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Multicenter Randomized Clinical Trial Evaluating the Effectiveness of the Lokomat in Subacute Stroke

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Objective. To compare the efficacy of robotic-assisted gait training with the Lokomat to conventional gait training in individuals with subacute stroke. *Methods.* A total of 63 participants <6 months poststroke with an initial walking speed between 0.1 to 0.6 m/s completed the multicenter, randomized clinical trial. All participants received twenty-four 1-hour sessions of either Lokomat or conventional gait training. Outcome measures were evaluated prior to training, after 12 and 24 sessions, and at a 3-month follow-up exam. Self-selected overground walking speed and distance walked in 6 minutes were the primary outcome measures, whereas secondary outcome measures included balance, mobility and function, cadence and symmetry, level of disability, and quality of life measures. *Results.* Participants who received conventional gait training experienced significantly greater gains in walking speed ($P = .002$) and distance ($P = .03$) than those trained on the Lokomat. These differences were maintained at the 3-month follow-up evaluation. Secondary measures were not different between the 2 groups, although a 2-fold greater improvement in cadence was observed in the conventional versus Lokomat group. *Conclusions.* For subacute stroke participants with moderate to severe gait impairments, the diversity of conventional gait training interventions appears to be more effective than robotic-assisted gait training for facilitating returns in walking ability.

Keywords: *Hemiplegia; Rehabilitation; Gait; Recovery of function; Robotics; Walking*

Body-weight supported locomotor training on a treadmill (BWSTT) has been the focus of intense investigations for nearly 20 years, beginning with the seminal work of Barbeau and colleagues.[1,2] Hesse et al[3] first evaluated this training modality in stroke populations, where it was demonstrated in a small group of subacute stroke participants that improvements in walking ability were greater following BWSTT than conventional physiotherapy. One uncertainty of this early work was whether the catalyst for improvements in walking ability resulted from the volume of steps practiced on the treadmill or the incorporation of body-weight support during training sessions. Visintin et al[4] investigated this by training 100 stroke participants on a treadmill, but only half received body-weight support. They found that the participants who received BWSTT demonstrated significantly greater gains in walking ability over those who received treadmill training with no weight support, although this was only true for participants who were elderly (eg, age >65) and had significant gait impairments (initial walking speed <0.2 m/s; <20 m in 6-minute walk test).[5]

A number of studies have continued to evaluate the efficacy of BWSTT and, more recently, have explored how the therapy can be improved by changing training conditions. For example, Sullivan et al[6] and Pohl et al[7] each evaluated the influence of training speeds on gait outcomes. Both of these studies found that participants trained at high speeds tend to show greater improvements in walking ability than those trained at slower rates. These and other studies using BWSTT in individuals poststroke demonstrate the effectiveness of the therapeutic paradigm, and have identified training factors that regulate intensity, which can directly impact the intervention outcomes.[8]

One of the recognized limitations with BWSTT is the significant demand it places on the therapists during training sessions. Specifically, manually assisting individuals with spastic hemiparesis at the impaired limb and/or trunk to facilitate continuous stepping may present significant physical challenges to skilled therapists. As a result, the consistency and duration of the training may be compromised. For example, if the level of assistance is constantly changing, which may occur if the therapist fatigues, the participants will have to not only adjust their motor control strategy to account for their impairments, but also the changing assistance provided by the therapist. The introduction of robotic devices has attempted to address these limitations (see Hidler et al[9] for a detailed review). Because these devices are actuated by

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motors, they can provide consistent, symmetrical time-unlimited training sessions. As such, even the most impaired individuals can begin intensive gait training early in their rehabilitation programs, which has been shown to be important in acute stroke recovery.[10,11]

Unfortunately there are only a few small-scale studies evaluating the efficacy of robotic gait training in individuals with hemiparetic stroke. The Gait Trainer (Reha-Stim, Berlin, Germany), developed by Hesse and colleagues,[12] was compared to BWSTT training in 30 subacute stroke participants using a crossover design study (A-B-A vs B-A-B).[13] In their study, participants who received more robotic-assisted therapy (eg, A-B-A group) experienced larger gains in walking speed than those who received more BWSTT (eg, B-A-B). A recent study compared Lokomat[14] (Hocoma AG, Volketswil, Switzerland) gait training with conventional gait training in 30 subacute stroke participants who were not ambulatory,[15] concluding that there were no differences in walking speed or independence, spasticity, or ability to perform other activities of daily living. The investigators did report that the Lokomat group increased the duration of single limb support on their paretic leg whereas the control group did not.

