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Against the odds: what to expect in rehabilitation of chronic spinal cord injury with a neurologically controlled Hybrid Assistive Limb exoskeleton. A subgroup analysis of 55 patients according to age and lesion level

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OBJECTIVE Age and lesion level are believed to represent outcome predictors in rehabilitation of patients with chronic spinal cord injury (SCI). The Hybrid Assistive Limb (HAL) exoskeleton enables patients to perform a voluntary controlled gait pattern via an electromyography-triggered neuromuscular feedback system, and has been introduced as a temporary gait training tool in patients with SCI. The aim of this prospective pre- and postintervention study was to examine functional outcomes as a function of age and lesion level in patients with chronic incomplete SCI (iSCI) or chronic complete SCI (cSCI) with zones of partial preservation (ZPP) by using the HAL as a temporary training tool.

METHODS Fifty-five participants with chronic iSCI or cSCI (mean time since injury 6.85 ± 5.12 years) were classified according to the American Spinal Injury Association (ASIA) Impairment Scale (AIS) and divided by age (< 50 or ≥ 50 years), independent of lesion level, and also into 4 homogeneous groups according to lesion level. The subgroups were as follows: Subgroup 1, tetraplegic iSCI (n = 13) (C2–8, AIS C [n = 8] and AIS D [n = 5]); Subgroup 2, paraplegic iSCI with spastic motor behavior (n = 15) (T2–12, AIS C [n = 8] and AIS D [n = 7]); Subgroup 3, paraplegic cSCI with complete motor paraplegia and absence of spastic motor behavior (n = 18) (T11–L4 [AIS A], and ZPP from L-3 to S-1); and Subgroup 4, paraplegic iSCI with absence of spastic motor behavior (n = 9) (T12–L3, AIS C [n = 8] and AIS D [n = 1]). The training paradigm consisted of 12 weeks of HAL-assisted treadmill training (5 times/week). Baseline status was documented prior to intervention by using the AIS grade, Walking Index for SCI II (WISCI II) score, the 10-meter walk test (10MWT), and the 6-minute walk test (6MinWT). Training effects were assessed after 6 and 12 weeks of therapy, without HAL assistance.

RESULTS Overall, a time reduction of 47% in the 10MWT, self-selected speed (10MWTsss) (< 50 years = 56% vs ≥ 50 years = 37%) and an increase of 50% in the 6MinWT were documented. The WISCI II scores showed a mean gain of 1.69 levels. At the end of the study, 24 of 55 patients (43.6%) were less dependent on walking aids. Age had a nonsignificant negative influence on the 10MWTsss. Despite a few nonsignificant subgroup differences, participants improved across all tests. Namely, patients with iSCI who had spastic motor behavior improved to a nonsignificant, lesser extent in the 6MinWT.

CONCLUSIONS The HAL-assisted treadmill training leads to functional improvements in chronic iSCI or cSCI, both in and out of the exoskeleton. An improvement of approximately 50% in the 10MWTsss and in gait endurance (6MinWT) can be expected from such training. The influences of SCI lesion level and age on functional outcome were nonsignifi-

ABBREVIATIONS AIS = ASIA Impairment Scale; ASIA = American Spinal Injury Association; BWSTT = body weight–supported treadmill training; CPG = central pattern generator; cSCI, iSCI = complete spinal cord injury, incomplete SCI; HAL = Hybrid Assistive Limb; ISNCSCI = International Standards for Neurological Classification of Spinal Cord Injury; LEMS = lower-extremity motor score; WISCI II = Walking Index for SCI II; ZPP = zones of partial preservation; 6MinWT = 6-minute walk test; 10MWT = 10-meter walk test; 10MWTsss = 10MWT, self-selected speed.

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cant in the present study. Older age (≥ 50 years) may be associated with smaller improvements in the 10MWTsss. An iSCI in paraplegic patients with spastic motor behavior may be a nonsignificant negative predictor in gait endurance improvements.

