EFFECT OF THE ROBOTIC-ASSISTED GAIT TRAINING DEVICE (Welwalk®) PLUS PHYSIOTHERAPY IN IMPROVING THE AMBULATORY FUNCTION IN SUB-ACUTE HEMIPLEGIC STROKE PATIENTS: ASSESSOR-BLINDED, RANDOMIZED CONTROLLED TRIAL

Mr. Natapatchakrid Thimabut

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ผลการฟื้นฟูการเดินของผู้ป่วยอัมพาตครึ่งซีกจากโรคหลอดเลือดสมองระยะกึ่งเฉียบพลันโดยใช้หุ่นยนต์ฟื้นฟูการเดิน (Welwalk®) ร่วมกับการทำกายภาพบำบัด: การทดลองแบบสุ่มปกปิดผู้ประเมิน

นายณฐภัทชกฤษฎ์ ทิมาบุตร

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
สาขาวิชาเวชศาสตร์คลินิก ไม่สังกัดภาควิชา/เทียบเท่า
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By	Mr. Natapatchakrid Thimabut
Field of Study	Clinical Sciences
Thesis Advisor	Associate Professor KRISNA PIRAVEJ, M.D.
Thesis Co Advisor	Instructor PATTARAPOL YOTNUENGNIT, M.D.

Accepted by the FACULTY OF MEDICINE, Chulalongkorn University in Partial Fulfillment of the Requirement for the Doctor of Philosophy

..... Dean of the FACULTY OF MEDICINE

(Professor SUTTIPONG WACHARASINDHU, M.D.)

DISSERTATION COMMITTEE

..... Chairman

(Associate Professor WASUWAT KITISOMPRAYOONKUL, M.D.)

..... Thesis Advisor

(Associate Professor KRISNA PIRAVEJ, M.D.)

..... Thesis Co-Advisor

(Instructor PATTARAPOL YOTNUENGNIT, M.D.)

..... Examiner

(Associate Professor JARIYA BOONHONG, M.D.)

..... Examiner

(Associate Professor Aurauma Chutinet, M.D.)

..... External Examiner

(Assistant Professor PARIT WONGPHAET, M.D.)

ณฐภัทชกฤษฎ์ ทิมาบุตร : ผลการฟื้นฟูการเดินของผู้ป่วยอัมพาตครึ่งซีกจากโรคหลอดเลือดสมองระยะกึ่งเฉียบพลันโดยใช้หุ่นยนต์ฟื้นฟูการเดิน (Welwalk®) ร่วมกับการทำกายภาพบำบัด: การทดลองแบบสุ่มปกปิดผู้ประเมิน. (EFFECT OF THE ROBOTIC-ASSISTED GAIT TRAINING DEVICE (Welwalk®) PLUS PHYSIOTHERAPY IN IMPROVING THE AMBULATORY FUNCTION IN SUB-ACUTE HEMIPLEGIC STROKE PATIENTS: ASSESSOR-BLINDED, RANDOMIZED CONTROLLED TRIAL) อ.ที่ปรึกษาหลัก : รศ. พญ.กฤษณา พิรเวช, อ.ที่ปรึกษาร่วม : อ. นพ.ภัทรพล ยศเนืองนิตย์

กว่าทศวรรษที่ผ่านมามีการศึกษาประสิทธิภาพของหุ่นยนต์ฟื้นฟูการเดินในผู้ป่วยโรคหลอดเลือดสมองอย่างกว้างขวาง หุ่นยนต์ฟื้นฟูการเดินเวลวอล์ค (Welwalk®) ถูกพัฒนาฟังก์ชั่นการเหยียด งอ หมุน ในการเคลื่อนไหว ตามหลักการทฤษฎีพื้นฐานของเรียนรู้ของระบบประสาทสั่งการในการเคลื่อนที่ เพื่อช่วยให้ผู้ป่วยโรคหลอดเลือดสมองสามารถกลับมาเดินได้ด้วยตนเอง

วัตถุประสงค์: เพื่อศึกษาผลการฟื้นฟูการเดินของผู้ป่วยอัมพาตครึ่งซีกจากโรคหลอดเลือดสมองระยะกึ่งเฉียบพลันโดยใช้หุ่นยนต์ฟื้นฟูการเดินเวลวอล์ค (Welwalk®) ร่วมกับการทำกายภาพบำบัด

ระเบียบวิธีวิจัย: การศึกษานี้เป็นการทดลองแบบสุ่มปกปิดผู้ประเมิน โดยสุ่มอาสาสมัครผู้ป่วยโรคหลอดเลือดสมอง ระยะกึ่งเฉียบพลันไม่เกิน 90 วัน และคะแนนความสามารถในการเดิน FIM-walking score ไม่เกิน 3 เป็น 2 กลุ่มคือ กลุ่มที่ได้รับการฟื้นฟูสมรรถภาพการเดินโดยใช้หุ่นยนต์ฟื้นฟูการเดินเวลวอล์ค (Welwalk®) ร่วมกับการทำกายภาพบำบัด และกลุ่มที่ได้รับกายภาพบำบัดเพียงอย่างเดียว อาสาสมัครจะได้รับการฟื้นฟูตามโปรแกรม โดยกลุ่ม Welwalk จะได้รับการฝึกด้วยหุ่นยนต์ฟื้นฟูการเดินเวลวอล์ค (Welwalk®) 40 นาที/วัน และฝึกเดินพื้นราบ 20 นาที/วัน ร่วมกับการทำกายภาพบำบัดพื้นฐาน 60 นาที/วัน ละกลุ่มควบคุมได้รับการฝึกเดินพื้นราบ 60 นาที/วัน ร่วมกับทำกายภาพบำบัดพื้นฐาน 60 นาที/วัน ทั้งสองกลุ่มได้รับการฝึก 5 วัน/สัปดาห์ นาน 6 สัปดาห์ (30 ครั้ง) ทำการตรวจประเมินคะแนนความสามารถในการเดินฟิมวอล์ค (FIM walking score) การทดสอบสมรรถภาพทางกายด้วยการเดิน 6 นาที (6-minute walk test: 6MWT) ความสามารถในการทำกิจวัตรประจำวัน (Barthel ADL index) และองค์ประกอบของตัวแปรการเดิน (gait parameter) ก่อนการฝึก (pretest), ฝึกครบ 15 ครั้ง (15^{th} session), ฝึก 30 ครั้ง (30^{th} session) แบบปกปิดผู้ประเมิน

ผลการศึกษา: จากการวิเคราะห์ความแปรปรวนพหุคูณ (MANOVA) ของผลการศึกษาทั้งหมดปฏิสัมพันธ์กับตัวแปรร่วมคืออายุและเพศพบว่า เมื่อเปรียบเทียบคะแนนความสามารถในการเดิน กลุ่ม Welwalk ดีกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ (Welwalk 5.00±0.36, control 3.46±0.49, p = 0.012) และจากผลการทดสอบความเปลี่ยนแปลงของสมรรถภาพทางกายด้วยการเดิน 6 นาที สามารถเดินได้ระยะทางมากกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ หลังการฝึกครั้งที่ 15 (Welwalk 74.85±17.69, control 15.58±4.04, p = 0.018) และมีการพัฒนาประสิทธิภาพในการเดินที่ดีกว่ากลุ่มควบคุมอีกด้วย (p = 0.008) การเปลี่ยนแปลงความสามารถในการทำกิจวัตรประจำวันพบว่ากลุ่ม Welwalk มีคะแนนสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญ หลังการฝึกครั้งที่ 30 (p = 0.000) อย่างไรก็ตามไม่พบความแตกต่างระหว่างทั้งสองกลุ่มในองค์ประกอบของตัวแปรการเดิน แม้ว่ากลุ่ม Welwalk จะมีแนวโน้มการพัฒนาสูงกว่ากลุ่มควบคุมก็ตาม ยกเว้นอัตราส่วนความสมมาตรของการเดิน ที่พบว่ากลุ่ม Welwalk มีแนวโน้มที่ดีกว่าอย่างมีนัยสำคัญ หลังการฝึกครั้งที่ 30 (p = 0.044)

สรุป: จากผลการศึกษาพบว่าการใช้หุ่นยนต์ฟื้นฟูการเดินเวลวอล์ค (Welwalk®) ร่วมกับการทำกายภาพบำบัด ช่วยเพิ่มความสามารถในการเดินและความสามารถในการทำกิจวัตรประจำวัน ของผู้ป่วยโรคหลอดเลือดสมองระยะกึ่งเฉียบพลัน ได้เร็วกว่าการทำกายภาพบำบัดเพียงอย่างเดียว

สาขาวิชา	เวชศาสตร์คลินิก	ลายมือชื่อนิสิต .....
ปีการศึกษา	2563	ลายมือชื่อ อ.ที่ปรึกษาหลัก .....
		ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

5974857030 : MAJOR CLINICAL SCIENCES

KEYWORD: Robotic-assisted Gait Training Device. Stroke. Hemiplegia. Gait training. Welwalk®

Natapatchakrid Thimabut : EFFECT OF THE ROBOTIC-ASSISTED GAIT TRAINING DEVICE (Welwalk®) PLUS PHYSIOTHERAPY IN IMPROVING THE AMBULATORY FUNCTION IN SUB-ACUTE HEMIPLEGIC STROKE PATIENTS: ASSESSOR-BLINDED, RANDOMIZED CONTROLLED TRIAL. Advisor: Assoc. Prof. KRISNA PIRAVEJ, M.D. Co-advisor: Instr. PATTARAPOL YOTNUENGNIT, M.D.

Over the last decades, the effectiveness of robot-assisted gait training devices has been extensively studied. Welwalk® has been developed to support ambulatory functions in stroke patients based on motor learning theory.

Objective: To investigate the effects of Welwalk® plus physiotherapy versus physiotherapy alone, in improving ambulatory function in subacute stroke patients with hemiplegia.

Methods: The study was an assessor-blinded, randomized controlled trial. Twenty-six subacute stroke patients with hemiplegia were randomized and allocated into either the Welwalk group or control. All patients received 30 training sessions (5 days/week for six weeks) which included standard physiotherapy treatment (60 min) and ambulation training (60 min). In the ambulation training session, the Welwalk group received robotic training (40 min) and ground ambulation training (20 min). The control group received only ground ambulation training (60 min). The outcomes were assessed at the initial session, the end of the 15th and the 30th sessions. Comparisons within group and between the groups were conducted.

Results: The Welwalk group showed greater improvements from baseline than control in: (1) the Functional Independence Measure (FIM)-walk score, at the end of the 15th session (P = 0.012), (2) the efficiency of FIM-walk, at the end of the 15th session (P = 0.008), (3) walking distance in the 6-minute walk test (6MWT), at the end of the 15th session (P = 0.018), (4) the Barthel Index for Activities of Daily Living (ADL), at the end of the 30th session (P < 0.001), and (5) gait symmetry ratio, at the end of the 30th session (P = 0.044). Other gait parameters showed the tendencies of improvement in the Welwalk group, but there were no significant differences.

Conclusion: Welwalk® plus physiotherapy showed early improvements in walking ability and Barthel ADL index compared with ground level training plus physiotherapy in subacute stroke patients with hemiplegia.

Field of Study:	Clinical Sciences	Student's Signature .....
Academic Year:	2020	Advisor's Signature .....
		Co-advisor's Signature .....