Although these studies provide an early look at the efficacy of robotic devices, they are generally limited in the number of participants enrolled. In this article, we present the results of a 5-year, randomized clinical trial, which compared robotic-assisted treadmill training with the Lokomat to conventional gait training in subacute stroke participants. The goal of the study was to determine whether stroke participants in the early stages of their injuries, who receive robotic-assisted gait training, improved their walking ability greater than those who received conventional gait training with therapist assistance. The National Rehabilitation Hospital (NRH) in Washington, DC, and the Rehabilitation Institute of Chicago (RIC) in Chicago, IL, participated in this study.

Method

Participants

Participants were recruited to the study by screening admissions at the NRH and the RIC, as well as from surrounding hospitals in the greater Washington, DC and Chicago areas that have stroke inpatient and outpatient services. Inclusion criteria for the study were as follows: hemiparesis resulting from unilateral ischemic or hemorrhagic stroke; no prior stroke; time since stroke onset <6 months; age >18 years; ability to ambulate 5 meters without physical assistance and a self-selected walking speed between 0.1 to 0.6 m/s; and could not be receiving any other physical therapy targeting the lower limbs.

Exclusion criteria included: severe osteoporosis; contractures limiting range of motion in the lower extremities; not ambulating prior to stroke; severe cardiac disease (New York Heart Association classification of II-IV); uncontrolled hypertension (systolic >200 mm Hg, diastolic >110 mm Hg); stroke of the brainstem or cerebellar lesions; uncontrolled seizures; presence of lower limb nonhealing ulcers; lower limb amputation; uncontrolled diabetes; cognitive deficits (<24 on the Mini-Mental State Examination[16]); and symptoms of depression (≥16 on the Center for Epidemiological Studies Depression Scale [CES-D][17]). All participants were required to provide informed consent approved by the institutional review boards (IRB) of the participating institutions.

A total of 72 participants met the inclusion and exclusion criteria over a 4-year period and were enrolled in the study. Prior to randomization, participants were stratified by their walking speed. Participants with severe gait impairments were classified as those with self-selected overground walking speeds between 0.1 to 0.4 m/s over 5 meters, whereas participants with moderate gait impairments walked between 0.4 to 0.6 m/s. After stratification, the participant was assigned to either the Lokomat group or the conventional group (see below) using a randomization table.

Participants were trained 3 days per week, for 8 to 10 weeks, for a maximum total of 24 sessions. Each session was 1.5 hours, and included setup, training, rest breaks, and break down with a total of 45 minutes allotted for the intervention. If a participant missed 5 consecutive training sessions, he or she was removed from the study. Throughout the training and in the period between the end of the study and the 3-month follow-up, participants were not allowed to receive physical therapy targeting their lower extremities.

Training Protocol

Training logs were maintained by the treating therapist. The logs consisted of 24 training session forms, as well as 4 sets of outcomes assessment forms. For each training session, therapists documented all of the activities the participant undertook within the session, including time on tasks, training parameters, and vitals.

Conventional Gait Training. Conventional gait training was performed by skilled and experienced physical therapists. The goal of the intervention was to facilitate improvements in walking ability, characterized by improved walking speed, endurance, postural stability, and symmetry. The structure of the intervention was customized to each individual's functional level. Early training sessions in very impaired individuals focused on static and dynamic postural tasks, trunk positioning, improving lower and upper extremity range of motion, and overground walking. As participants progressed in these areas, or entered the study at a higher functioning level, higher-level balance and gait activities were performed. Such activities included walking speed tasks, symmetry of lower limb movements, stair climbing, and locomotor training on a treadmill. As treadmill training is now commonly used in many rehabilitation settings, the conventional gait training group was allowed up to 15 minutes per session as deemed appropriate.

Lokomat Gait Training. For the Lokomat group, participants were fitted with a harness so that a portion of their body weight could be supported when walking in the device. The first training session focused on patient setup and adjustments within the device, and allowed the participant to acclimate to robotic-assisted walking. To minimize the incidence of skin abrasions, soccer-style shin guards were placed on the participant's shins prior to walking in the Lokomat. All participants in the Lokomat group were initially trained using a foot lifter on the forefoot of the affected leg to help provide toe clearance during swing. As ankle strength and control improved in the participant, the tension was reduced in the straps. In some sessions the tension would begin at low levels, however, as the participant fatigued, the tension was increased. If the participant's ankle function progressed to the point where he or she was able to demonstrate volitional dorsiflexion, we would begin the training session with no strap but would often add the strap during the session (eg, as the participant fatigued). In some participants, function and endurance progressed to the point where we were able to keep the strap off for the entire session.