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KEY WORDS chronic spinal cord injury; Hybrid Assistive Limb; exoskeleton; locomotion; rehabilitation; subgroup analysis

Following a spinal cord injury (SCI), the majority of neurological and therefore ambulatory recovery occurs within the 1st year. After this period, recovery appears to be nearly completed, maintaining a constant neurological level.[27] Whereas patients with complete SCI (cSCI) demonstrate segmental improvements around the lesion level, those with incomplete SCI (iSCI) experience a substantially greater functional and neurological recovery.[6] The literature suggests that the extent of neurological recovery depends on lesion level; a patient's age; neurological impairment (as measured by the International Standards for Neurological Classification of Spinal Cord Injury [ISNCSCI]); and immediate, intensive, and individually tailored physiotherapy.[34,37] In patients with iSCI, intensive gait training leads to substantial improvements in walking functions.[7,15] Restoration of motor functions is based on the fundamental concept that repeated execution of a motor task induces plasticity and functional and structural reorganization of neuronal circuits in the injured brain and spinal cord.[29,40]

The central pattern generator (CPG) is known as a neuroanatomical structure that consists of a neuronal network cluster in the spinal cord.[10,13,14,26] The CPG is involved in the generation of a stepping-like movement in the supine and upright position in humans, and is relevant for locomotion.[24,25] To achieve a relevant level of independent locomotion, the CPG uses sufficient supraspinal input as well as afferent feedback from the peripheral nervous system.[24,25] Body weight–supported treadmill training (BWSTT) is an established primary rehabilitative therapy for patients with iSCI and those with cSCI with zones of partial preservation (ZPP), and may be effective in improving functional ambulation in patients with chronic SCI.[3,19] Depending on the severity of the injury, BWSTT often requires the assistance of multiple physiotherapists, thus hampering regular and intensive therapy, a crucial factor in the optimum recovery of motor function.[34] To facilitate a greater duration of therapy, while allowing for more physiologically accurate and reproducible gait patterns in therapy, driven gait orthoses like the Lokomat (Hocoma AG) have been developed.[3,4,9,38]

More recently, various wearable and mobile exoskeletons have been introduced and used not only for therapeutic purposes but as medical and assistive daily use walking aids. However, most available exoskeletons are controlled by posture and use autonomously generated predefined gait patterns for passive mobilization of patients with SCI by direct motion support.[2] In contrast, the neurologically controlled Hybrid Assistive Limb (HAL, Cyberdyne Inc.) exoskeleton offers an active electromyography-triggered neuromuscular feedback system (Fig. 1). Amplifying minute bioelectrical signals in the lower extremities of patients with iSCI or patients who have cSCI with ZPP, the HAL exoskeleton allows for a voluntarily driven range of motion.[1,2,33] Several studies have indicated that BWSTT with HAL is not only feasible and safe in patients with acute and chronic SCI, but that it increases their functional mobility, over-ground walking, muscle strength, and motor functions when outside the HAL exoskeleton.[1,5,30] Nevertheless, the literature continues to suggest that post-SCI neurological and ambulatory recovery depends on a patient's lesion level and age, as well as their initial AIS grade.[7,8,34,37] Lesion characteristics (low AIS grade) and age (≥ 50 years) especially seem to be negative predictors for functional recovery following SCI.[34,37]

The purpose of this study was to compare the functional outcomes of patients with chronic SCI in 4 injury-level groups following 12 weeks of HAL-assisted BWSTT in a pre- and postintervention prospective study design. The groups were defined as incomplete tetraplegia, incomplete paraplegia with spastic motor behavior, patients with incomplete conus medullaris and/or cauda equina SCI, and patients who had complete conus and/or cauda SCI with ZPP. Furthermore, all outcomes were independently analyzed as a function of age (< 50 years vs ≥ 50 years).

Methods

This study was registered with the Deutsches Register Klinischer Studien (DRKS) database (https://drks-neu.uniklinik-freiburg.de/drks_web/setLocale_DE.do); its registration no. is DRKS00010250. All participants were classified according to the ISNCSCI, using the American Spinal Injury Association (ASIA) Impairment Scale (AIS).

