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ORIGINAL ARTICLE



# Evaluation of Gait Training with Treadmill Versus Rehabilitation on Ground Methods in Hemiparetic Patients with Temporospatial and Kinematic Data

# İbrahim Halil Ural<sup>1</sup>, Murat Özkaya<sup>2</sup>, Ayşe Yalıman<sup>3</sup>

<sup>1</sup>Department of Physical Medicine and Rehabilitation, İstanbul Beykent University Faculty of Medicine, İstanbul, Türkiye <sup>2</sup>Department of Physiotherapy, İstanbul Beykent University of Health Sciences Türkiye Faculty of Medicine, İstanbul, Türkiye <sup>3</sup>Department of Physical Medicine and Rehabilitation İstanbul University Faculty of Medicine, İstanbul, Türkiye

### Abstract

**Introduction:** Gait disorders can occur in different forms in hemiplegic patients. Restoring a rapid, safe, and independent gait is the main goal of neurorehabilitation after stroke. Gait training with a treadmill became popular in rehabilitation. The treadmill allows for a large number of steps in a training session and a large amount of task-specific exercise can be performed.

**Methods:** Twenty patients were enrolled in this prospective, randomized, and controlled study. The patients were divided into two groups. With computerized gait analysis, the temporospatial parameters of gait and kinematics of lower extremity joints and pelvis were evaluated. Functional evaluation was performed with a 10-m walking time (sec) and the Functional Independence Measure (FIM) - mobility and locomotion score.

**Results:** The changes in the kinematic analyses in both groups showed that walking was more economical and functional in the treadmill group. Treadmill training stimulated functional changes on the paretic side. In the ground group, changes occurred mostly in the pelvis and leg on the healthy side, and in this way, the walking function was improved. At the same time, it was determined that the gains in the motor abilities of the paretic lower extremity, 10-m walking time, FIM mobility, and locomotion scores were higher in patients who were rehabilitated in the early period and who were given walking training on the treadmill.

**Discussion and Conclusion:** Treadmill training in stroke-related hemiplegia can develop gait speed and safety in hemiplegia. Since treadmill treatments are more reachable and cheaper, they can be preferred in the rehabilitation of the gait in stroke-related hemiplegia.

Keywords: Brain plasticity; gait analyses; hemiplegia; stroke rehabilitation; treadmill.

ndependent ambulation is an important rehabilitation goal for hemiplegic patients. Two-thirds of stroke patients hospitalized in the acute period are unable to walk independently. Gait disorders can occur in different forms<sup>[1,2]</sup>. Since stride length and cadence determine walking speed, a decrease in one or both of these parameters may cause a decline in walking speed in hemiplegic patients<sup>[3]</sup>.

**Correspondence:** İbrahim Halil Ural, M.D. Department of Physical Medicine and Rehabilitation, İstanbul Beykent University Faculty of Medicine, İstanbul, Türkiye **Phone:** +90 533 733 81 23 **E-mail:** ihural@gmail.com



Twenty-five percent of patients remain wheelchair-bound, 60% have markedly reduced walking capacity, and speed 3 months after stroke<sup>[4]</sup>. Therefore, restoring and correcting gait rapidly, safely, and independently are the main goal of neurorehabilitation after stroke<sup>[5]</sup>.

Since the term brain plasticity entered, the literature on gait training using the treadmill or other robotic rehabilitation methods has become increasingly popular methods in rehabilitation. Electrophysiological studies have shown that rehabilitation in hemiparetic or hemiplegic patients stimulates the re-activation of masked latent pathways in the brain. Usually, this reorganization occurs as a result of the formation of new synaptic connections. Treadmill or robotic rehabilitation systems can stimulate brain plastic-ity<sup>[6,7]</sup>. Treadmill systems can include a lift system with body weight support, or they can be supported by handrails. The treadmill allows for many numbers of steps in one training session, and a large amount of task-specific exercise can be performed<sup>[8,9]</sup>.