With the device properly adjusted, the Lokomat initiated stepping patterns after which the participant was instructed to follow. Specifically, their goal was to move their legs like the device, trying to minimize the amount of assistance provided by the Lokomat. For this first session, up to 40% body-weight support was provided to allow participants to focus on establishing the timing in their gait patterns under only moderate intensity levels. Initial walking speeds were normally around 1.5 km/h (0.42 m/s).

In subsequent sessions, training intensity was increased progressively by changing walking speed, level of body-weight support, and duration of continuous walking. The amount of body-weight support was fixed so that the participant could achieve adequate knee extension during stance and toe clearance during swing at 1.5 km/h (0.42 m/s). When this level of weight support was found, the speed of the Lokomat was increased in increments of 0.2 km/h (0.06 m/s) per session up to 3.0 km/h (0.83 m/s) with fixed body-weight support. When the participant was able to ambulate at that level of body-weight support at the highest speed, the level of weight support was reduced in increments of 5% to 10% per session and the speed reduced (if necessary).

If a participant's walking ability improved to the point that he or she could ambulate at the highest training speed under his or her full body weight, the guidance force was reduced in the Lokomat, which effectively decreases the amount of assistance the device provides. At 100% guidance force, the device offers maximal assistance in achieving symmetrical, consistent gait patterns. At 0% guidance force, the device only compensates for the weight and inertia of the linkages, but will not move the limbs. The ultimate goal for each participant was to have him or her walk for a total of 45 minutes in the Lokomat under no body-weight support, at 3.0 km/h (0.83 m/s), and 0% guidance force.

During Lokomat training, the participant was instructed to try and match the movement of the Lokomat. A computer monitor located in front of the participants provided them with biofeedback of their performance at both the hip and knee joints. The biofeedback provided an estimate of participant performance during robotic-assisted stepping so that participants could alter the timing and magnitude of their leg movements to reduce performance errors. Therapists also provided constant verbal encouragement and cueing during the training. It should be noted that at low levels of body-weight support, an error signal in the kinematic trajectory of the Lokomat would terminate walking when participants did not generate substantial volitional activity to continue stepping. This safety feature helped ensure that the participant was engaged and not completely passive thereby letting the Lokomat do all the work.

Cardiovascular and Health Monitoring. Blood pressure and heart rate were taken prior to, during, and following training. If cardiovascular measures were elevated above the American College of Sports Medicine[18] guidelines for cardiac patients during exercise testing, training ceased and a physician was consulted. Training was reinitiated following physician clearance.

Outcome Measures

Outcome measures were evaluated for each participant prior to training, after 12 and 24 sessions, and at a 3-month follow-up exam. Primary outcome measures were participants self-selected overground walking velocity over 5 meters and walking distance assessed through the 6-minute timed walk. Therapists closely guarded participants during gait testing, but did not provide physical assistance. For gait speed, participants were timed with a stopwatch as they walked a 5-meter marked distance.[19] For the 6-minute walk test, participants walked through continuous hallways clear of obstacles and with minimal foot traffic.

Secondary measures included the Berg Balance Test,[20] Functional Ambulation Category (FAC),[3] NIH Stroke Scale (National Institutes of Neurological Disorders and Stroke, National Institutes of Health, US), Motor Assessment Scale,[21] Rivermead Mobility Index,[22] Frenchay Activities Index,[23] and SF-36 Health Survey.[24] We also measured each participant's cadence using the Gait Rite at NRH (CIR Systems, Havertown, PA) or Gait Mat II at RIC (E.Q. Inc, Chalfont, PA). With this group of outcome measures, we were able to look at improvements in function, as well as the impact of these improvements on quality of life measures.

Standardizing Training and Outcome Assessments

To help minimize variability in training strategies and outcomes assessments between training centers, detailed training manuals were developed prior to the study, which included methods of recruiting, participant enrollment, training methods

for the Lokomat and conventional groups, outcomes assessment procedures, and data collection and management procedures. All staff affiliated with the study, including physical therapists, research coordinators, and evaluators, were required to review these procedures with the principal investigators (J. Hidler for NRH and T. G. Hornby for RIC).