Inclusion criteria were defined as chronic incomplete paraplegia or tetraplegia at any spinal cord lesion level (AIS C or D), or chronic complete paraplegia (AIS A) after suffering lesions of the lower lumbar spine (from conus medullaris to cauda equina) with ZPP. However, independent of injury level and AIS grade, patients had to have some residual motor function of hip and knee extensor and flexor muscle groups to trigger and control the exoskeleton (Frankel and Janda Grade 1/5 or 2/5).[16] Exclusion criteria included the absence of residual motor functions in the lower extremities, severe limitations of range of motion in hip and knee joints (e.g., contracture, immobilizing spasticity), pressure sores, cognitive impairment, body weight > 100 kg, nonconsolidated fractures, epilepsy, and severe heart insufficiency.

Patient Population

Between January 2012 and June 2016, 70 participants were screened; 10 were excluded and 5 dropped out due to extended pause or other reasons (Fig. 2). Accordingly, 55

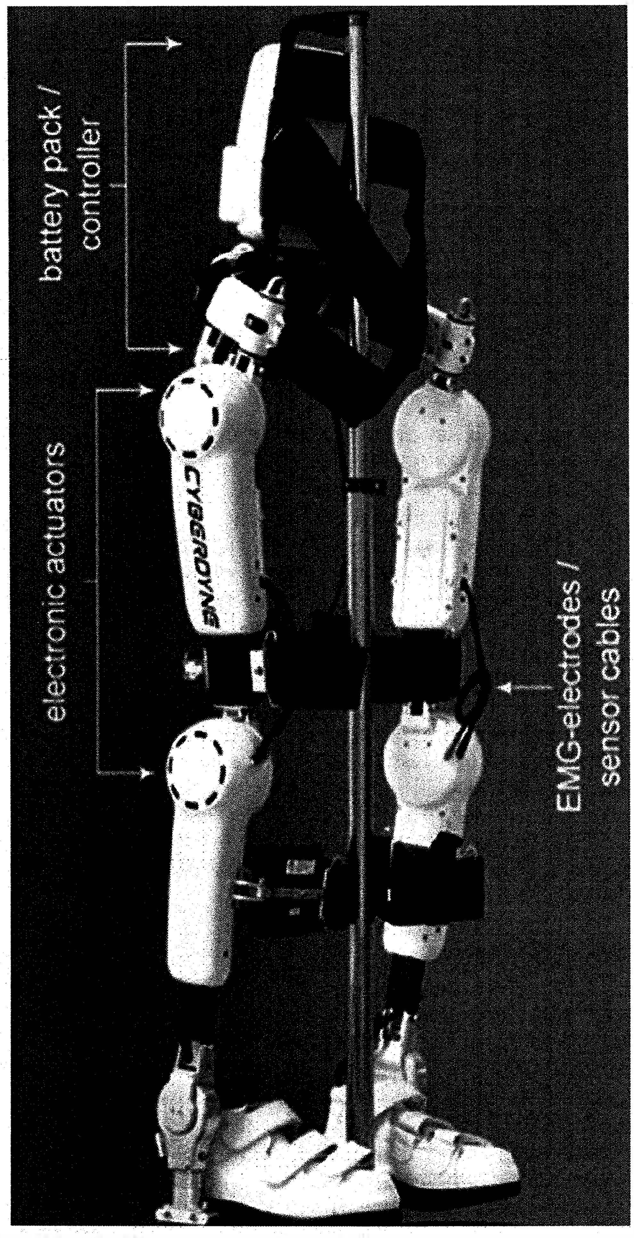

FIG. 1. Photograph of the HAL exoskeleton. Copyright Cyberdyne. Published with permission. EMG = electromyography.

patients (12 females and 43 males) with chronic (> 1 year since trauma) SCI were included and formed the present cohort. All lesions occurred between C-2 and L-4. Eighteen patients were classified as AIS A, 24 as AIS C, and 13 as AIS D (Table 1).

The mean age at the time of enrollment was 44.3 ± 13.9 years (range 16–68 years). The average time between a patient's SCI and the beginning of the HAL-assisted BWSTT was 6.85 ± 5.12 years (range 1–22 years). Three patients did not suffer traumatic SCIs. In these cases, paraplegia occurred secondary to intramedullary ependymoma (n = 1), myelitis transversa (n = 1), and spontaneous syringomyelia with unknown origin (n = 1).