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CHAPTER I

INTRODUCTION

1. Background and Rationale

Stroke is the major health problem worldwide.[1] It is the second major cause of death for people above 60 years old, and the fifth major cause in people aged 15 to 59 years old concerning the World Health Organization (WHO). The problem affects approximately 6.2 million people for a global death on stroke each year, and 6 percent of people will have stroke in their life time worldwide.[2]

In Thailand, stroke is one of the major causes of death and long term disability.[3] The country annual morbidity and mortality from stroke were 352.3 and 38.7 per 100,000 population respectively in 2014.[4] Hemiplegia is one of the most nationwide disabilities resulting from stroke.[5] Hemiplegic stroke patients usually have difficulty with everyday activities; especially, the ambulatory function.[5, 6] To reduce movement disabilities in sub-acute stroke is easier to improve gait performance than chronic stroke.[7] Gait rehabilitating strategy is based on activating the muscles to stimulate the central nervous system. The specific movement patterns and intensive training program are concerned the most important factors for rehabilitation.[8] Thus, current researchers and clinicians try to find the best way that can improve brain recovery and return sub-acute stroke patients to restoration of independent gait.[9]

In recent years, the robotic-assisted gait training device has heightened concern about the highly effective use for gait rehabilitation in sub-acute hemiplegic stroke patient.[10, 11] The devices have been developed in various models during the last few years.[12] They can be classified in to two categories, namely end-effector (GEO, GT1,etc.) and exoskeleton (LOKOMAT, etc.). The end-effector is the gait trainer type that held the patient's feet in place on the foot plate with partial body weight support, and the robot will drive the patient's feet to move directly. The exoskeleton has been developed differently. It worn over both lower extremities directly controls hip and knee joint while walking on treadmill with or without partial

body weight support.[13] Although both of robotic-assisted types are the effective way for gait training, the exoskeleton has limitations in uses. Exoskeleton restricted range of motion of the pelvis because of its rigid control over hip joints.[14, 15] Moreover, it can cause a stress-related joint from misalignment between orthotic joint and patient's joint. Thus, it may be less effective use in stroke patients.[13, 14, 16]

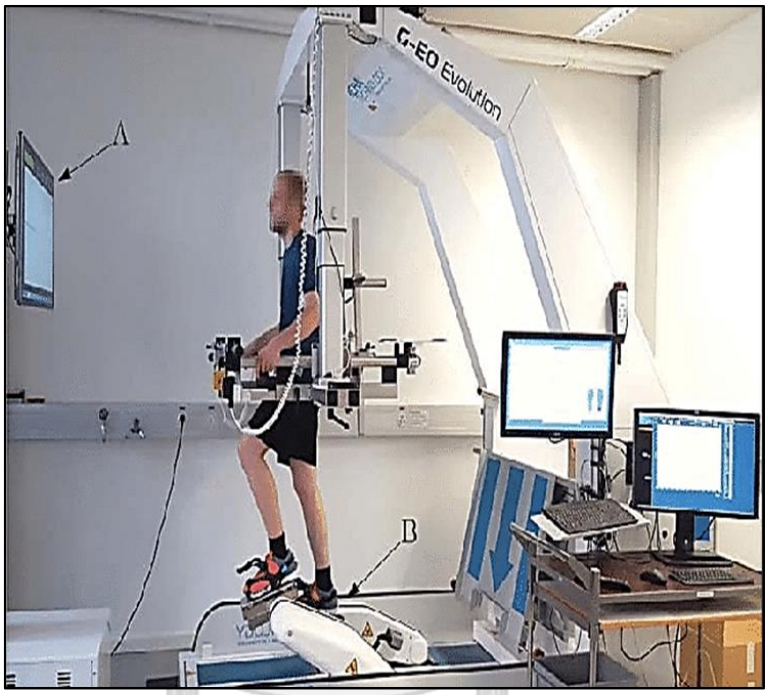


Figure 1 G-EO system end-effector gait rehabilitation robot[17]

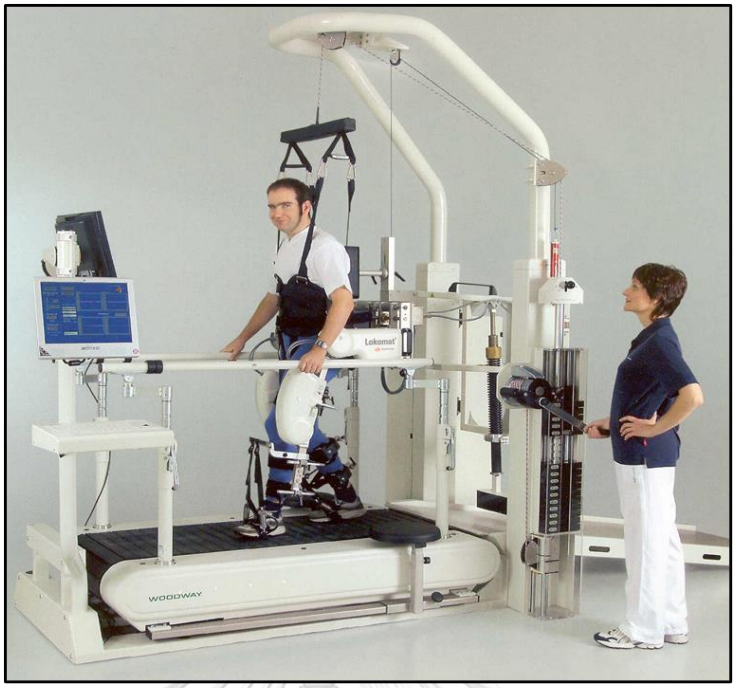


Figure 2 LOKOMAT[18]

The Gait Exercise Assist Robot (Welwalk®) that has been developed in the collaboration between Toyota Motor Corporation and the Department of Rehabilitation Medicine, School of Medicine, Fujita Health University, Japan is an adapted exoskeleton type of the locomotor rehabilitation robot. Welwalk® is on demand partial exoskeleton robot that provides a way of dealing with exoskeleton's problems.

Its components include a knee-ankle-foot robot, a low floor treadmill, a safety suspending device (can be used as for body weight support), a robot weight support device, a monitor for patient use, and a control panel. The system determines the gait cycle from the pressure sensor on the plantar region of the robot and the knee joint angle, and executes flexion and extension of the knee joint at the appropriate timing.[12] It uses the motorized orthosis to control hip and knee joint during walking on treadmill as the exoskeleton type, and lets patients to put their effort into weight shifting and stepping in walking as end-effector type. Besides, it does not harm joint strain due to misalignment between orthotic joint center and

true center of movement of patient's joints. Its ability to trigger walking training according to unloading of the hemiparetic leg may leads to better clinical outcome.

Over the last decades, the effectiveness of exoskeleton type of the robotic-assisted gait training devices have been widely studied, Saito et al. published one study in sub-acute post-stroke hemiplegic patients which reported comparable effects on gait function between the Welwalk® robotic training and conventional gait training.[12, 13] However, its effect was not clear in their study because there were a few patients recruited. Therefore, the aims of this study are to advance on the knowledge of study whether using of Robotic-assisted gait training device plus physiotherapy would improve the ambulatory function in sub-acute post-stroke hemiplegic patients.

Figure 3 The Gait Exercise Assist Robot (Welwalk®)

2. Research question

Whether the Robotic-assisted gait training device plus physiotherapy would improve the ambulatory function in sub-acute post-stroke hemiplegic patients.

3. Study Design

A prospective, single-blinded, randomized controlled trial study

4. Objectives

To compare the effect of Robotic-assisted gait training device plus physiotherapy to the effect of physiotherapy alone on the ambulatory function in sub-acute hemiplegic stroke patients.

To determine the improvement in efficiency of FIM walk on the ambulatory function in sub-acute hemiplegic stroke patients.

Sub-objective:

To determine the improvement in 6-minute walk test, gait parameters, and Barthel ADL index in sub-acute hemiplegic stroke patients.

To identify satisfaction and facilitation of using Robotic-assisted gait training device in sub-acute hemiplegic stroke patients.

5. Hypothesis

Using Welwalk® rehabilitation robot plus physiotherapy can improve ambulatory function in sub-acute hemiplegic stroke patients.

6. Conceptual Framework

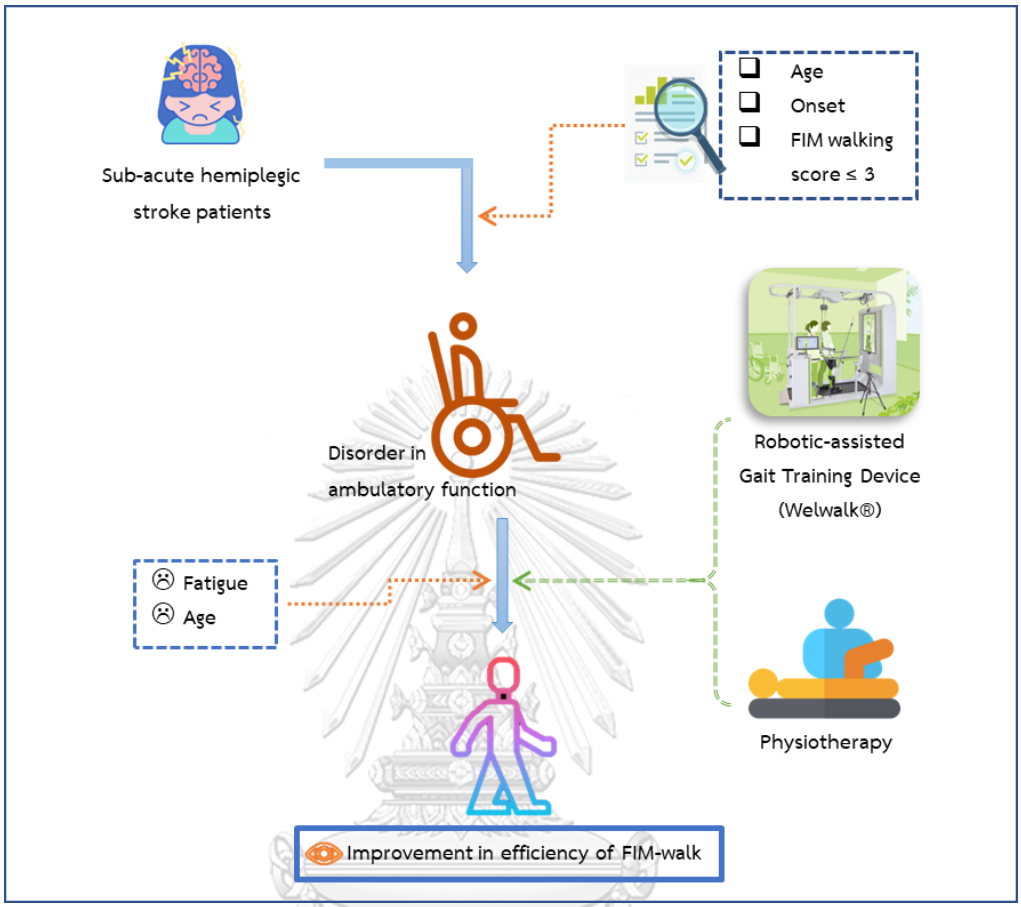


Figure 4 Conceptual framework

7. Keywords

Robotic-assisted Gait Training Device, Stroke, Hemiplegia, Gait training, Welwalk®

8. Operational definition

Stroke

Stroke is a condition of poor blood flow to the brain causes cell death. There are two main types of stroke: ischemic, due to lack of blood flow, and hemorrhagic, due to bleeding. Both cause parts of the brain to stop functioning (NIH, 2014).

9. Expectable benefits

- The benefits of using Welwalk® rehabilitation robot training in combination with standard physiotherapy can assist movement function in sub-acute post-stroke hemiplegic patients.
- Welwalk® can facilitate walking function in activities of daily living (ADL) for sub-acute post-stroke hemiplegic patients.