Statistical Analyses

Demographics and initial participant characteristics were compared between the Lokomat and conventional groups. Student's *t* tests were used to test for differences in means for continuous variables and chi-square tests were used to test for differences in proportions for categorical variables. Changes in outcomes (Δ) were calculated by subtracting the baseline value from the value obtained at each of the three follow-up visits. The analysis of covariance (ANCOVA) method was used to determine the effect of group assignment on the primary outcome measures of change in walking speed and walking distance, while adjusting for number of days poststroke (see below). A P value < .05 was considered statistically significant. Data in the text, tables, and figures is presented as mean ± standard error, unless indicated otherwise. All analyses were performed using SAS version 9.1.3 (Cary, NC).

Results

Of the 72 participants enrolled in the study, 9 withdrew or were removed because of poor attendance or a decline in health, which was unrelated to the study. The remaining 63 participants completed the 24 training sessions. At NRH a total of 39 participants were trained, 17 Lokomat and 22 conventional. At RIC a total of 24 participants were trained, 17 Lokomat and 8 conventional. At the 3-month follow-up evaluations sessions, 5 Lokomat and 2 conventional participants did not participate. Reasons for lost follow-ups included 1 death, 3 moved to another city, and 3 declined to return.

Table 1 lists the demographics of subjects who participated in the study. A total of 33 participants completed the Lokomat training protocol while 30 participants completed conventional gait training. Despite random assignment, age was statistically different between the groups (mean difference, 5.3 years), whereas differences in days poststroke and side of lesion nearly reached the significance level. All of the other measures were not statistically different at baseline assessment.

Because age and days poststroke could influence recovery patterns observed in the study, the relationships between improvements in walking speed and endurance and each of these variables were investigated using a linear regression model. We found that age was not related to improvements in walking speed or 6-minute distance, however days poststroke were highly significant for distance (P = .009) and borderline significant for walking speed (P = .13) where earlier interventions were correlated with higher gains in these outcome measures.[10,11] Therefore, statistical corrections were made in all of our outcome measures to account for differences in days poststroke, while no corrections were made for age.

Table 1
Summary of Participant Characteristics by Treatment Group

	Lokomat (n = 33)	Conventional (n = 30)	*P*
Age (SD, range)	59.9 (11.3, 30-79)	54.6 (9.4, 36-78)	.05
Days poststroke (SD)	110.9 (62.5)	138.9 (60.9)	.08
Gender (M/F)	21/12	18/12	.77
Side of stroke (R/L)	11/22	17/13	.06
Ischemic/hemorrhagic	26/7	21/9	.47
Baseline CES-D	8.2	7.4	.58
Baseline Folstein MMSE	26.7	26.8	.58

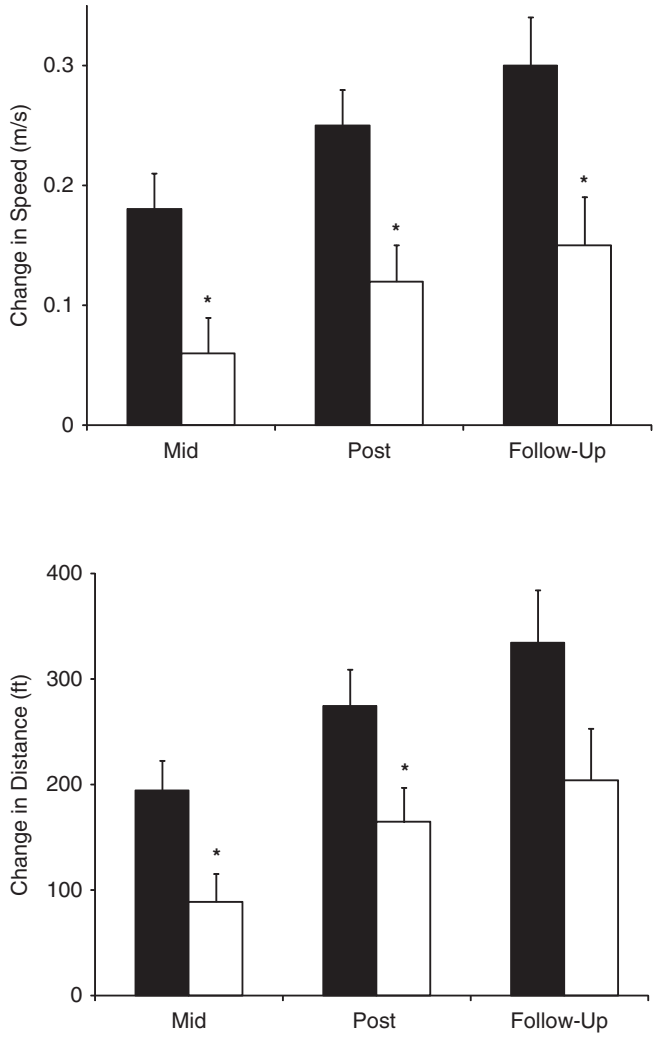
Abbreviations: M, male; F, female; R, right; L, left; CES-D, Center for Epidemiological Studies Depression Scale; MMSE, mini-mental state examination.