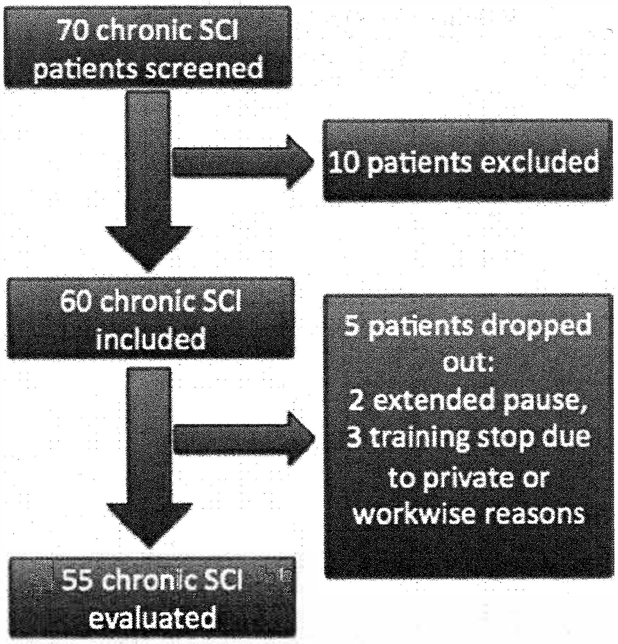

FIG. 2. Flow chart of included, excluded, and evaluated patients.

Patients were divided into 4 homogeneous subgroups according to lesion level and neurological status. Subgroup 1 (n = 13) was defined by cases of incomplete tetraplegia (C2–8, AIS C [n = 8] and D [n = 5]). Subgroup 2 (n = 15) was defined by cases of incomplete paraplegia with spastic motor behavior (T2–12, AIS C [n = 8] and D [n = 7]). Subgroup 3 (n = 18) was defined by cases of complete paraplegia with an absence of spastic motor behavior (T11–L4, AIS A) and ZPP from L-3 to S-1. Subgroup 4 (n = 9) was defined by cases of incomplete paraplegia with an absence of spastic motor behavior (T12–L3, AIS C [n = 8] and D [n = 1]). To describe the influence of age on rehabilitation and training outcomes, patients were also divided by age < 50 years versus ≥ 50 years, independent of lesion level.

Intervention and Training Paradigm

All participants underwent BWSTT 5 times per week using the HAL robot suit exoskeleton (Cyberdyne, Inc.; Fig. 1) for a 12-week period. The mean number of training sessions was 58.78 ± 2.37.

The training was performed on a treadmill (Woodway, Inc.) with adjustable body weight support and speed, under the supervision of a physiotherapist and a medical doctor. The exoskeleton's weight, which was between 14 and 17 kg depending on the suit size, was always compensated by the body weight support during the treadmill training. Additionally, up to 30% of the individual body weight was neutralized during the initial training sessions. A 10-m walk test (10MWT) without the HAL was performed before and after each session in addition to regular physiotherapy. Overall, each training session lasted approximately 90 minutes.

