes are not normally distributed, Wilcoxon signed-rank test will be used). 2) Analyses will be performed to determine the relationships between the change of outcome measures and EAW training time (including sessions, up time, walking time, or total number of steps per session and across all sessions) using correlation coefficients, regression analyses (stepwise and logistic), analyses of covariance, and nonparametric analyses as appropriate. 3) An additional exploratory post

hoc analyses will be to determine the relationship of participant's' baseline characteristics with successful use of the exoskeleton. This post hoc analysis would serve as pilot data to begin to determine who is a good candidate for EAW training during AIR for a future study.

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