Improvements in Overground Walking Speed and Endurance

Figure 1 shows the changes in self-selected walking speed and distance for midevaluations, posttraining evaluations and at the 3-month follow-up evaluations. All data are expressed as a change from baseline values. At study entry, there were no differences between groups for the average self-selected walking speeds (Lokomat, 0.34 ± 0.03 m/s; conventional, 0.35 ± 0.03 m/s; P = .77). By midtraining evaluations, the Lokomat group increased its walking speed by 0.06 ± 0.03 m/s, which was significantly less than the conventional group that improved by 0.18 ± 0.03 m/s (P = 0.03). At posttraining evaluations, the Lokomat group demonstrated a 0.12 ± 0.03 m/s increase in walking speed, whereas improvements in the conventional group were 0.25 ± 0.03 m/s (P = .002). At the 3-month follow-up evaluation, the change in walking speed from baseline for the Lokomat group was 0.15 ± 0.04 m/s, whereas the change in the conventional group was 0.30 ± 0.03 m/s. (P = .006).

Similar training effects between groups were observed in distance ambulated during the 6-minute walk (Figure 1). At baseline, there were no differences between groups (Lokomat, 387.8 ± 43.4 ft; conventional, 440.7 ± 46.4 ft; P = .4). At the midtraining evaluations, the conventional group improved by 194.1 ± 28.7 ft compared to 88.6 ± 26.9 ft for the Lokomat group (P = .01). At the completion of the training, the conventional group continued to progress at a faster rate than the Lokomat group, improving 274 ± 35.4 ft from baseline compared to 164.6 ± 32.5 ft for the Lokomat group (P = .03). At the 3-month follow-up evaluation, both groups continued to improve their endurance, where the conventional group improved by 334.5 ± 49.8 ft from baseline while the Lokomat group improved 204.1± 48.8 ft from baseline (P = .07). Although this difference was not statistically significant, the gains for the conventional group were 64% greater than the Lokomat group.

Figure 1
Changes in Walking Speed and 6-Minute Walk Distance for Both Groups With Respect to Baseline Values



Note: Black, conventional gait training; white, Lokomat gait training. *$P < .05$.

Table 2
Mobility and Function Measures

Measure	Lokomat (n = 33) Mean (SD)	Conventional (n = 30) Mean (SD)	P*
Motor Assessment Scale			
Baseline	27.7 (1.8)	29.4 (1.8)	.51
ΔMidtraining	2.7 (0.7)	2.7 (0.8)	.99
ΔPosttraining	3.5 (0.8)	4.5 (0.9)	.44
Δ3-month follow-up	4.1 (1.1)	4.6 (1.1)	.75
Functional Ambulation Category			
Baseline	3.3 (0.2)	3.7 (0.2)	.23
ΔMidtraining	0.5 (0.2)	0.4 (0.2)	.77
ΔPosttraining	0.7 (0.2)	0.7 (0.2)	.84
Δ3-month follow-up	0.7 (0.2)	1.0 (0.2)	.40
Berg Balance test			
Baseline	36.7 (1.9)	39.9 (2.0)	.25
ΔMidtraining	3.1 (0.9)	5.5 (1.0)	.08
ΔPosttraining	6.0 (0.9)	6.6 (1.0)	.67
Δ3-month follow-up	6.0 (1.2)	7.0 (1.2)	.54
Rivermead			
Baseline	9.5 (0.5)	11.3 (0.6)	.03*
ΔMidtraining	1.3 (0.4)	1.1 (0.4)	.73
ΔPosttraining	2.0 (0.3)	1.6 (0.3)	.36
Δ3-month follow-up	2.6 (0.4)	2.2 (0.5)	.53
Gait assessment cadence (steps/min)			
Baseline	67.2 (5.8)	65.3 (6.4)	.83
ΔMidtraining	–0.9 (5.6)	8.8 (6.3)	.26
ΔPosttraining	5.5 (5.3)	13.7 (6.0)	.32
Δ3-month follow-up	7.3 (6.1)	15.0 (6.9)	.42

*P value represents between-group differences, adjusting for days poststroke.
Δ Indicates change in outcome measure from baseline.