Outcome Measures

Between-group differences in functional outcomes and

TABLE 1. Demographic data in 55 patients with SCI

Case No.	Sex	Age (yrs)	Time Since Trauma (yrs)	SCI Level	AIS Score/ ZPP
1	M	38	13	T-8	C
2	M	62	1	L-1	C
3	M	34	1	T-12	A/L-3
4	F	53	1	L-1	C
5	M	41	16	L-1	A/L-3
6	M	51	10	L-2	A/L-3
7	F	39	19	T-11	A/S-1
8	M	53	3	T-12	D
9	M	50	5	T-12	C
10	F	32	8	C-7	C
11	M	68	20	T-12	D
12	M	65	7	T-12	C
13	M	21	3	T-4	C
14	M	16	4	C-5	D
15	F	54	6	L-1	A/L-3
16	M	45	2	T-10	C
17	M	49	2	L-1	A/L-3
18	F	31	8	L-1	A/L-4
19	M	37	3	C-2	C
20	F	54	6	T-10	C
21	F	47	7	C-5	C
22	M	53	4	C-4	C
23	M	23	1	L-1	A/L-3
24	M	56	20	C-8	C
25	M	52	10	L-1	D
26	M	27	2	L-1	C
27	F	44	18	L-3	C
28	M	60	7	L-4	A
29	M	25	7	C-6	D
30	M	19	1	T-4	D
31	M	53	5	T-6	D
32	M	45	3	L-1	C
33	F	45	8	C-6	C
34	M	60	7	C-7	D
35	M	53	4	T-6	C
36	M	50	7	T-9	C
37	M	68	2	T-6	D
38	M	27	2	T-11	A/L-4
39	M	64	4	L-2	A/L-3
40	M	36	7	T-12	A/L-4
41	M	23	1	T-12	A/L-3
42	F	32	4	T-7	D
43	M	46	12	C-4	D
44	M	36	1	L-1	A/L-3
45	M	55	20	C-4	C
46	M	38	2	L-2	A/L-3
47	F	18	4	L-3	C
48	F	51	3	T-4	C
49	M	50	4	L-1	A
50	M	39	18	C-6	D
51	M	51	22	L-1	A/L-3
52	M	56	2	T-2	D
53	M	52	10	L-2	C
54	M	48	4	C-6	C
55	M	43	9	T-12	A/L-3

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TABLE 1. Demographic data in 55 patients with SCI

walking capability after 3 months of daily HAL locomotion training were investigated. The physiotherapists were involved in neither the study design nor data analysis. Outcomes were evaluated at baseline, at 6 weeks, and at 12 weeks of training. Treadmill-associated data (walking distance, speed, and time) acquired while using the HAL exoskeleton were recorded continuously. However, functional measurements were performed without the exoskeleton. Gait speed, number of steps, and required assistance to walk a 10-m distance were assessed using the 10MWT in self-selected speed (10MWTsss).[35] The 6-minute walk test (6MinWT) was performed to determine gait endurance through evaluation of the distance and assistance required while walking for 6 minutes. Subjects were instructed to walk at their preferred speed and rest if they felt unable to continue the 6MinWT.[28,36] To determine patients' ambulatory capacity we used the Walking Index for Spinal Cord Injury II (WISCI II).[11]

Statistical Analysis

Descriptive analysis of the demographics (age, sex) and injury characteristics was done using frequency distributions for categorical data and means for continuous variables, to provide general information about the study population. Data analysis was performed using a repeated-measurement ANOVA with the inner subject factor of time (baseline, 6-week, and 12-week condition). All significant main effects underwent post hoc analysis (Bonferroni). The differences were considered statistically significant at $p < 0.05$. Data were analyzed using SPSS software (version 18.0).

Ethics Statement

All participants gave written informed consent to participate in this trial. They confirmed consent for anonymized data publishing. The ethics committee of BG University Hospital Bergmannsheil and the Ruhr University Bochum approved the study protocol. This study was conducted according to the principles expressed in the Declaration of Helsinki.

Results

The HAL-Assisted BWSTT

All patients showed improved treadmill performance using the HAL exoskeleton. Participants demonstrated