CHAPTER II

LITERATURE REVIEW

Research about rehabilitation robotic assistive devices have grown rapidly and the number of therapeutic rehabilitation robotic-assisted gait training technology has increasingly developed in recent year. Robotic rehabilitation therapy can affect motor recovery after stroke with certain advantages. There are two types of robotic assisted-gait training technology: end-effector and exoskeleton. End-effector type work by applying mechanical forces to the distal segments of limbs with offering the advantage of easy setup. Conversely, exoskeleton device is commonly designed for automated gait training on a treadmill with the reinforced orthosis. The orthosis has robotic axes aligned with the anatomical axes of the wearer; therefore, it provides direct control of individual joints, which can minimize abnormal posture or movement.[14] Both end-effector and the exoskeleton devices are very complicated and more expensive. Though the devices are highly effective use for locomotor training, exoskeleton has limitation on pelvis restriction that decrease chance of active weight shifting in stroke patients.[13, 14] Regarding this problem of exoskeleton type, Welwalk® rehabilitation robot training is developed to deal with this problem because it has a new improved design as an adapted on demand partial exoskeleton type. It also may be better and suitable for stroke patients than the original one.

Newly design of the robotic assistive gait training device: an adapted-on demand partial exoskeleton robotic-assisted gait training device

The exoskeleton type is the wearable device that work in tandem with the user. It places on the user's body and acts as reinforce or restore human performance. Although the exoskeleton type has proven to be effective complements to conventional physiotherapy in patients with sub-acute stroke, it limits to improve the active weight shifting in stroke patients. Therefore, patients may wear any kind of ankle-foot orthosis (AFO) or knee ankle-foot orthosis (KAFO) to prevent knee instability.[19, 20] Due to the limitation of structural design, all of the

exoskeleton robot only allows overground walking training, and shows lack of variations in the gait patterns.[13] This would cause much harm on patients whose hip range of motion are severely impaired. During the patient is using the robotic legs, the speed of the motor drive for the exoskeleton must match with speed of the treadmill, in order to ensure the safety of the patient.[10]

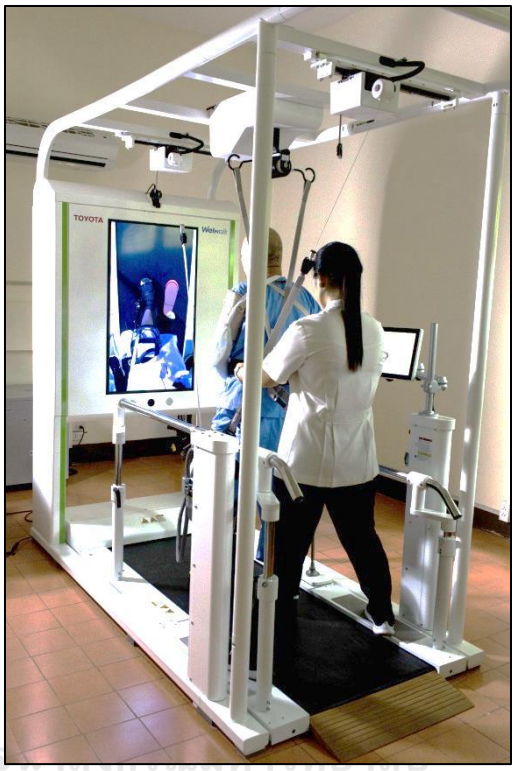


Figure 5 The Gait Exercise Assist Robot (Welwalk®)

In 2017, The Gait Exercise Assist Robot (Welwalk®) has been developed in the collaboration between Toyota Motor Corporation and Department of Rehabilitation Medicine, School of Medicine, Fujita Health University is an adapted-on demand partial exoskeleton type. The robot designed to provide a highly efficient gait exercise environment for post-stroke hemiplegic patients, which assists only the hemiplegic lower limb and allows flexible adjustments of the motor learning variables. The device is composed of a knee-ankle-foot robot, a low floor treadmill, a safety suspending device (can be used as a body weight support device), a robot

weight support device, a monitor for patient use, and a control panel. The robot controls gait cycle from the pressure sensor and the knee joint angle and adjusts flexion and extension of the knee joint at the appropriate timing. For this structural design, patients can create a chance of active weight shifting to achieve the final goal of the independent walking. One of the characteristics of Welwalk® is enriched feedback, the monitor at the front can display either the full-length image (mirror image) or the foot image. When foot image is selected, the target position of foot contact with the floor is displayed as overlay. As acoustic feedback, the device can be set to emit a sound of success when the weight on the hemiplegic side exceeds the set value, and a sound of failure when the knee gives way. On the control panel for use by the therapist, more detailed information including weight bearing on the hemiplegic side and trajectory of the center of foot pressure can be displayed at real time.[12]

Hirano et al. studied the effectiveness of Gait Exercise Assist Robot (GEAR) in stroke patients with hemiplegia. GEAR was used as the gait training assist system in their study. In patients with severe paralysis and gait disturbance requiring the use of a knee-ankle-foot orthosis, gait training using GEAR combined with conventional physiotherapy was compared with physiotherapy alone. Six patients who met the following criteria were recruited: patients with hemiplegia caused by primary supratentorial intracerebral hemorrhage or cerebral infarction, within 60 days after onset, aged 20 to 75 years, Functional Independence Measure (FIM) walking score ≤ 3, Stroke Impairment Assessment Set (SIAS) lower extremity total score ≤ 6, and use of a knee-ankle-foot orthosis. Rehabilitation was conducted for a maximum of 3 hours a day, including 40 min of gait training using GEAR. The primary outcome measurement was the improvement in efficiency of FIM-walk, defined as the gain in FIM walking score from the baseline to supervised walking divided by the number of weeks required. The study found that the mean improvement in efficiency of FIM walk was 1.0 in the GEAR group and 0.54 in the control group and was significantly higher in the GEAR group. This study demonstrated that gait training using GEAR may facilitate early improvement in gait independence.[12]

From the literature reviews, we found that the effective of using the adapted-on demand partial exoskeleton type may improve gait function and motor recovery. However, the benefits and advantages of using the adapted-on demand partial exoskeleton type in gait training for sub-acute hemiplegic stroke patients need more studies in clinical aspect. Therefore, we aim to advance on the knowledge of study whether using of Welwalk® rehabilitation robot training plus physiotherapy would affect the ambulatory function in sub-acute post-stroke hemiplegic patients.

CHAPTER III

RESEARCH METHODOLOGY

1. Study Design

A prospective, single-blinded, randomized controlled trial study

2. Flow diagram of Methodology

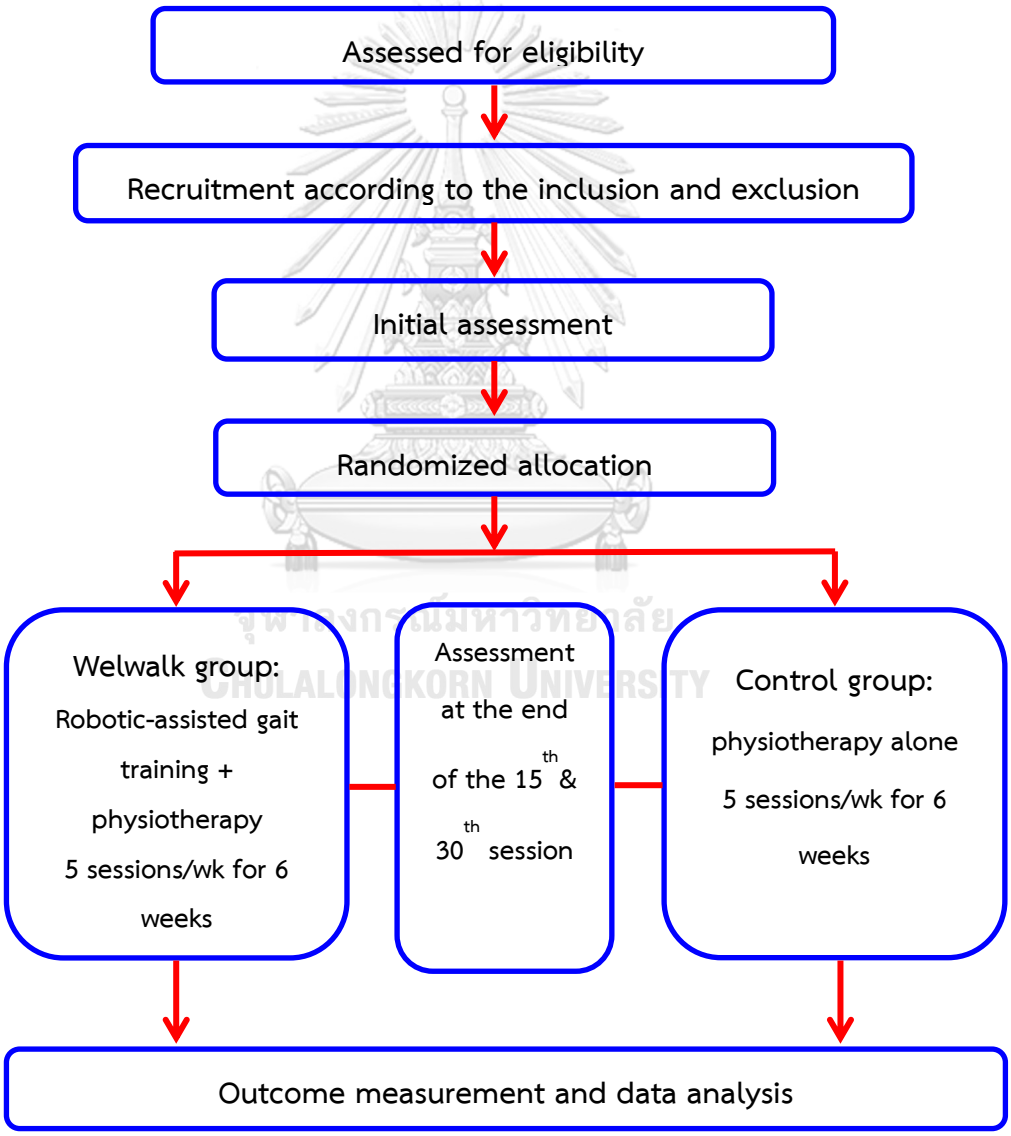


Figure 6 Flow diagram

3. Subjects

Sub-acute hemiplegic stroke patients at King Chulalongkorn Memorial Hospital and Thai Red Cross Society Rehabilitation Center, Thailand.

3.1 Inclusion criteria

1. Patients or family gave written informed consents to participant in this study
2. Patients with first episode hemiplegia caused by primary supratentorial intracerebral hemorrhage or cerebral infarction
3. Patients meet the following criteria at the initial assessment:
    - Within 90 days after onset
    - Aged 20-79 years
    - Body weight is between 40-80 kg.
    - Functional Independence Measure (FIM) walking score ≤ 3
    - Brunnstrom stage of lower extremity ≤ 3
    - Able to understand the meaning of the study and follow the instruction

3.2 Exclusion criteria

1. History of myocardial infarction
2. Symptom of angina / arrhythmia
3. Symptom of respiratory disorders
4. Muscular or other neurological disorders such as diabetic neuropathy
5. Communicable infection
6. Joint contracture / limb deformity that affects walking: range of motion of hip < 5-degree, knee extension < -5-degree, ankle dorsiflexion with knee extension position < 5-degree
7. Heterotopic ossification that restricts the range of motion of joints of lower extremities

8. Being vulnerable to fracture such as severe osteoporosis of spine, lower extremities
9. Incontinence of urine or feces
10. Poor control of hypertension: BP ≥ 180/120 mmHg
11. Inadequate control of tachycardia: HR ≥ 120 bpm
12. Training restriction due to reduce cardiac function or respiratory dysfunction
13. Visual or auditory impairment hindering training
14. Pregnant patient
15. Recent participation in other clinical trials

3.3 Sampling and allocation

Simple sampling and Randomized allocation by using computerized program.