This study aims to evaluate the effectiveness of gait training with a treadmill in patients with stroke-related hemiparesis with quantitative temporospatial and kinematic data obtained by gait analysis and clinical assessment scales and to compare to the traditional rehabilitation approach.

# **Materials and Methods**

This study is performed with the permission of the Ethical Committee of Istanbul University Istanbul Medical Faculty (approval number: 1110, date: July 26, 2005). This research was conducted in accordance with the Declaration of Helsinki. Twenty patients were enrolled in this prospective, randomized, controlled, and a pilot study. The patients were randomized in order of admission. The written informed consent form was received from all participants before the study. Hemorrhagic or ischemic stroke etiology may cause differences in the spontaneous recovery process and this may contribute to the difference in functional endstates between ischemic and hemorrhagic stroke patients. For these reasons, we included patients with stroke, whose etiology is ischemic, and the posterior irrigation area of the brain and the cerebellum is not affected.

Inclusion and exclusion criteria are given in Table 1.

### Method

The patients were divided into two groups:

- 1. Group 1 (Treadmill group-TG): Walking training on the treadmill
- 2. Group 2 (Floor Group-FG): Walking training on flat ground.

### Table 1. Inclusion and exclusion criteria

Inclusion criteria

- Ischemic stroke,
- A maximum of 12 months has elapsed since the date of the cerebrovascular attack when the patients started walking training,
- The Functional Ambulation Category score of 3, 4, or 5
- Being able to walk 10 m without using any device and without assistance

### Exclusion criteria

- Having a high cardiovascular risk to exercise walking on the treadmill
- Presence of an orthopedic pathology that disrupts the normal gait pattern before or after cerebrovascular disease
- Dementia, sensory aphasia, denial syndrome, and severe cognitive dysfunction (mini-mental state test score < 23)</li>
  Presence of lesions in the irrigation area of the posterior cerebral artery or in the cerebellum

In both groups, additional physiotherapy included a range of motion, stretching, and strengthening exercises as conventional physiotherapy. Gait training on a treadmill or flat surface was applied for a minimum of 15-maximum 20 min, depending on the patient's tolerance. In both groups, walking training was applied 5 days a week for 4 weeks. During the research, the affected upper extremities were treated when needed. Computerized gait analysis was performed before and after the gait training. Evaluations with functional assessment measurements were performed before the treatment and 3<sup>rd</sup> month after the completion of the treatment.

During the treadmill walking, blood pressure and heart rate were monitored intermittently. Speed was kept variable throughout the exercise and was started from 0.9 km/h and increased up to 2.6 km/h according to the patient's tolerance.

### **Evaluation Measurements**

Measurements were evaluated in two ways. With computerized gait analysis, the temporospatial parameters of gait and kinematics of lower extremity joints and pelvis were evaluated. Functional evaluation was performed with a 10-m walking time (sec) and the Functional Independence Measure (FIM) - mobility and locomotion score. FIM - mobility and locomotion score is calculated through the items which measure walking and stepping. In these items, walking is evaluated at a given time and given distance and stepping 12–14 steps independently and comfortably.[10] The patients who are in grades 3, 4, or 5 in these items are included in the research.

### **Computerized Gait Analysis**

The walking characteristics of patients were determined by a 3D motion analysis system consisting of 6 high-speed (100 ps) cameras (Elite System, BTS S.p.A, Milan, Italy). Walking parameters were determined by allowing them to walk at normal speed on the 15-m walkway. The timedistance parameters of three randomly selected from at least 5 repetitions walks obtained from each case were evaluated and the arithmetic averages of these parameters were calculated. In kinematic evaluation, reflective markers were placed on the 7<sup>th</sup> cervical vertebra, sacrum, bilaterally on the acromion, superior anterior iliac crest, trochanter major, lateral mid-thigh, lateral epicondyle, fibular head, lateral mid-calf, ankle lateral malleolus, heel, and 5<sup>th</sup> metatarsophalangeal joint of the patients during walking (Fig. 1).