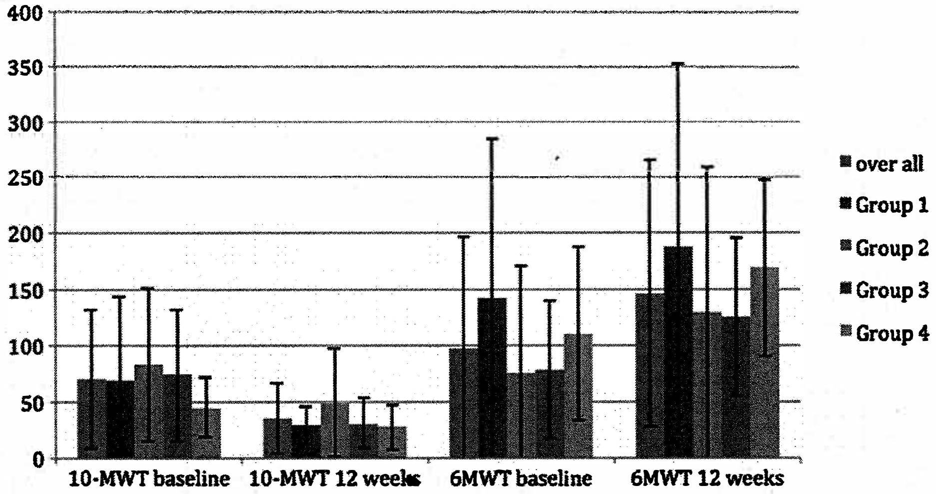

FIG. 3. Graph showing functional outcome evaluated by the 10MWT (seconds) and the 6MinWT (meters) overall and for each subgroup at baseline and after 12 weeks of training. *Whiskers* represent the SD in Figs. 3–6.

an overall significant increase ($p \leq 0.001$) in mean walking speed from 0.85 ± 0.31 km/hour (range 0.5–1.8 km/hour) at baseline to 1.83 ± 0.63 km/hour (range 0.8–3.0 km/hour) at 12 weeks of training. The cumulative mean walking time at baseline was 12.59 ± 4.72 minutes and increased significantly ($p \leq 0.001$), to 29.55 ± 5.61 minutes after 12 weeks of training. Walking time and walking speed improvements showed no significant differences between subgroups. Although the results were nonsignificant, Subgroup 2 demonstrated a slower walking speed. An increase in the mean ambulated distance ($p \leq 0.001$) from 185.64 ± 134.70 m to 887.38 ± 357.79 m on the treadmill while using the HAL suit was observed across all groups. The mean ambulated distance in Subgroups 1, 3, and 4 showed relatively greater improvement than that in Subgroup 2. There were no significant differences in walking speed, time, or distance as a factor of patients' age.

Functional Outcomes Without HAL Assistance

Significant improvements in all over-ground gait assessments (10MWTsss, 6MinWT) were observed across the cohort. The mean time for the 10MWTsss significantly decreased ($p \leq 0.001$) from baseline (70.45 ± 61.50 seconds) to 12 weeks (35.22 ± 30.80 seconds). There were no significant differences between subgroups. As observed on the treadmill, Subgroup 2 showed smaller functional improvements, yet these differences were statistically nonsignificant (Fig. 3).

Across all patients, a significant increase ($p \leq 0.001$) in the mean ambulated distance in the 6MinWT from 97.81 ± 95.80 m to 146.34 ± 118.13 m was observed. There were no significant differences between subgroups (Fig. 3).

Analyzed as a function of age, a significantly larger improvement in the 10MWTsss was observed in the younger group (baseline, 64.06 ± 59.3 seconds; 12 weeks, 28.27 ± 19.25 seconds) versus the older group (baseline, 69.52 ± 53.59 seconds; 12 weeks, 43.87 ± 39.46 seconds). In contrast, no significant differences in walking speed and time during the HAL-assisted BWSTT were observed in the 2 age groups (Fig. 4).

The WISCI II scores improved significantly across all subjects (baseline mean score, 9.35 ± 5.12; 12-week mean score, 11.04 ± 4.52; $p \leq 0.001$). A significant improvement in the WISCI II score was detected in Subgroups 1 and 3 ($p \leq 0.001$). Subgroups 2 and 4 presented no significant differences in pre- and postintervention assessments. Of the overall cohort of 55 patients, 24 (43.6%) were less dependent on walking aids after 12 weeks of HAL-assisted BWSTT (Fig. 5). The WISCI II scores showed no difference in improvement as a function of age (Fig. 6).

Overall, in the 10MWTsss the most improvements occurred during the 4th and 10th week of the training period. Nearly a plateau was reached at the 12-week evaluation. This is documented by larger improvements from baseline to 6 weeks than from 6 to 12 weeks (mean time for 10MWTsss at baseline, 70.45 ± 61.5 seconds; at 6 weeks, 46.24 ± 41.28 seconds; and at 12 weeks, 35.2 ± 30.8 seconds).