4. Materials and methods

The study was approved by the Institutional Review Board of the Faculty of Medicine, Chulalongkorn University (IRB No. 641/60), and was registered on the Thai Clinical Trials Registry (TCTR) website (www.clinicaltrials.in.th) by named "Effect of the Robotic-assisted Gait Training Device (Welwalk®) plus physiotherapy in improving the ambulatory function in sub-acute hemiplegic stroke patients: investigator-blinded, randomized controlled trial" (TCTR20180419004). All eligible sub-acute hemiplegic stroke patients in this study were recruited from January 2018 till January 2021 for research at King Chulalongkorn Memorial Hospital and Thai Red Cross Society Rehabilitation Center, Thailand. All patients participated in the study after themselves or their families had provided written informed consent before data collection. All information and patient identifiers were kept anonymous to strictly protect patient confidentiality.

4.1 Method of assignment to study groups

A prospective, assessor-blinded, parallel-group, randomized controlled trial was conducted. The inclusion and exclusion criteria were described in previous

section. 26 patients were randomized assigned to either the Welwalk group (n=13) or the control group (n=13) by an independent person who selected numbers from sealed envelopes containing numbers chosen by a random number generator. The randomization was restricted to permuted blocks of different sizes. Each random permuted block was transferred to a sequence of consecutively numbered, sealed, opaque envelopes that are stored in a locked drawer until required. As each patient formally entered the trial, the researcher opened the next envelope in the sequence in the presence of the patient.

4.2 Materials/Instruments

The Gait Exercise Assist Robot (Welwalk®) is an adapted-on demand partial exoskeleton robotic-assisted gait training device. The system determines the gait cycle from the pressure sensor on the plantar region of the robot and the knee joint angle and executes flexion and extension of the knee joint at the appropriate timing. It uses the motorized orthosis to control hip and knee joint during walking on treadmill as the exoskeletal type, and lets patients to put their effort into weight shifting and stepping in walking as end-effector type.[21]

4.2.1 Mechanism of the Gait Exercise Assist Robot

Welwalk® system includes a knee-ankle-foot robot/robotic orthosis (Figure 7), a low floor treadmill, a safety suspending device/a body weight support, a robot weight support device, a monitor for patient use (Figure 8), and a control panel (Figure 9).

Figure 7 A knee-ankle-foot robot/robotic orthosis

The knee ankle-foot robot is worn only on the hemiplegic limb. The robotic knee joint has a motor attached, and the weight can be canceled by the robot weight support device. Therefore, the patient will feel free during walking. Moreover, a pressure sensor is set up at the plantar region of the robotic leg for the determination of gait cycle at the appropriate timing. The effort of the patient can be accompanied with minimal assistance from the early stage of gait training until the final gait pattern without excessive compensatory motion, with minimal assistance.[21]

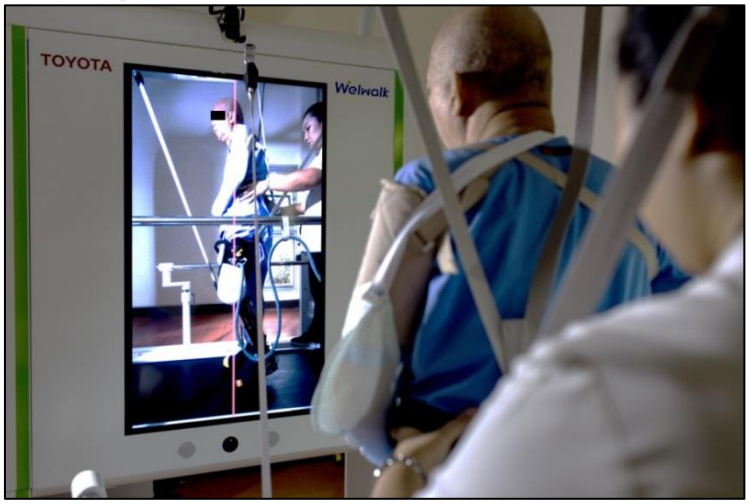


Figure 8 A monitor for patient use

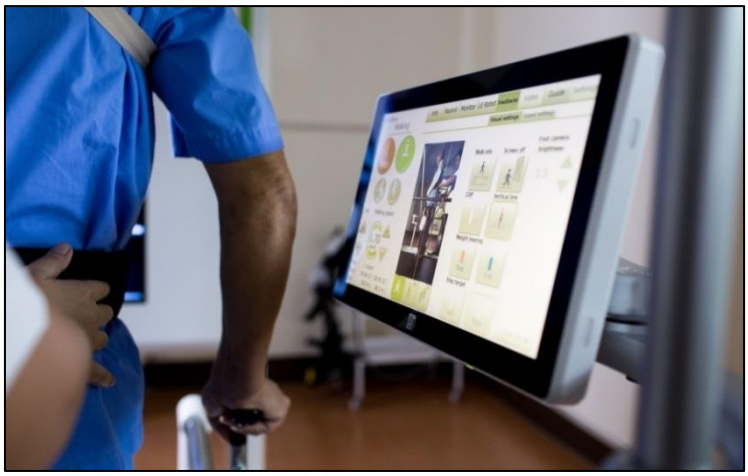


Figure 9 A control panel

4.3 Assessment tools

FIM-walking score

The FIM instrument, a reliable and valid score, is used to assess gait ability. Seven categories (1-7) are distinguished to give detail on the physical support needed by patient while walking, irrespective of the technical aids used. Level 1 indicates a patient who cannot walk at all or needs the help of two therapists. Level 7 indicates a patient who can walk independently; however, level 5 is considered enough for independent walking. An assessor assessed the Functional Ambulation Category from the patients walked a 50 meters distance.[22]

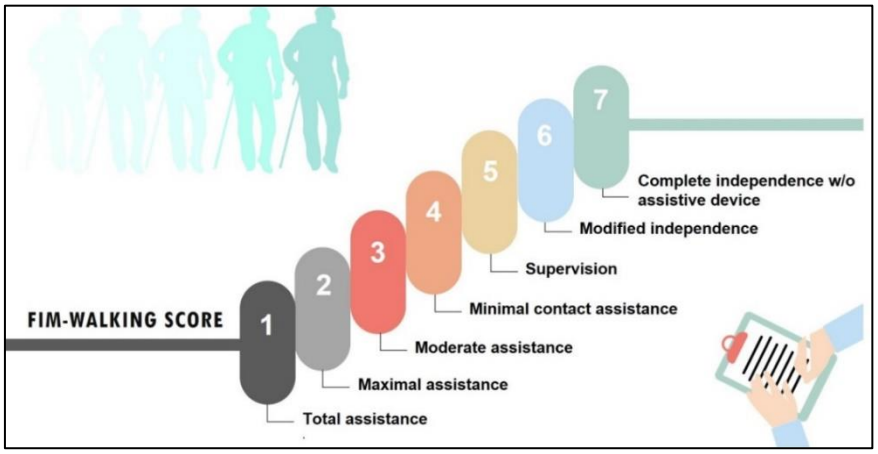


Figure 10 Evaluation of FIM-walk

XSENS

The improvement of gait parameters verified by XSENS (Figure 11). It is a kinematic 3D motion capture and inertial sensors based upon data fusion algorithms. This device can evaluate motion analysis, gait speed, cadence, step length, step width, and gait symmetry as the quantitative data.[23]

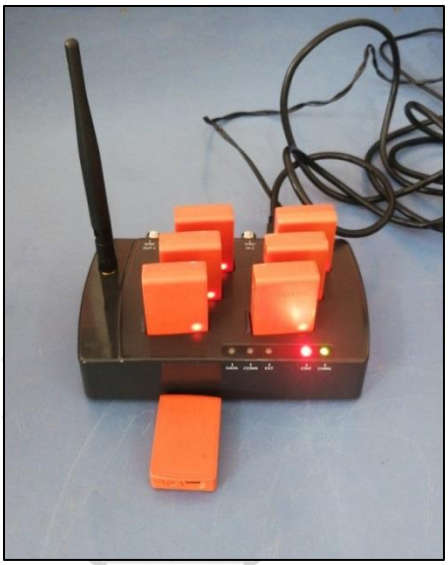


Figure 11 XSENS

In this study, the sensors will be placed on pelvis and lower limb, since the improving of walking ability is only defined. Pelvis: place the sensor on the sacrum. Upper leg: a few centimeters above mid-thigh, on the outer side of the leg. It is recommended placing the sensor on the IT band, between the quadriceps and hamstrings muscles. Lower leg: a few centimeters below the knee. Foot: place the sensor in the middle of the foot, and consider to leave enough room on either side of toe and ankle motion does not influence the sensor (Figure 12). A biomechanical model is represented for walking ability (Figure 13), and then the data can be analyzed by a visual 3D program (Figure 14).

Figure 12 The placement of XSENS sensor

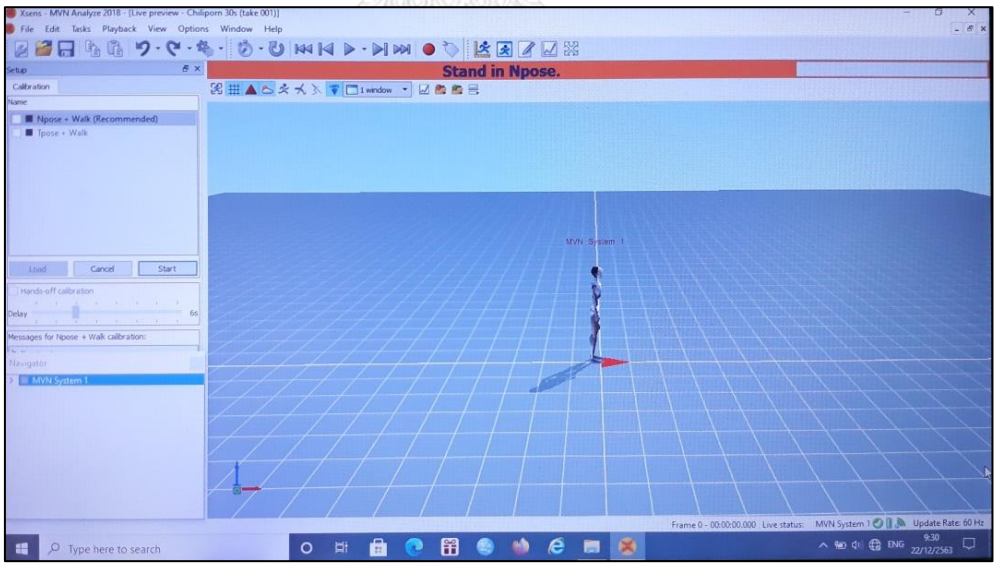


Figure 13 A biomechanical model

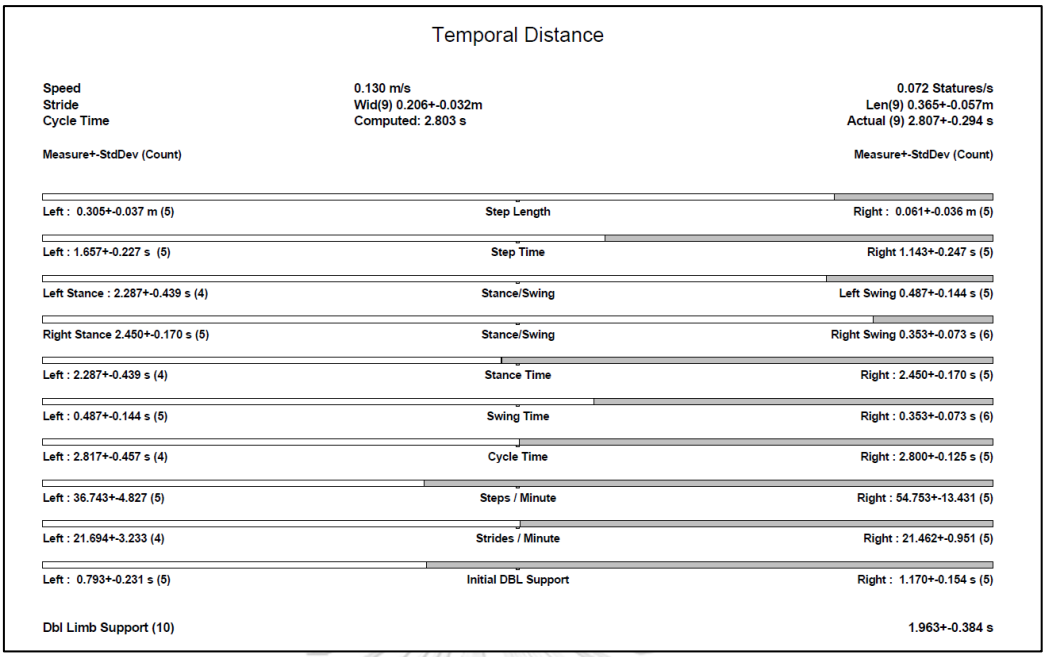


Figure 14 Data analyzed by visual 3D program

6-Minute Walk Test (6MWT)

The 6-Minute Walk Test is a sub-maximal exercise test used to assess aerobic capacity and endurance. The distance covered over a time of 6 minutes is used as the outcome by which to compare changes in performance capacity.[24]

4.4 Experimental tasks

A prospective, assessor-blinded, parallel-group, randomized controlled trial was conducted. The inclusion and exclusion criteria were described in previous section. 26 patients were randomized and assigned to either the Welwalk group (n=13) or the control group (n=13) by an independent person who selected numbers from sealed envelopes containing numbers chosen by a random number generator. The randomization was restricted to permuted blocks of different sizes. Each random permuted block was transferred to a sequence of consecutively numbered, sealed, opaque envelopes that are stored in a locked drawer until required. As each patient

formally entered the trial, the researcher opened the next envelope in the sequence in the presence of the patient.