In kinematic analysis, the only motion is examined. The position of the trunk, pelvis, legs, and feet in frontal, sagittal, and transverse plains, joint angles, linear and angular velocities, and accelerations are measured and recorded as numerical data. The signals coming from the markers which are placed on certain points of the lower extremities are monitored by cameras. The data of each joint are calculated during the walking cycle. Kinematic parameters were calculated for the right and left legs by averaging at least 3 walks. Then, the right and left legs were separated into paretic and normal legs. In each group, the averages of the paretic and normal leg kinematics were taken and the values before and after the treatment were compared on a group basis (paretic legs TG/FG, normal legs TG/FG). Temporospatial and kinematic variables are given in Table 2.

### **Statistical Analysis**

SPSS 13.0 (the Statistical Package for the Social Sciences, SPSS Inc. Version 13.0. Chicago) software was used for statistical analysis of the data. " $p \le 0.05$ " was considered statisti-

# <image><image><image>

**Figure 1.** Gait analysis laboratory, placement of the cameras and marker and computer imagening of the gait.

### Table 2. Temporospatial and Kinematic Variables

- Stance phase (time %)
- Swing phase (time %)
- Double support times (time %)
- Step time for each leg
- Anterior stride length
- Speed
- Sway velocity
- Step length
- Number of steps per minute (cadence)
- Average walking speed
- Step widths
- Movements of the pelvis in three planes
- (frontal-sagittal-transverse):
  - o Maximum pelvic up-down motion and range of motion
  - o Maximum pelvic forward-backward motion and range of motion
  - o Maximum pelvic internal-external rotation and range of motion

• Movements of the hip joint in three planes (coronal-sagittal-transverse):

- o Maximum flexion-extension values and ranges of motion o Maximum adduction-abduction values and ranges of motion
- o Maximum internal/external rotation values and ranges of motion
- Movement of the knee joint in the sagittal plane:
   Maximum flexion-extension values and range of motion
- Movement of the ankle joint in the sagittal plane:
- o Maximum dorsi-plantar flexion and range of motion

cally significant in the analyses. "Chi-square – Fisher's Exact Test" was used to determine whether the gender distribution was homogeneous according to the treatment groups. The non-parametric "Wilcoxon Signed-Rank Test" was used to compare clinical assessment scales, swing phase kinematics, and other kinematic data before and after treatment. The non-parametric "Mann–Whitney U-test" was used to compare the differences between the two groups. Since this study is a pilot study, power analyses were not performed before the study.

## Results

The patients were homogeneous in terms of pre-treatment age, disease duration, gender, clinical assessment measures, and temporospatial characteristics of gait (p>0.05). 12 male and 8 female patients were included to this research. Demographic data are given in Table 3 and the distribution of the gender of the participants is given in Table 4.

	Treadmill Group (n=10)	Ground Group (n=10)	<b>p</b> *	
	Average±SD (Median)	Average±SD (Median)		
Age (years)	50.8±12.55/(53)	53.8±6.56/(54)	0.622	
Disease duration (months)	4.2±3.45/(3)	5.2±4.61/(3)	0.877	
* Mann–Whitney U-test.				

### **Table 3.** Demographic data of the participants

#### Table 4. Distribution of the gender of the participants

	Treatment Group	
Tread	nill Groun	d
7	4	11
3	6	9
10	10	20
3 10	10	

\*p=0.185 (Chi-square – Fisher's exact test).

Results of clinical evaluation scores in TG are given in Table 5. Results of clinical evaluation scores in TG are given in Table 6. Results of lower extremity kinematics are given in Table 7. Results of swing phase kinematics of walking are given in Table 8.

FIM mobility and locomotion scores were significantly higher at the  $3^{rd}$ -month follow-ups and 10-m walking time was significantly shortened in 1-month follow-up in all patients (p<0.05).