Discussion

We investigated the functional outcome of 55 patients with chronic cSCI or iSCI after 12 weeks of HAL-assisted BWSTT (mean 58.78 sessions). Using the 10MWTsss and 6MinWT results and the WISCI II scores of patients assessed while not wearing the HAL exoskeleton, we analyzed functional outcomes according to age and lesion level. To our knowledge, this is the first subgroup analysis of outcomes in patients with chronic SCI after they have undergone HAL-assisted BWSTT. The reasons for dividing the 55 patients with SCI into the above-mentioned subgroups were neuroanatomical. We used strict anatomical borders, pathophysiological signs like spinal spasticity, and the AIS grade for generating the subgroups.[21] The subgroups were similar to those in other studies focusing on SCI rehabilitation.[3,4,9,34,37]

The present study demonstrated homogeneous improvements in all treadmill HAL-supported tests. Neither age, lesion level, nor neurological status demonstrated significant influence on treadmill performance outcomes. Addi-

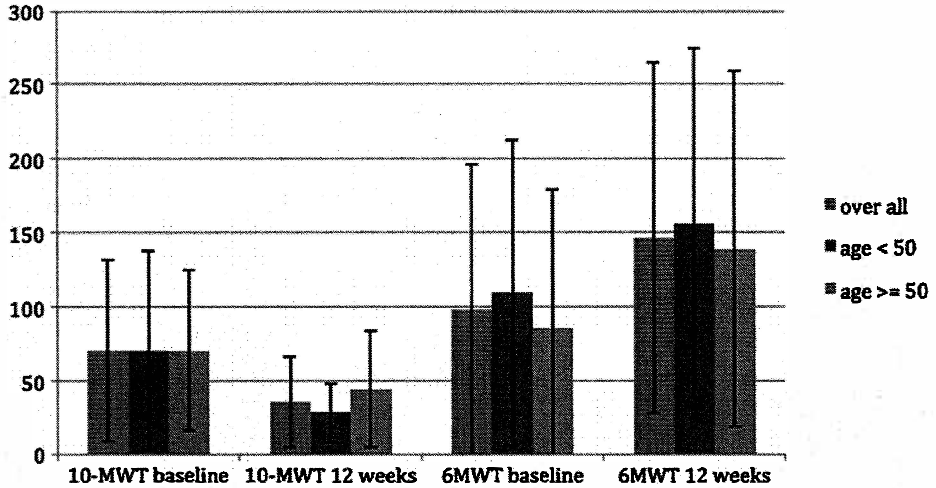

FIG. 4. Graph showing functional outcome evaluated by the 10MWT (seconds) and the 6MinWT (meters) overall and according to age (< 50 years and ≥ 50 years) at baseline and after 12 weeks of training.

tionally, all participants showed a continuous functional improvement in non-HAL–assisted functional measures over the 12-week training period. Maximum improvement occurred between Weeks 4 and 10. This clearly represents a training-induced improvement rather than spontaneous recovery, underlined by a mean gain of 1.69 levels in the WISCI II score across all patients.

During the training period all patients' walking ability increased considerably. This is evidenced by an approximately 47% improvement in short-distance gait speed (10MWTsss) and a roughly 50% improvement in endurance (6MinWT). Twenty-four of 55 patients (43.6%) were less dependent on walking aids than they were before starting the training.

All subgroups improved significantly on the 10MWTsss. Subgroup 2 (patients with incomplete paraplegia in whom spastic motor behavior was present) showed slightly less improvement. Gait endurance (6MinWT) showed no differences among the subgroups. In contrast, the 10MWTsss demonstrated greater improvements in the younger cohort (approximately 56%) than in the older cohort (approximately 37%).