The Welwalk group was received 30 sessions of assigned treatment protocol of robotic gait training for 40 minutes by the therapist who was well-trained for Welwalk training, ground level ambulatory training 20 minutes plus standard physiotherapy 60 minutes a day, five days a week for six weeks. During the training, the therapist set the degree of robot assistance according to the patients' walking ability to prevent the compensatory movements and provided minimum support or guidance as needed. The body weight support was allowed to use if patients were unable to keep their trunk straight. The attending therapist supervised usage and types of visual and auditory feedback. The use of the treadmill cane was also accepted to stabilize walking on Welwalk without the therapist's assistance. Each Welwalk training was carried out by one well-trained therapist. The control group was received ground level ambulatory training for 60 minutes plus standard physiotherapy 60 minutes a day, five days a week for six weeks. All outcomes were evaluated at baseline, at the end of the 15th session (3rd week), and at the end of the 30th session (6th week). In addition, gait parameters; gait speed, cadence, step length, step width including gait symmetry were evaluated by using XSENS.

Figure 15 Welwalk training

Table 1 The contents and amount of time of physiotherapy

Group	Amount of time of physiotherapy (minutes)			Total (minutes)
	Welwalk training	Level-walk training	Other physiotherapy training	
Welwalk® (n = 13)	40	20	60	120
Control (n = 13)	0	60	60	120

The Welwalk group and the control group were also blinded to their measurement outcome to avoid potential expectation bias. Patients were instructed not to inform the assessors of their intervention status.

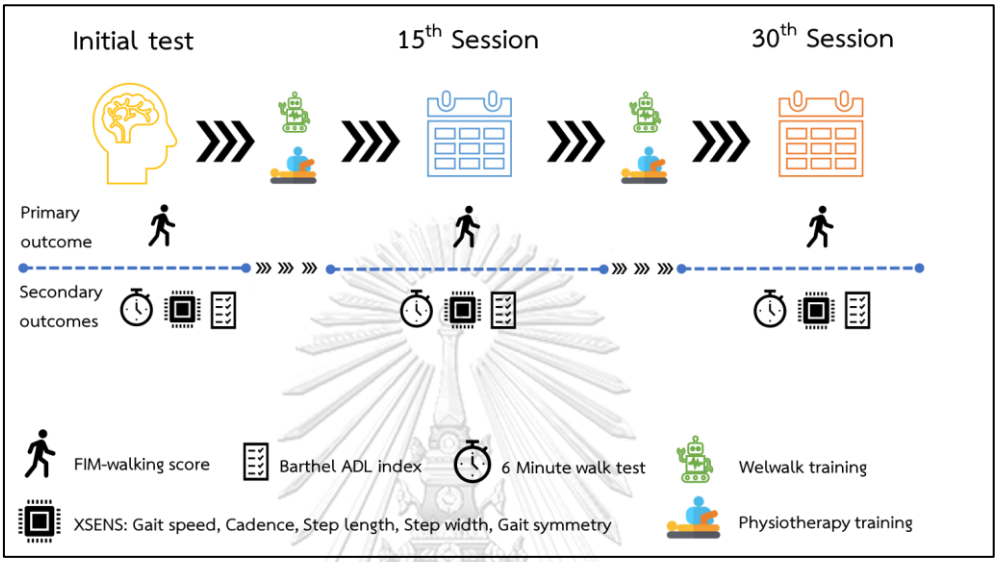


Figure 16 Assessment Time Scale

The study site was at Thai Red Cross Rehabilitation Center, Samutprakarn Province, Thailand. Marker poles were set as 10-meter apart for the evaluation, and every 1 meter had a marker for easy observation. Three cameras were used to record during walking; camera I was at the left side, camera II was at the right side, and camera III was at the end of the walkway. In evaluation, the therapist helped to reckon time for 6MWT. Safety was concerned for a long duration of study.

The measurements were separated into 2 rounds of the walking test for the objective information. Round I, participants were assigned to walk around the marker poles which set as 10 meters apart for FIM walking score and 6MWT (Figure 17). Round II, XSENS was used to assess functional ambulatory data only, and participants just walked a 10-meter distance. Some participants were afraid of the unsatisfied walking during using XSENS. They tried to correct themselves as unnatural walking habit. However, all participants were asked to try out using XSENS for a couple of

times before the evaluation. The data were collected only one time for each experiment. Three cameras were used to record VDO for the reinspection. The participants took a rest for 15 minutes before starting to do the next experiment to avoid fatigue.

Figure 17 Study site

Figure 18 A safety concern in data collection

5. Data collection

Outcome assessments were carried out with 2 data collectors (1 orthotist and 1 doctor) who were blinded to group allocation to prevent potential recorder and ascertainment bias. Patients were blinded to their measured scores to address potential expectation bias. Patients were instructed not to inform the assessors of their intervention status.

Primary outcome variable was the improvement of walking ability by evaluate the FIM-walk score and efficiency of FIM-walk defined by the following formula:

$$\text{Improvement in efficiency of FIM-walk} = \frac{\text{5-FIM score at the baseline}}{\text{Number of sessions to reach FIM walking score of 5}}$$

Secondary outcome variables were the improvement of 6-minute walk test (6MWT) and gait parameters verified by XSENS e.g., gait speed, cadence, step length, step width, and gait symmetry.

In addition, Barthel ADL Index regarding activities of daily living (ADLs), with zero indicating complete dependence and with the highest score in each sub-item signifying complete independence. The reliability and validity of the Barthel ADL index will be established.

5.1 Variables

Independent variable:	Using a Welwalk® rehabilitation robot training plus physiotherapy
Dependent variable:	Improvement in efficiency of FIM-walk
Confounders:	Fatigue (Solution: determine a resting period.)
	Age (Solution: exclude from the study because of age-related disabilities)

6. Statistical consideration

Score of the FIM-walk, XSENS's data, Barthel ADL index, and Length of hospitalization demonstrate as quantitative data/numerical data (discrete data and interval scale) and Degree of satisfaction of Welwalk® training demonstrates as qualitative data.

6.1 Sample size calculation

$$\text{N per group} = \frac{2(Z_{1-\frac{\alpha}{2}}+Z_{1-\beta})^2+(t-1)\rho}{t(\frac{\Delta MCD}{\sigma})}$$

According to Hirano et at. Effectiveness of Gait Exercise Assist Robot (GEAR) for stroke patients with hemiplegia.[25]

Significance level (alpha)	0.05
Power (1 – β)	80%
Standard deviation of outcome	0.36
Sample size required per group	8
Plus 20% drop out	= 13
Total sample size required	13 subjects/group
Total participants	26 participants

6.2 Statistical analysis

Baseline data:

- Student T test is used for quantitative data will be presented as Mean and Standard Deviation (SD)

- Chi-square test is used for qualitative data will be presented as Number and Percentage.

To compare data between 2 groups of treatment

- Multivariate analysis of covariance (MANCOVA) is used to determine the potential baseline covariances to the FIM related outcomes (FIM score at each evaluation, FIM score improvement and FIM efficiency) also with the other secondary outcomes.

To compare data within each group of treatment

- General linear model for repeated measure ANOVA was used to examine the relationship between the proportion data of discordant pair and proportion data of difference within each group of treatment.

Statistical analysis will be performed by using the IBM SPSS Statistics program (version 22.0) which has been supported the concurrent user license by Chulalongkorn University, and p-value lesser than 0.05 will be considered as statistically significant.

7. Ethical consideration

1. The proposal was approved by ethical review board of the Faculty of Medicine, Chulalongkorn University.
2. All participants gave the informed consent before participating in the research.
3. All participants were received all information and details of the research and the experiment as well, and they could independently make decision to participate in the research.
4. The participant’s/volunteer's information was kept confidential. In recording, there were no name and any information that identify the subject of the participant/ volunteer.
5. This research did not harm the participants/volunteers. Because the study was

almost no harm or risk at all. The equipment and device in this research were not exposed to the skin of the participants/volunteers, and there was no direct burial into the body (non-invasive). There was no use of drugs or chemicals in this research.

6. In this research, there were clear criteria for entry and exit, and randomly entered the study group without any bias.
7. There were a Prosthetist & Orthotist (PO) and Rehabilitation Engineer and an Physical Therapy (PT) took care of the participants throughout the experiment for preventing accident.
8. During the study, all participants were free to withdraw at any time.

CHAPTER IV

RESULTS AND DISCUSSION

Results

Thirty sub-acute hemiplegic stroke patients were enrolled in the study. Four subjects were dropped out for various reasons such as scabies, musculoskeletal pain, seizure & depression, and knee pain & personal problem. Thus, 26 patients were finally included.