### Discussion

Independent ambulation is one of the main goals of rehabilitation and a key element for independence in stroke. <sup>[9]</sup> Because there are various forms of stroke, it is difficult to form homogeneous groups with stroke patients in research. We tried to standardize the participants as much as possible. In this research, FIM-mobility and locomotion scores and 10-m walking time showed statistically significant advances which continued for 3-month follow-up in both groups. However, the shortening in 10-m walking time was more in TG at the end of the research and 2 times more than FG in 3-month follow-up.

At the swing phase kinematics of gait in the sagittal plane, the ankle dorsiflexion angle per unit time decreased significantly in both groups, but there was no significant difference between the groups. However, in the swing phase, knee and hip flexion angles per unit time increased significantly in the TG but decreased significantly in the FG.

Animal studies<sup>[11]</sup> show that treadmill training in the early period after cerebral infarction improves the functional status, which is due to the changes at the cellular level that occurs in and around the infarcted area of the central nervous system. Hence, treadmill training in the restoration of gait may be a more appropriate approach in the early period of rehabilitation.

Hip and knee flexion and internal rotation of the pelvis and the decrease in hip raise in the swing phase of the paretic leg increased in the treadmill group. Since the hip and knee muscles are larger muscle groups, and they consume the greatest amount of energy expended during walking, it can be concluded that gait training on the treadmill pro-

Table 5. Clinical evaluation scores in treadmill group before and after the treatment				
Treadmill Group	Before treatment	After treatment	3. months	
	Average±SD	Average±SD	Average±SD	
	(meters)	(meters)	(meters)	
FIM Mobility score	30.2±4.37/(31)	31.8±3.16/(32)	33.2±2.53/(35)	
Ten-meters walking time (seconds)	17.8±3.74/(17.5)	13.6±2.87/(13.69)	13.6±3.56/(12.75)	

**Table 6.** Clinical evaluation scores in ground group before and after the treatment

Ground Group	Before treatment Average±SD (meters)	After treatment Average±SD (meters)	3. months Average±SD (meters)
FIM mobility score	29.8±3.49/(29.5)	30.9±2.81/(30.5)	31.7±2.75/(32.5)
10-m walking time (seconds)	21.9±6.74/(19.95)	18.9±6.30/(16.54)	19.8±6.18/(17.3)

# Table 7. Lower extremity kinematics

Joint	Paretic leg		Normal leg	
	Pre-treatment	Post-treatment (3 months)	Pre-treatment	Post-treatment (3 months)
Ankle dorsi/plantar flexion Treadmill group				
Maximum DF	11.81°	10.47°	12.53°	11.71°
Minimum PF	3.66°	6.15°	2.29°	1.31°
Total ROM	15.47°	16.63°	14.82°	13.02°
		p<0.001		p<0.001
Ankle dorsi/plantar flexion				
Floor group				
Maximum DF	11.74°	6.71	17.13°	15.52°
Minimum PF	7.32°	9.29	-2.97°*	-0.94°*
Total ROM	19.06°	16.00°	14.16°	14.58°
		p<0.001		p<0.001
Knee flexion and extension				
Treadmill group				
Maximum	36.58°	39.92°	56.74°	50.54°
Minimum	5.40°	3.07°	2.78°	1.31°
Total ROM	31.18°	36.85°	53.96°	49.23°
		p=0.366		p<0.001
Knee flexion and extension				
Floor group				
Maximum	35.26°	34.71°	55.78°	57.23°
Minimum	4.50°	0.21°	13.48°	7.50°
Total ROM	30,76°	34.50°	42.30°	49.73°
		p<0.001		p<0.001
Hip abduction and adduction *				
Treadmill group				
Abduction	7.64°	13.46°	12.03°	7.98°
Adduction	0.20°	-3.28°	-4.54°	-1.39°
Total ROM	7.84°	10.18°	7.49°	6.59°
		p<0.001		p<0.001
Hip abduction and adduction				
Floor group	5.000	6.000		7 7 40
Abduction	5.99°	6.93°	5.65°	7.76°
Adduction	3.07°	-0.04°	-0.13°	-1.32°
Iotal ROM	9.06°	6.89°	5.52°	6.44°
11: A		p<0.001		p<0.001
Hip flexion and extension **				
Ireadmill group	26.169	27.76	26.11	22.20
Flexion	26.16°	27.76°	36.11	33.30
Extension	1.97°	0.74°	6.54	9.31
ROM	28.13°	28.50°	42.65°	42.61°
		p>0.05		p<0.001
Hip flexion and extension				
Floor group	20 710	27.00	20.00	24.50
FIEXION	28.7 I <sup>°</sup>	27.98	39.90	34.59
Extension	-3.U9 <sup>-</sup> ^	1.92	-1.U2 <sup>^</sup>	0.09
KUM	25.02°	29.18	38.88	41.28°
		p<0.001		p<0.001