Improvements in Mobility and Function

Changes in walking ability, function, and balance were also evaluated using numerous clinical measures (see Outcome Measures). As shown in Table 2, in general, there were no statistically significant differences in improvements between the Lokomat and conventional groups. Both groups improved on the FAC, the Rivermead Mobility Index, Berg Balance test, and Motor Assessment Scale from baseline to all evaluations sessions. For the Motor Assessment Scale and Berg Balance test, most participants made the largest gains from baseline to the midtraining evaluation session and then continued to improve at a lower rate. For FAC and the Rivermead Mobility Index, participants tended to exhibit a slow and steady improvement throughout the duration of the study. Notably, the Lokomat group had a lower baseline Rivermead score than the conventional group (9.5 compared to 11.3; $P = .03$), although the clinical significance of this difference is uncertain.

Cadence (steps/min) was used as secondary spatiotemporal measures of gait quality. Following training, the conventional group improved its cadence from baseline by 15 steps/min while the Lokomat improved its cadence by 7.3 steps/min, with differences maintained at the 3-month follow-up evaluation session (Table 2). Although the conventional group exhibited a 2-fold difference in cadence compared to the Lokomat group, the difference was not statistically significant.

Changes in Stroke Impairment, General Health, and Activities of Daily Living

Table 3 lists changes in overall health and well-being of study participants for both groups. Overall, both groups improved in all of these measures with no statistically significant differences between groups.

Discussion

The findings of this multicenter randomized clinical trial, comparing robotic-assisted gait training with the Lokomat to conventional gait training, indicate that the use of conventional rehabilitation strategies elicits greater improvements in

Table 3
Measures of Stroke Impairment, General Health, and Activities of Daily Living

Measure	Lokomat (n = 33) Mean (SD)	Conventional (n = 30) Mean (SD)	*P**
National Institutes of Health Stroke Scale			
Baseline	5.5 (0.6)	5.9 (0.6)	.65
ΔMidtraining	−0.7 (0.3)	−1.2 (0.3)	.24
ΔPosttraining	−0.9 (0.3)	−1.8 (0.4)	.07
Δ3-month follow-up	−1.2 (0.4)	−1.5 (0.4)	.55
Frenchay Activities Index			
Baseline	16.1 (1.5)	18.7 (1.5)	.23
ΔMidtraining	1.8 (1.2)	1.3 (1.3)	.78
ΔPosttraining	2.6 (1.3)	2.6 (1.3)	.99
Δ3-month follow-up	4.5 (1.3)	6.4 (1.3)	.32
Rand 36-Item Health Survey			
General health			
Baseline	67.6 (3.4)	67.8 (3.6)	.97
ΔMidtraining	−1.1 (2.6)	−2.6 (2.7)	.69
ΔPosttraining	1.1 (2.7)	0.9 (2.9)	.97
Δ3-month follow-up	3.0 (3.3)	1.0 (3.3)	.68
Social functioning			
Baseline	63.7 (5.1)	61.2 (5.4)	.74
ΔMidtraining	7.2 (5.0)	6.7 (5.3)	.94
ΔPosttraining	15.6 (5.3)	8.2 (5.6)	.35
Δ3-month follow-up	17.9 (5.7)	10.4 (5.7)	.36

**P* value represents between-group differences, adjusting for days poststroke.
Δ Indicates change in outcome measure from baseline.

overground walking speed and distance in individuals with moderate to severe gait impairments following subacute, unilateral stroke. Those individuals who were provided repeated, consistent locomotor training with the Lokomat improved in virtually every outcome measure we monitored. However, conventional training proved more effective for this population. Our original hypotheses were that the Lokomat would be more effective than conventional gait training at improving walking ability since participants can practice a high volume of steps in the device and also because the device promotes symmetric movements. We also expected that providing the participants biofeedback of their walking performance would help ameliorate compensatory strategies that are common in stroke.[25] Since the onset of the present clinical trial, research findings from our labs as well as others offer possible explanations for the differences in outcomes between Lokomat and conventional gait training.