CONSORT Flow Diagram

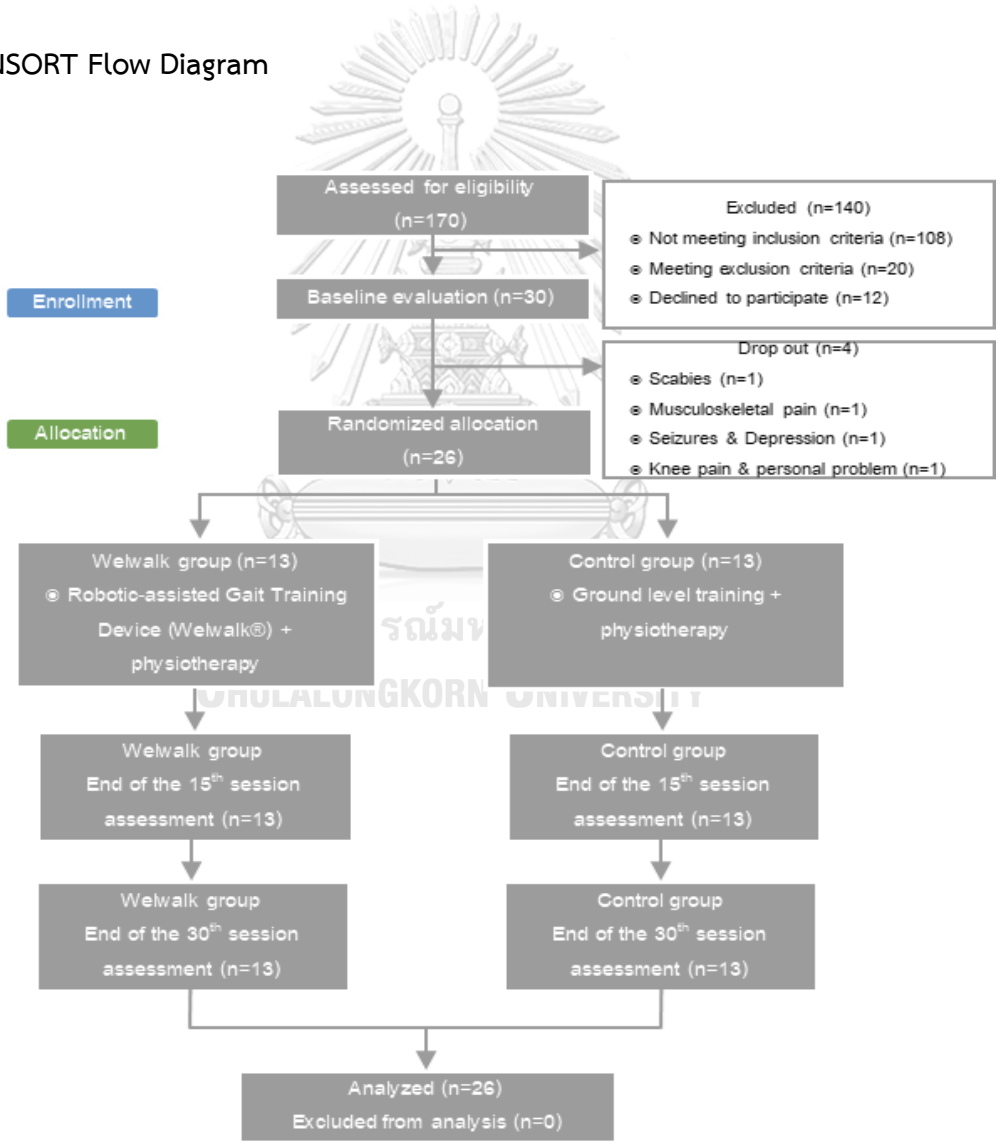


Figure 19 CONSORT Flow Diagram

Table 2 Demographic data

Variable	Welwalk Group (n=13)		Control Group (n=13)	
Age, y*	52.77±12.56		62.77±8.51	
Gender, %	6 Male	(46.2)	10 Male	(76.9)
	7 Female	(53.8)	3 Female	(23.1)
Affected side, %	7 Right	(53.8)	4 Right	(30.8)
	6 Left	(46.2)	9 Left	(69.2)
Onset, d*	56.15±23.71		72.54±20.12	
BMI*	23.49±4.20		24.43±3.43	
Cause of stroke, %	Ischemic	(61.5)	Ischemic	(53.8)
	Hemorrhage	(38.5)	Hemorrhage	(46.2)

*Mean±SD

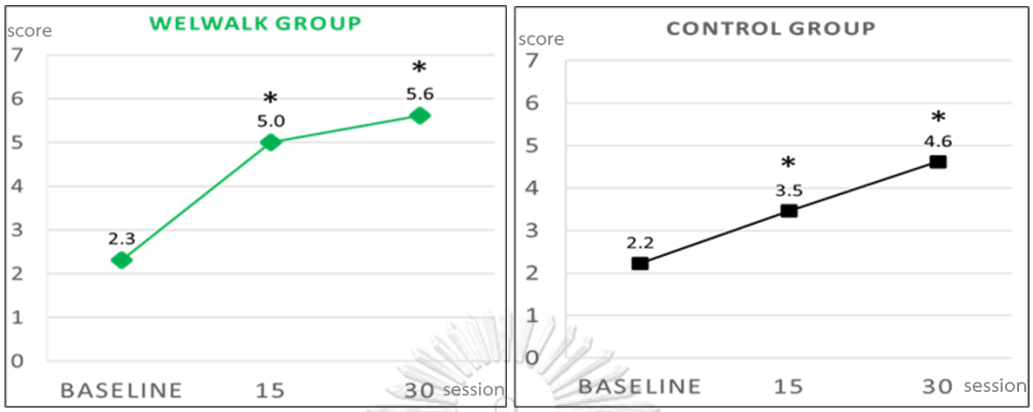
The average age of stroke patients in Welwalk group was 53 years old, and in control group was 63 years old. Welwalk group had 7.60% of male less than female, but control group had 53.8% of male more than female. Welwalk group had 7.60% of right affected side more than left side, but control group had 6.10% of left affected side more than right side. The average onset of Welwalk group was 56 days, and control group was 72 days. For BMI, the average BMI of stroke patients in Welwalk group was 23, and in control group was 24. The underweight and obesity were found only in Welwalk group as 7.7%. Welwalk group had 7.7% of normal weight more than control group, but the overweight had gone up 2 times in control group. In addition, ischemic stroke was higher than hemorrhagic stroke in both Welwalk and control group as 23% and 7.6%, respectively.

1. Primary outcome

1.1 FIM walking score

When compare the FIM-walk score at the 15th and 30th sessions of treatment with their own baseline in each group. Both Welwalk and control groups showed statistically significant improvement at both time points of evaluation ($P<0.05$). FIM-

walk score of Welwalk group were 5.00±1.29, 5.62±1.04 while control group were 3.46±1.76, 4.62±1.56 at the end of the 15th and 30th session, respectively. (Figure 20).



* Significant improvement from baseline

Figure 20 FIM walking score: compare within group

When comparing the outcomes between groups of treatment, multivariate analysis of covariance (MANCOVA) was used to identify the significance covariables that related to the primary outcome (the FIM score and FIM efficiency.) Age and sex were the 2 significant covariables with the P-value of 0.009 and 0.020, respectively. While other demographic parameters including of the onset of stroke, the side affected, the cause of stroke, and the BMI demonstrated as non-significant variables with P value > 0.05.

From ANCOVA analysis of the FIM related outcomes compared between groups of treatment by adjusting the covariables of age and sex, Welwalk group had a significantly higher FIM-walk score at the end of the 15th sessions (5.00±1.29 vs 3.46±1.76, p=0.012) and non-significant higher score at the end of the 30th sessions (5.62±1.04 vs 4.62±1.56, p=0.070).

Welwalk group also showed better improvement in FIM score in the first half of treatment protocol (from baseline to the end of the 15th session) in which the FIM score increase 2.69±1.11 point, while the FIM score in control group increased 1.23±1.17 point (p<0.001). But in the second half of treatment protocol (from 15th to the end of the 30th session), the Welwalk group had lesser improvement in FIM-walk

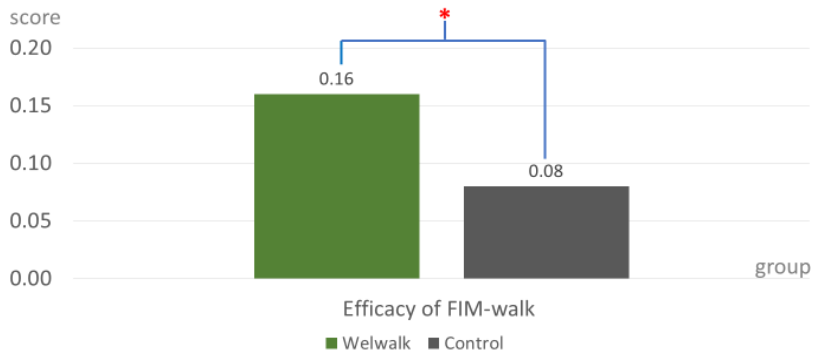
score (0.62±0.65 point) compare with control group (1.15±0.80 point) but not statistically significant (p=0.083). Overall, Welwalk group still had better improvement in FIM walk score when considered the whole treatment protocol (from baseline to the end of the 30th session) with the 3.31±0.85 point while the control group had 2.38±1.12 point improvement from baseline (p=0.004). (table 4)

1.2 Improvement in efficiency of FIM-walk

Reference*	Our study
• Improvement in efficiency of FIM-walk = $\frac{5 - \text{FIM score at the baseline}}{\text{Number of weeks to reach FIM walking score of 5}}$	• Improvement in efficiency of FIM-walk = $\frac{5 - \text{FIM score at the baseline}}{\text{Number of sessions (15/30) to reach FIM walking score of 5}}$

Figure 21 Equation for Improvement in efficiency of FIM-walk

Based on the reference article, the improvement in efficiency of FIM-walk was divided by number of weeks to reach FIM 5. While our study the improvement score was divided by number of sessions that patients could reach FIM 5 after received the training for 15 sessions or 30 sessions.



* Significant difference between groups

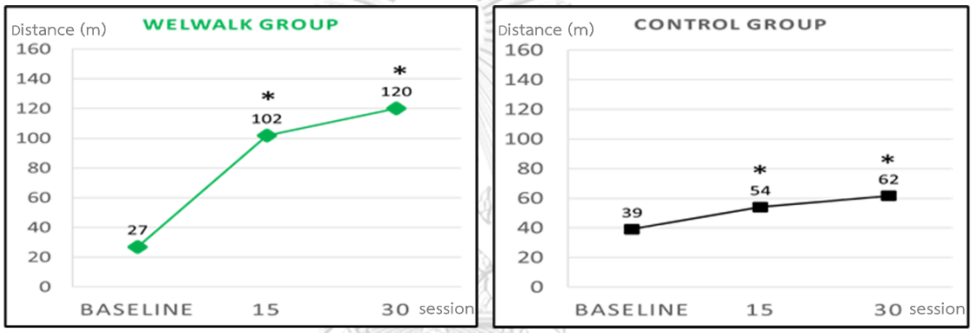
Figure 22 Improvement in efficiency of FIM-walk (FIM ≥ 5; considered as no. of sessions)

As the ANCOVA analysis results, the efficiency of FIM-walk showed higher improvement in Welwalk group than control group (p=0.008) that was similar to the reference article.

2. Secondary outcomes: Clinical evaluation

2.1 6-Minute walk test (6MWT, meters)

6MWT of both groups showed significant increase of walking distance at the end of the 15th and 30th session compare with each group's baseline (Welwalk: 101.78±66.66, 120.08±115.50, control: 44.68±24.98, 55.14±27.54, p<0.05).



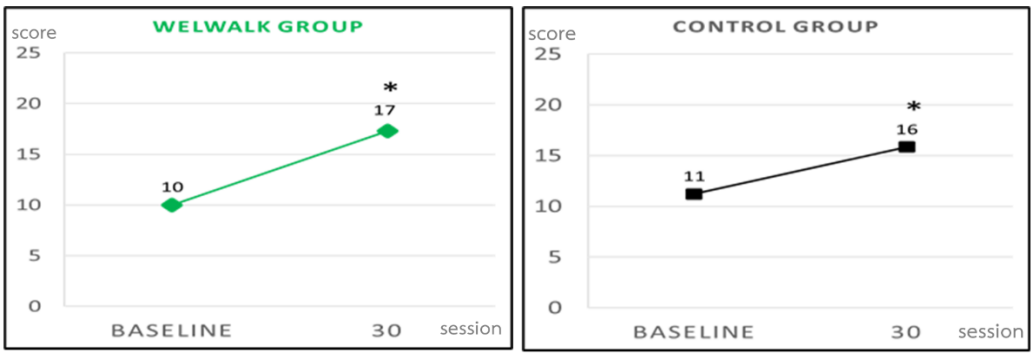
* Significant improvement from baseline

Figure 23 6MWT (m): compare within group

The comparison between groups using ANCOVA showed Welwalk group had a significantly greater improvement from the baseline to the 15th session with 74.83 m. while control group had only 15.53 m. (p=0.018)

2.2 Barthel ADL index

At the end of treatment protocol, both Welwalk and control group gained a significant improvement (Welwalk: 17.31±2.10, control: 15.85±2.27, p<0.001) comparing with each group's baseline Barthel score.