## Table 7. Lower extremity kinematics

Joint	Paret	Paretic leg		Normal leg	
	Pre-treatment	Post-treatment (3 months)	Pre-treatment	Post-treatment (3 months)	
Hip rotation					
Treadmill group ***					
Total ROM	-2.30°	−7.80° p<0.001	-5.08°	–0.93° p<0.001	
Floor group ***					
Total ROM	-1.38°	−1.99° p<0.001	-1.14°	–5.81° p<0.001	
Pelvic obliquity		·		·	
Treadmill group					
Up	5.11°	4.83° p<0.001	-1.30°	0.63° p<0.001	
Down	2.15°	-1.16°	-5.66°	-3.87°	
Pelvic obliquity		p<0.001		p<0.001	
Floor group					
Up	5.84°	6.71° p<0.001	-0.63°	–1.27° p<0.001	
Down	0.66°	1.28° p<0.001	-5.86°	−6.60° ¤<0.001	
Pelvic rotation		·		·	
Treadmill group					
Max. Int. Rot.	5.14°	6.55°	5.74°	3.82°	
Max Ext Pot	7 20°	μ<0.001 4 24°	2 110	p<0.001 5 10°	
Mdx. Ext. NOL.	-7.20	p<0.001	-3.44	p<0.001	
Pelvic rotation					
Floor group					
Max. Int. Rot.	5.77°	-1.04°	3.93°	7.33°	
		p<0.001		p<0.001	
Max. Ext. Rot.	-4.58°	-6.47°	-4.60°	0.21°	
		p<0.001		p<0.001	
Pelvic tilt Treadmill group					
Anterior	10.08°	11.75°	10.90°	12.25°	
		p<0.001		p<0.001	
Posterior	4.04°	4.60°	3.55°	6.10°	
		p<0.001		p<0.001	
Pelvic tilt					
Floor group					
Anterior	12.78°	9.92°	12.53°	9.92°	
		p<0.001		p<0.001	
Posterior	5.64°	3.68°	4.88°	4.13°	
		p<0.001		p<0.001	

ROM: Range of motion, DF: Dorsiflexion, PF: Plantarflexion, Max. Int. Rot.: Maximum internal rotation, Max. Ext. Rot.: Maximum external rotation, \* Angles are given as (-) since the movement cannot pass to the direction of adduction. \* \* Angles are given as (-) because the movement cannot pass to the extension direction. \*\*\* Angles (-) indicate that it is in external rotation.