One of the distinct limitations with the Lokomat is the restriction the device places on the participant's trunk and pelvis. Specifically, the Lokomat firmly compresses the participant's pelvis in the frontal plane just above the greater trochanters, with sagittal plane restraints using a posterior pad with adjustable straps. As such, during walking with the robotic device, pelvis movement is restricted. In our previous work,[26] we found that healthy participants will exhibit greater frontal and sagittal plane pelvic movement when walking freely on the treadmill versus walking with robotic assistance in the Lokomat. These restrictions prevent pelvic rotation and weight shifting between legs, which then translate to limited movement of the trunk. Restricting such movement during Lokomat training may alter the muscular work for propulsion[27] and medial/lateral stability[28] required during ambulation.[29] Such restrictions may also alter the acceleration patterns of the lower limbs, as Regnaux and colleagues[30] found that during Lokomat walking, participants tended to exhibit abnormal acceleration and deceleration from toe-off to heel contact.

Upper extremity motion is also restricted in the Lokomat because of the nature of the linkages. When walking in the device, the Lokomat linkages extend approximately 14 cm off each side of the participant's hips. As a result, for stroke participants with arm impairments and even those without neurological injury, it is very difficult to swing the arms when walking in the device. Others have suggested that bipedal locomotion in humans is under quadrupedal control[31] and have advocated the use of arm swing during gait training.[32] For individuals without neurological injury, there is some evidence to suggest that upper extremity activities can enhance lower extremity muscle activity during locomotor-like tasks.[33] In participants with stroke, however, despite a correlation between paretic upper limb function and independent ambulation,[34] there is insufficient data indicating that differences in upper extremity activity alter lower limb activity and/or recovery.

In addition to the restrictions the Lokomat places on the motion of the participant's arms and trunk, we believe another factor limiting its effectiveness is the guidance and feedback participants receive when walking in the device. Our previous data demonstrate that, despite movement of the limbs through normal "symmetrical" walking patterns, lower extremity muscle activity[29,35] and joint moments[36,37] produced by participants are altered substantially during Lokomat versus unassisted or therapist-assisted walking. For example, during swing, healthy participants tend to adduct their leg, while the paretic leg in stroke participants generates a strong abduction moment,[37] consistent with previously reported synergistic patterns.[38] The swing phase EMG activity is also altered when compared to unassisted or therapist-assisted treadmill walking in neurologically impaired participants, specifically demonstrating reduced hip flexor activity.[29,35] Unfortunately participants are unaware of these altered joint moments and muscle activation patters as they only see the kinematic patterns of their legs. Thus without an appropriate error signal of motor performance, motor learning will be significantly compromised.

Similar to the restraint at the pelvis and trunk, robotic guidance may reduce volitional muscle activity and subsequent learning.[39] Although participants constantly received verbal encouragement during training sessions, their effort level may not have always been at the highest level because the Lokomat provides the necessary assistance to complete the movement trajectory. Furthermore, the lack of variability in kinematic trajectories of the lower limbs during walking in the Lokomat may limit the amount of error experienced during training, which is thought to critical for successful motor adaptation as investigated in animal[40] and human studies.[41]

Another potential cause for less recovery in the Lokomat group may be the speeds of gait training in the Lokomat. Pohl et al[7] found that individuals with subacute stroke (average 16 weeks poststroke), who were trained on a treadmill at their maximum safe walking speed, demonstrated better outcomes in walking ability than those who received slower treadmill training and conventional gait training (using facilitative reflex or neurodevelopmental techniques). Similar findings have been reported in chronic stroke.[6] In our training paradigm, the maximum training velocity we were able to achieve on the Lokomat was 3.0 km/h (or equivalently 0.83 m/s), which was the top speed of the device when we started the study. Because one of our inclusion criteria was that the self-selected walking speed of participants ranged from 0.1 to 0.6 m/s, it is likely that the maximum walking speed of many of these participants exceeded 0.83 m/s, so that the slower training speeds may have been insufficient to maximize improvements in gait speed.