* Significant improvement from baseline

Figure 24 Barthel ADL index: compare within group

Welwalk group also had a significant greater gain of Barthel ADL index compared to the control group (7.31±1.89 vs 4.62±0.96, p<0.001) as shown in table 4.

3. Secondary outcomes: Gait analysis

3.1 Comparison within group

The gait analysis was analyzed using XSENS to evaluate the spatiotemporal parameters including the gait speed (m/s), cadence (step/min), step length (cm), step width (cm), and gait symmetry ratio. There was a significant improvement of the cadence at the end of the 15th sessions in both groups. (p<0.05) while other parameters also had a tendency of improvement in both groups but not statistically significant. (table 3, figure 25-29)

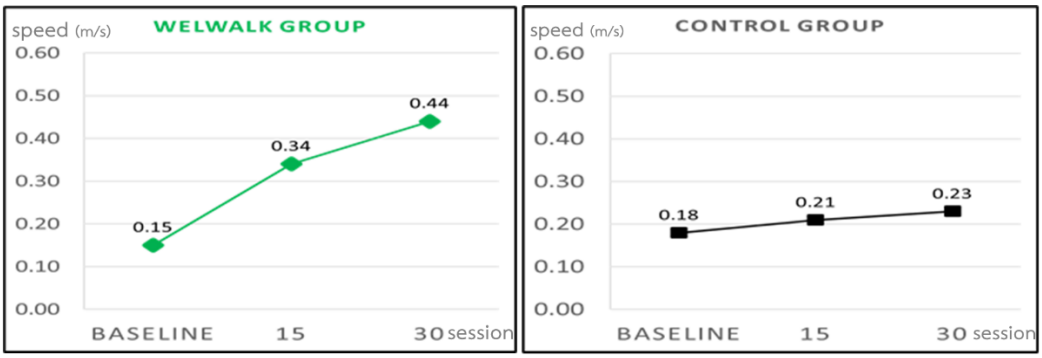
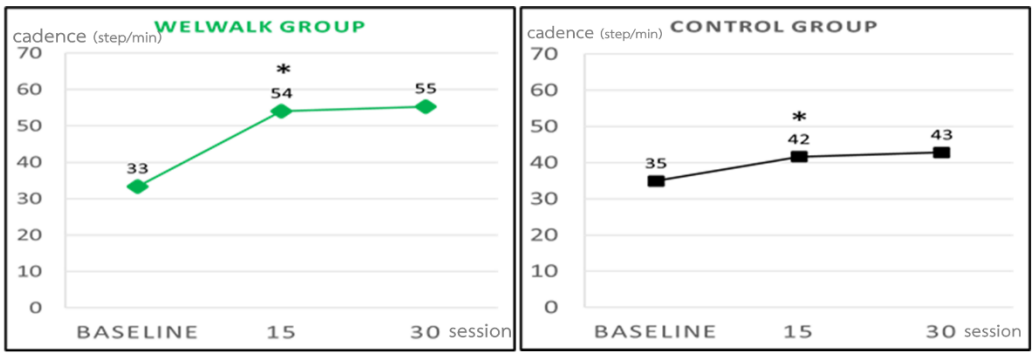


Figure 25 Gait speed (m/s)



* Significant improvement from baseline

Figure 26 Cadence (step/min)

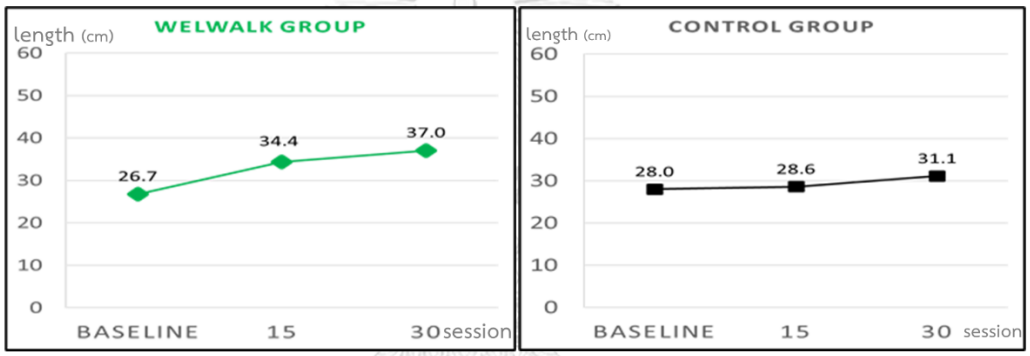


Figure 27 Step length (cm)

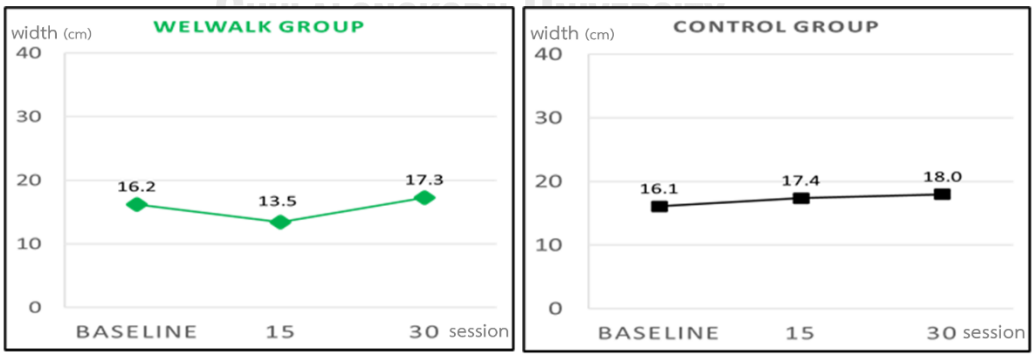


Figure 28 Step width (cm)

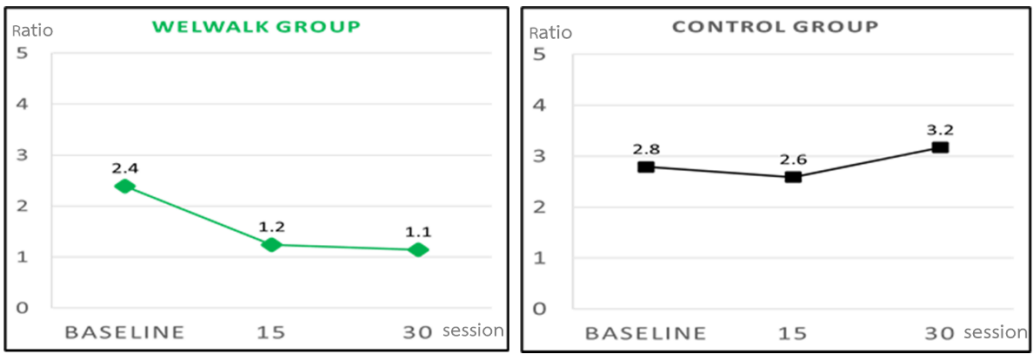


Figure 29 Symmetry ratio

3.2 Comparison between groups

By comparing the results from the Welwalk group with the control group using ANCOVA and adjusting the covariables of age and sex, the gait symmetry ratio at the end of the 30th session of the Welwalk group (1.14±0.75) was significantly different from the control group (3.17±4.14). (p=0.044) There was no other significant difference outcome in the gait sped, cadence, step length, and step width. (table 4)

Table 3. Primary outcome: FIM walk score

Parameters	Session	Within group comparison				Between group comparison		
		Welwalk		Control		Mean difference	P value**	95%CI
		Mean±SD	*P* value*	Mean±SD	*P* value*			
FIM walking score	baseline	2.31±0.95		2.23±0.83		0.08	0.453	(0.65, 0.80)
	15th	5.00±1.29	≤0.001†	3.46±1.76	0.007†	1.54	0.012†	(0.29, 2.79)
	30th	5.62±1.04	≤0.001†	4.62±1.56	≤0.001†	1.00	0.070	(0.07, 2.07)
FIM difference	0 to15th	2.69±1.11		1.23±1.17		1.46	≤0.001†	(0.54, 2.38)
	15th to 30th	0.62±0.65		1.15±0.80		0.54	0.083	(0.05, 1.13)
	0 to 30th	3.31±0.85		2.38±1.12		0.92	0.004†	(0.12, 1.73)
FIM efficacy		0.16±0.10		0.08±0.08		0.08	0.008†	(0.01, 0.15)

* paired T test

** ANCOVA

† significant p<0.05

Table 4. Secondary outcomes: Clinical evaluation and Gait spatiotemporal parameters

Parameters	Session	Within group comparison				Between group comparison		
		Welwalk		Control		Mean difference	P value**	95%CI
		Mean±SD	*P* value*	Mean±SD	*P* value*			
6MWT (m)	baseline	26.96±13.55		29.14±19.90		2.18	0.384	(11.81, 16.17)
	15th	101.78±66.66	0.004†	44.68±24.98	0.008†	57.11	0.055	(14.94, 99.28)
	30th	120.08±115.50	0.037†	55.14±27.54	0.011†	64.94	0.220	(6.11, 135.99)
6MWT difference (m)	0 to15th	74.85±63.77		15.58±13.99		59.26	0.018†	(20.14, 98.38)
	15th to 30th	18.15±66.18		10.33±21.83		7.82	0.902	(33.69, 49.33)
	0 to 30th	26.96±13.55		29.14±19.90		67.08	0.162	(2.77, 136.93)
Barthel index	baseline	10±2.61		11.23±2.31		1.23	0.212	(0.77, 3.23)
	30th	17.31±2.10	≤0.001†	15.85±2.27	≤0.001†	1.46	0.084	(0.31, 3.23)
Barthel index difference	0 to 30th	7.31±1.89		4.62±0.96		2.69	≤0.001†	(1.46, 3.93)
Gait speed (m/s)	baseline	0.16±0.08		0.18±0.13		0.02	0.648	(0.07, 0.11)
	15th	0.34±0.24	0.066	0.21±0.14	0.678	0.14	0.140	(0.02, 0.29)
	30th	0.44±0.39	0.081	0.23±0.11	0.545	0.21	0.142	(0.03, 0.45)
Gait speed difference (m/s)	0 to15th	0.19±0.25		0.03±0.08		0.16	0.077	(0.00, 0.32)
	15th to 30th	0.09±0.19		0.02±0.1		0.07	0.357	(0.05, 0.20)
	0 to 30th	0.28±0.40		0.05±0.12		0.24	0.117	(0.01, 0.48)
Cadence (step/min)	baseline	33.35±10.10		34.96±18.22		1.61	0.852	(10.32, 13.53)
	15th	54.02±20.17	0.018†	41.62±20.1	0.043†	12.40	0.127	(3.90, 28.70)
	30th	55.32±29.85	0.080	42.86±17.1	0.091	12.47	0.376	(7.22, 32.16)