Table 8. Swing phase kinematics of walking					
Joint	Pre-treatment	Post-Treatment	р		
Ankle					
Treadmill Group					
Maximum DF	1.56°	-1.27°*			
Maximum PF	3.67°	6.14°			
ROM in swing phas	ie 5.23°	4.87°	p<0.001		
Ankle					
Floor Group					
Maximum DF	-1.91°*	-4.54°*			
Maximum PF	7.33°	9.30°			
ROM in swing phas	e 5.42°	4.76°	p<0.001		
Knee flexion					
Treadmill Group					
Maximum	36.58°	39.92°			
Minimum	13.03°	11.43°			
ROM in swing phas	e 23.55°	28.48°	p<0.001		
Knee Flexion					
Floor Group					
Maximum	35.27°	34.72°			
Minimum	13.38°	11.97°			
ROM in swing phas	e 21.89°	22.75°	p<0.001		
Hip flexion					
Treadmill Group					
Maximum	26.16°	27.77°			
Minimum	11.63°	13.84°			
ROM in swing phas	e 14.53°	13.93°	p<0.001		
Hip flexion					
Floor Group					
Maximum	28.72°	27.98°			
Minimum	11.45°	10.19°			
ROM in swing phas	e 17.27°	17.79°	p<0.001		

ROM: Range of motion, DF: Dorsiflexion, PF: Plantarflexion, Max. Int. Rot.: Maximum internal rotation, Max. Ext. Rot.: Maximum external rotation, \* Angles are given as (-) since the movement cannot pass to the direction of adduction. \* \* Angles are given as (-) because the movement cannot pass to the extension direction. \*\*\* Angles (-) indicate that it is in external rotation. DF: Dorsiflexion, PF: Plantarflexion, ROM: Range of motion.

vided a more economical gait pattern in terms of energy spent while walking.

Visintin et al.<sup>[12]</sup> found better results with training with body weight support treadmill (BWST) about independency in speed and endurance in patients who were walking dependently. On the other hand, they observed that combining body weight support to treadmill training in patients who were walking independently did not provide superiority over these parameters<sup>[13]</sup>. Laufer et al.<sup>[14]</sup> reported that stroke patients can tolerate treadmill training without body weight support at the early phase of the rehabilitation. In our study, instead of the BWST, the classical treadmill with handrail support and with no modification was used. Based on the results of Visintin et al.,<sup>[12,13]</sup> it can be thought that treadmill training without body weight support will not affect the final situation, since our patients were able to walk independently at the beginning of the treatment.

Bayat et al.<sup>[15]</sup> obtained that stroke patients walked faster on normal ground than on a treadmill, and they could increase their speed much more during walking on the ground. It was determined that the stride length was statistically significantly greater and the cadence was lower in ground walking compared to treadmill walking<sup>[15]</sup>. Harris-Love showed that during the treadmill gait, while the stance and single support phase ratios and stance/swing phase ratios increased in the paretic leg, they decreased in the healthy leg, thus providing a more harmonious and symmetrical gait pattern than the over-ground gait<sup>[9]</sup>. In our study, no significant change was found in the temporospatial parameters of gait after treatment in either treatment group. The fact that there was no significant change in the temporospatial parameters before and after the treatment in the TG. Hence, it suggested that the harmonious and symmetrical gait pattern on the treadmill could not be transferred to normal gait, at least in the short term.

Weight transfer with BWST in the stance phase, singledouble support ratios of walking, and tibialis anterior and guadriceps muscle activation in the stance phase are more symmetrical with gait training given on the treadmill<sup>[16-18]</sup>. In our study, when the kinematics of the lower extremities were examined, the maximum flexion angle and range of motion of the knee on the paretic side increased in TG after treatment, while both decreased in the normal leg. In the FG, both the maximum flexion angle and range of motion of the knee in the normal leg increased, and the difference between the healthy side and paretic side in a range of motion increased. In the TG, during the entire gait cycle, hip abduction and flexion per unit time of the paretic leg increased, while it decreased in the normal leg. During the entire walking cycle in the FG, hip abduction per unit time increased, while hip flexion decreased in both legs. In addition, the pelvic obliquity angles of both legs that changed during the walking cycle approached each other in the neutral position direction in the TG, while diverged in the FG. We concluded that the TG walked more symmetrically in terms of lower extremity and pelvis kinematics than the FG. It is seen that compensatory changes due to motor deficiencies occur in the paretic leg in TG, while it occurs more in the healthy leg in FG.