In addition to the lack of blinded assessment of outcomes, there are two possible limitations with the study that should be considered. First, one of the problems with testing a new technology, such as the Lokomat, is the rapid improvements in the design and control of these devices that occur in a short period of time. However, to deliver a consistent protocol across all participants trained, we were unable to take advantage of some of the new features of the Lokomat. For example, extensive work has been done on the Lokomat to develop comprehensive biofeedback and cooperative control strategies (see Riener et al[42] for review), which may improve outcomes. Neither of these latest technologies was used in this study. Although feedback was provided during training sessions in the Lokomat, the feedback was restricted to the hip and knee joints in the sagittal plane only and was based on data from the previous step rather than real-time performance. Real-time biofeedback and enhanced control strategies may facilitate gains in motor recovery[9] and may be a necessary adjunct to robotic-assisted gait training. The second limitation with the study is that participants in the Lokomat group only received robotic-assisted treadmill training and no conventional gait training. In the clinical setting, gait training would likely be multidisciplinary, where participants would receive robotic-assisted gait training as needed, with therapist-assisted treadmill walking and conventional gait training. Indeed, our recent investigations have indicated some key differences between walking on a treadmill compared to walking overground.[43] Such a multidisciplinary approach to gait retraining has been suggested previously[44] and incorporated using the Lokomat.[45] Pohl and colleagues[46] have recently shown that this approach is an effective strategy for treating individuals with acute nonambulatory stroke. For this study, attempts to combine therapies would have necessitated increases in our sample size substantially. A follow-up study could include a progressive approach to gait training in stroke survivors based on attainment of certain locomotor milestones and progression to the next intensity.

Our results are in contrast with previous reports in subacute stroke participants with limited walking ability,[15,47] although consistent with data in ambulatory individuals with chronic stroke[48] and spinal cord injury.[49] In the study by Husemann et al[15] 30 individuals, 28 to 200 days poststroke, were either provided gait training using the Lokomat for 20 sessions, with an additional 20 conventional gait training sessions, or 40 sessions of conventional gait training. Prior to and following the 40 sessions performed over 4 to 5 weeks, evaluations of walking ability and other functional measures revealed no differences in changes in fastest comfortable walking speed over 10 m or FAC, although there were small differences in single limb stance time favoring Lokomat training. The lack of group differences in this study could be explained by the extent of recovery of stroke participants following initial injury. Specifically, mean duration poststroke in this study was approximately 80 to 90 days and participants could not walk without substantial physical assistance. Duncan et al[50] previously showed that for severely impaired stroke participants, the majority of recovery occurs in the first 30 days, whereas after 90 days, improvements in function are minimal. Accordingly, results in the Husemann study, where participants entered the study with a fastest comfortable walking speed of 0.12 to 0.14 m/s, only improved by 0.06 to 0.08 m/s after 40 sessions of therapy. Such minimal changes may indicate the limited recovery potential in walking ability regardless of the intervention. In the present study, participants walked with an average self-selected walking speed of 0.3 m/s at study entry and were independent ambulators. Thus, we believe the participants trained in our study had much greater potential for improvements in walking ability than those in the Husemann study.

Our results also differ from those reported by Mayr et al.[47] In that study, 16 subacute stroke participants averaging 2.8 months poststroke were trained using the Lokomat (treatment A) and conventional treatment (treatment B) using an A-B-A versus B-A-B design, with each phase lasting 3 weeks (5 sessions per week). Of the participants trained, 12 of the 16 participants required full support by a physical therapist to walk overground, while 3 required a walking aid and verbal assistance. They reported that participants in the A-B-A group demonstrated greater gains in nearly all measures of walking ability and lower limb function. As addressed previously, a more impaired participant population at an extended duration poststroke may be confounders, which limit the utility of their findings. Additionally, this study utilized a crossover design, where it is likely that the different phases were likely coupled and not independent. Finally, the low sample size may limit the statistical power. Despite such limitations, perhaps training with the Lokomat followed by therapist-assisted or overground gait training is an appropriate multidisciplinary approach to improving walking ability in severely impaired participants with neurological injury.[45]

Differences in results between our study and previous work emphasize the need to interpret findings cautiously. That is, impairment levels, time poststroke, and other key factors that strongly influence stroke recovery need to be considered when comparing outcomes of rehabilitation studies. Although the

present study clearly demonstrates that conventional therapy is more effective at improving walking speed and endurance than Lokomat training, this can only be confirmed for the demographic of individuals we trained. Extrapolating our findings to stroke patients at different periods after stroke, different impairment levels, lesion locations, etc, is likely to lead to erroneous predictions of the effectiveness of treatment interventions. Future studies will need to evaluate robotic-assisted gait training at various stages poststroke, and in individuals with a range of lower extremity deficits.

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