Cadence difference (step/min)	0 to15th	20.66±22.34		6.65±8.4		14.01	0.120	(0.35, 27.67)
	15th to 30th	1.31±13.05		1.24±11.6		0.06	0.516	(9.93, 10.06)
	0 to 30th	21.97±31.34		7.9±11.61		14.07	0.425	(5.65, 33.8)
Step length (m)	baseline	0.27±0.13		0.28±0.12		0.01	0.706	(0.09, 0.12)
	15th	0.34±0.17	0.689	0.29±0.1	1.000	0.06	0.528	(0.06, 0.17)
	30th	0.37±0.19	0.415	0.31±0.1	1.000	0.06	0.773	(0.06, 0.18)
Step length difference (m)	0 to15th	0.08±0.21		0.01±0.13		0.07	0.448	(0.08, 0.21)
	15th to 30th	0.03±0.15		0.02±0.09		0.00	0.694	(0.10, 0.11)
	0 to 30th	0.1±0.23		0.03±0.15		0.07	0.640	(0.09, 0.23)
Step width (cm)	baseline	0.16±0.06		0.16±0.09		0.00	0.724	(0.06, 0.06)
	15th	0.14±0.07	0.705	0.18±0.07	1.000	0.04	0.205	(0.02, 0.10)
	30th	0.18±0.05	1.000	0.18±0.05	1.000	0.01	0.895	(0.04, 0.05)
Step width difference (cm)	0 to15th	0.03±0.08		0.01±0.07		0.04	0.408	(0.02, 0.10)
	15th to 30th	0.04±0.05		0.01±0.08		0.03	0.239	(0.02, 0.09)
	0 to 30th	0.01±0.07		0.02±0.09		0.01	0.803	(0.06, 0.07)
Symmetry ratio	baseline	2.39±2.65	0.461	2.79±2.51	1.000	0.40	0.642	(1.69, 2.49)
	15th	1.24±1.15	0.230	2.59±3.43	1.000	1.35	0.292	(0.72, 3.43)
	30th	1.14±0.75		3.17±4.14		2.03	0.044†	(0.50, 4.55)
Symmetry ratio difference	0 to15th	1.15±2.72		0.20±4.60		0.95	0.660	(2.11, 4.01)
	15th to 30th	0.10±0.97		0.57±4.94		0.67	0.349	(2.34, 3.69)
	0 to 30th	1.25±2.32		0.38±3.59		1.62	0.067	(0.85, 4.09)

* paired T test

** ANCOVA

† significant p<0.05

Discussion

This study demonstrated the effectiveness of the Robotic-assisted Gait Training Device (Welwalk®) plus physiotherapy in improving the ambulatory function in sub-acute hemiplegic stroke patients. Regarding MANCOVA analysis, the multivariate showed age and gender significantly influenced on the recovery of sub-acute hemiplegic stroke patients (p<0.05). Petrusevicience D. and Krisciunas AV.[26] studied the influence of factors on independence of patients after stroke in early rehabilitation stage, and they found the older patients had more expressed functional disorders, and worse functional recovery comparing with younger patients. The functional status was better in men than women at the start of rehabilitation training.

From MANCOVA analysis of all outcomes compared between groups of treatment by adjusting the covariables of age and gender, the Welwalk group gained independent level of walking (FIM walking score ≥ 5) at the end of the 15th session significantly higher than control group who received ground level training. When considered the improvement in efficiency of FIM-walk as number of sessions, the Welwalk group showed higher significant improvement than the control group. The results were similar to previous study[25, 27] in 2017, Hirano S. et al. studied the effectiveness of gait exercise assist robot (GEAR) for stroke patients with hemiplegia, their results also showed significant difference between Welwalk and control group.[25] Ii and Hirano et al. studied about an effectiveness of Welwalk in hemiparetic stroke patients with matched control and their results showed Welwalk group got higher FIM-walk efficiency than control group significantly.[27] However, the time of FIM-walk score assessment in our study was different from their studies. We evaluated the FIM-walk score every 3 weeks (at the end of the 15th session and 30th session) while Ii T et al. did the evaluation every week and Hirano et al. evaluated every 2 weeks.

The FIM-walk score changed at the end of the 15th session or the 1st half changing and at the end of total session showed significant difference in our study. The result was not similar to the study of Hirano S. et al.[27] Their study demonstrated no significant differences between both Welwalk and control group. This may be caused by several reasons, firstly our study was randomized control trial. Secondly, our study was done at Thai Red Cross Rehabilitation Center that had the specialist team, and intensive training program. Thirdly, our study period was long enough to see the improvement of patients' walking ability clearly. Thus, the result showed the walking ability in Welwalk group was faster improvement than the control group in first half of training period and slow improvement later on.

Welwalk® was developed from prototype, GEAR which the visual feedback functions for patients have been added. The improvement of walking ability after Welwalk training maybe facilitated by many systems consisted in Welwalk® such as knee-ankle foot orthosis type robot, a low floor treadmill, a safety suspension device which can be used for body weight support, a robot weight support device, a

monitor for patients, and a control panel. These systems determine the gait cycle from the pressure sensor and knee joint angle and executes flexion and extension of the knee joint at appropriate timing. The torque for assisting knee extension and force for assisting swing-out of the paralyzed lower limb with robot weight support can be regulated using the control with these mechanisms, stroke patients can practice Welwalk training repetitively with voluntary activity and improve their walking performance.

When comparing FIM–walking score between groups at the end of the 30th session, there was no significant difference. This may be caused by the ceiling effect of Welwalk training after the 15th session. There were around 70% of stroke patients in Welwalk group gained independent walking at the end of the 15th session but therapist allowed them to continue Welwalk training according to the research protocol. However, the advantage of Welwalk training in faster improvement of walking ability may encourage patients to engage to rehabilitation training and improve their quality of life.

Cheng PY and Lai PY[13] studied the effectiveness of Exoskeleton robots and End-effector robots on training methods and gait biomechanics. The limitations of both robotic systems were found that the exoskeleton type could cause a stress-related joint from misalignment between orthosis joint and patient joint, and the end-effector type could cause knee instability during training. When compared with Welwalk®, our study found its robotic orthosis was easily adjustment to correct knee joint position between patient's joint and orthosis joint. So, the orthosis of Welwalk® provided the better support to knee joint with shorter set up time than exoskeleton type. Moreover, Welwalk® could prevent knee instability during swing phase because it could reinforce knee performance and could lock the position of leg during walking but the end-effector types could not do these functions.

As the MANCOVA analysis, 6MWT difference showed the tendency of significantly longer walking distance in Welwalk group than control group at the end of the 15th session when compared to the baseline. This result suggested Welwalk training can improve patients' walking endurance and capacity. In 2017, Molteni F and et al.[28] studied the feasibility and the clinical effects of an over-ground walking

training with a wearable powered exoskeleton in sub-acute and chronic stroke patients. They found 6MWT was statistically significant improvements at the three assessment periods for both experimental group and control group. Furthermore, the study of Beretta E and et al.[29] about the comparison between a treatment solely based on conventional physiotherapy (CP) with a program combining Robotically-driven orthoses (RDO) training with CP exerted proximal-to-distal differential recovery on the lower limbs in children with hemiplegia, early after acquired brain injury, and their study found 6MWT was significantly increased in the experimental group more than the control group. So that, the robotic training plus physiotherapy was better than the physiotherapy alone on the improvement of walking ability in the early stage of stroke patients.

Barthel ADL index had increased in both Welwalk and control groups. The result was comparable to DEGAS study of Pohl et al.[30] Their multicentre trial was to compare the effect of repetitive locomotor training using the electromechanical gait trainer (Gait Trainer GT I; Reha-Stim, Berlin, Germany) in combination with physiotherapy to the effect of physiotherapy alone in subacute, non-ambulatory stroke patients. Barthel ADL Index (0-100) was assessed before study onset, at the end of the four-week treatment period and at the follow-up six months after study end by a blind assessor. The Barthel Index was not differed between groups at follow-up. Our study showed the Barthel ADL index improved significantly at the end of the 30th session in both groups when compared to the baseline as MANCOVA analysis. After adjusting the covariables of age and gender by MANCOVA analysis, the Welwalk group gained higher than the control group significantly. This result was confirmed to the study of Morreale M and et al.[31] that investigated the early versus delayed rehabilitation treatment in hemiplegic patients with ischemic stroke: proprioceptive or cognitive approach? Their study found the Barthel ADL index significantly changed between early versus delayed groups at 12 months. Wei J and et al.[32] studied the Intermittent pneumatic compression combined with rehabilitation training improves motor function deficits in patients with acute cerebral infarction, and they found the Barthel ADL index of the treatment group were also

significantly higher than the control group. However, our study did not evaluate at the end of the 15th session so we may not know the early effect of Welwalk.

For the secondary outcomes from XSENS evaluation, there was no significant difference in almost all gait parameters except cadence when compared within group at the end of the 15th session. However, gait speed, cadence, step length, and step width demonstrated the tendency of higher improvement in Welwalk group. In 2013, Mehrholz J et al. reviewed the effects of automated electromechanical-and robotic-assisted gait-training devices for improving walking after stroke by Cochrane Review. They concluded electromechanical-assisted gait training in combination with physiotherapy improved stroke patients' independent in walking with moderate-quality evidence but did not significantly increase walking velocity.[33] Regarding the gait symmetry, the result showed the trend that Welwalk training can improve the walking asymmetry in Welwalk group better than control group. Symmetry ratio showed significant difference between both Welwalk and control group at the end of the 30th session as MANCOVA analysis. The results were similar to previous study of Munari D and et al.[34] which studied about an effectiveness of high-intensity treadmill training improves gait ability. Their study found the symmetry ratio of high-intensity treadmill training was significant difference when comparing with low-intensity treadmill training. Lee H-J and et al.[35] studied about the training for walking efficiency with a wearable Hip-Assist Robot in stroke patients, and they found the spatiotemporal gait symmetry ratio of stroke patients became closer to normal range after gait training.

The present study suggested that Welwalk training combined with standard physiotherapy effected the improvement of stroke patients' walking ability faster than ground level walking.

CHAPTER V

CONCLUSION, LIMITATION, AND SUGGESTION

Conclusion

This study suggested that Welwalk training plus physiotherapy can improve walking ability and Barthel ADL index faster than ground level training plus physiotherapy in sub-acute hemiplegic stroke patients.

Limitation

This study has some limitations. Firstly, this effectiveness study included stroke patients in sub-acute stage from one rehabilitation centre, acute or chronic stage and multicenter study are recommended. Secondly, we did not evaluate patients' walking ability every week which may not be able to detect the change of FIM-walk score at the earliest. Measurement of FIM-walk score weekly is suggested in further study. Thirdly, we neither record the time from starting of Welwalk training to until no need assistance on Welwalk nor from no need assistance on Welwalk training to no need assistance on level walking which may reflect the effectiveness of Welwalk training in stroke patients' independent walking ability clearly.

All patients who underwent Welwalk training as well as the Welwalk training therapist were very satisfied with the training and there was no adverse effect.

Suggestion

Hardware of Welwalk®

An uninterruptible power supply (UPS) of welwalk® had a short lifespan as 7 - 8 months, but the general UPS batteries lifespan should be 5 – 10 years.[36] In the study, the UPS was broken two times in 1½ years, and it took at least 3 months for importing from Japan to replace a new one. Finally, it was broken again in the third time and other UPS was required for the replacement. The new one was work very well until now (more than 2 years of using), so that Toyota should improve the efficiency of UPS battery cycle of Welwalk® for the long lifespan.

Software of Welwalk®

Welwalk® cannot save data automatically when power outage since the problem was found during the UPS broken. Thus, Welwalk® should upgrade its software for the autosave and backup.

Technical use

Welwalk® is not recommended to patients who have an inability of standing. It would be better, if the robotic orthosis of Welwalk® can provide a function of the active weight balance and standing reinforcement. Patients will benefit to move out bed early and will allows overground walking training rapidly.

Despite our therapists were very satisfied to use Welwalk®, the position of therapists during training was uncomfortable. The therapists had standing separate leg on either side of treadmill. It caused low back pain to the therapists. Thus, Welwalk® should provide a portable chair or a foldable chair for the therapist's sitting during training.

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VITA

NAME	Natapatchakrid Thimabut
DATE OF BIRTH	23 April 1984
PLACE OF BIRTH	Ubon Ratchathani
INSTITUTIONS ATTENDED	Faculty of Medicine, Chulalongkorn University
HOME ADDRESS	109 Moo 3, Chaeng Sanit Road, Khuaengnai Subdistric, Khuaengnai Distric, Ubon Ratchathani, Thailand 34150
AWARD RECEIVED	Advanced Rehabilitation Training For Gait & Motion Analysis and Robotic-Assisted Gait Training Device (Welwalk)