Daly et al.<sup>[19]</sup> obtained no significant increase in peak swing hip flexion in both groups before and after treatment in which swing phase kinematics of gait was used as an evaluation criterion. They suggested that the improvement may be due to activity-related central nervous system plasticity. However, the fact is different from Daly et al. In animal studies, it has been shown that the application of treadmill training in the early period after cerebral infarction improved the functional status, which is due to the changes at the cellular level that occurs in and around the infarcted area of the brain. For this reason, treadmill training may be a more appropriate approach in the early period of gait rehabilitation.

Two important mechanisms reduce the activity duration and intensity of the muscles participating in a movement. The first is the mechanism that reduces the displacement of the body's center of gravity (CG), and the other is the controlled, economical contraction of the muscles. The movement of the pelvis in all three planes increases in hemiparetic patients. Accordingly, displacement of CG to above normal and is an important indicator of decreased walking efficiency<sup>[20]</sup>. In our study, a significant decrease was observed in the pelvic obliquity A/T during the walking cycle of the paretic leg in TG, while a significant increase was observed in the other group. Maybe this increases the effectiveness of walking positively in the TG. In our study, pelvic internal rotation A/T in the swing phase and throughout the gait cycle of the paretic leg increased in the TG but significantly decreased in the FG. This is due to the compensation of the changes in the paretic legs. An increase in hip and knee flexion and internal rotation of the pelvis in the swing phase of the paretic leg in the TG and a decrease in hip raising movement were concluded that gait training on the treadmill provided a more economical gait pattern in terms of energy consumed while walking.

In our study, hip abduction and external rotation angles in the paretic leg were found to be significantly increased in the TG. Hip abduction and external rotation of the normal leg were decreased in the TG while increased in the FG. These results can be interpreted that the disorder of motor control and gait asymmetry in hemiplegic patients were tried to be corrected by compensatory movement changes that occurred more in the paretic leg in the TG and the normal leg more in the FG.

The design and the homogeneity as much as possible of the study groups increase the reliability of our results. Since no need for special rehabilitation equipment, the organization of the research is easy, and the use of computerized analysis systems increases the accuracy of the data. Although we think that these are the strong sides of our research, we consider that evaluating similar groups with BWST and robotic rehabilitation devices could increase this strength. Besides, increasing the number of subjects in groups could also increase the power of the data.

### Conclusion

The changes detected in hip and knee flexion, pelvic rotation, pelvic tilt, pelvic obliquity, and swing phase kinematics in both lower extremities in the kinematic analyses in both groups showed that walking was more economical and functional in the TG, and treadmill training stimulated positive functional changes in the pelvis and legs, especially on the paretic side. On the other hand, changes that developed in the FG occurred mostly in the pelvis and leg on the healthy side, and in this way, the walking function was improved. At the same time, it was determined that the gains in the motor abilities of the paretic lower extremity, 10-m walking time, and FIM mobility and locomotion scores were higher in patients who were rehabilitated in the early period and who were given walking training on the treadmill.

**Ethics Committee Approval:** This study is performed with the permission of the Ethical Committee of Istanbul University Istanbul Medical Faculty (approval number: 1110, date: July 26, 2005).

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**Authorship Contributions:** Concept: A.Y., M.Ö., İ.H.U.; Design: A.Y., M.Ö.; Supervision: A.Y.; Fundings: A.Y., M.Ö., İ.H.U. Materials: M.Ö., İ.H.U.; Data collection and proccesing: M.Ö., İ.H.U.; Analysis os Interpretation: M.Ö., İ.H.U.; Literature search: M.Ö., İ.H.U.; Writing: M.Ö., İ.H.U.; Critical review: A.Y.

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