Conventional or driven gait orthosis BWSTT is roughly as effective as alternative SCI therapies described in the literature and focusing on functional improvement.[23] However, a direct comparison of HAL-associated results with other clinical trials focusing on rehabilitation of chronic SCIs is missing. Furthermore, such a comparison is difficult due to training paradigm and study population differences. Nevertheless, compared with other studies the reduction of required walking aids in the 10MWT is higher after HAL-assisted BWSTT.[22,23,39]

In contrast to previous findings in the literature, the lesion level and patients' age were not significantly associated with training-related functional improvements in chronic iSCI or cSCI. Only the 10MWTsss showed greater

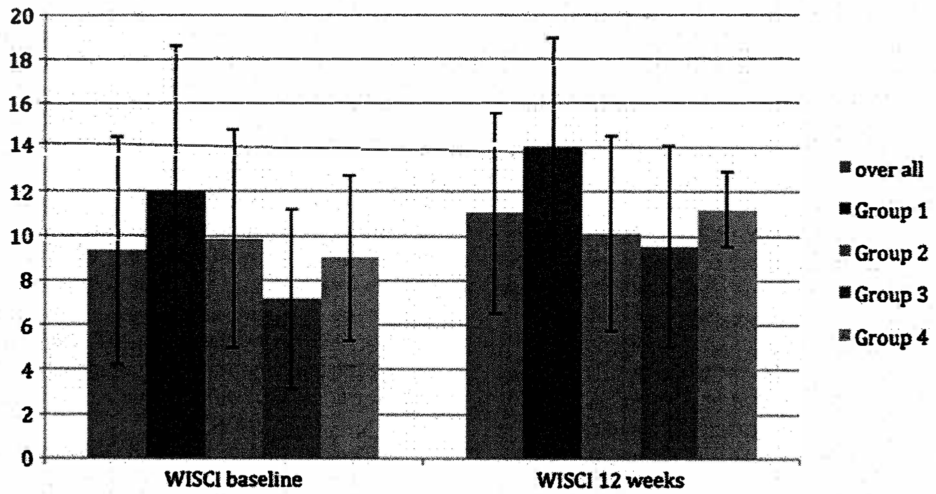

FIG. 5. Graph showing patients' ambulatory capacity measured by the WISCI II overall and for each group at baseline and after 12 weeks of training.

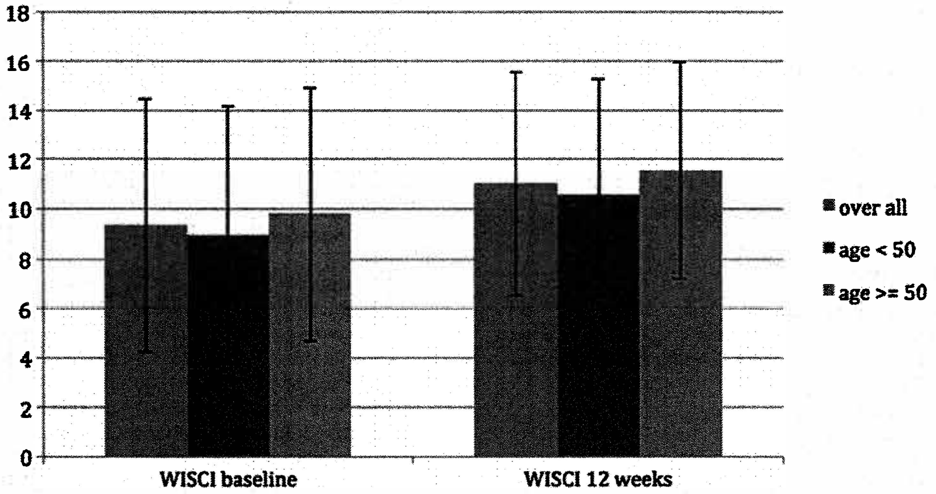

FIG. 6. Graph showing patients' ambulatory capacity measured by the WISCI II overall and according to age (< 50 years and ≥ 50 years) at baseline and after 12 weeks of training.

improvements in the younger age group. Incomplete SCI lesions of the thoracic spine, including spastic motor behavior, appear to be a nonsignificant negative predictor for training-related improvements. Furthermore, it is of interest that Subgroup 1 (patients with iSCI and tetraplegia) and Subgroup 3 (patients with conus and/or cauda iSCI) improved less in gait endurance (6MinWT) relative to Subgroups 2 and 4. An explanation might be that Subgroups 1 and 3 are more adapted to their pretraining walking abilities. This is specifically highlighted by the higher level of functional walking abilities in Subgroups 1 and 3 at baseline. Therefore, they may have a smaller range for improvements.

The findings of the present study demonstrate that neurologically controlled exoskeleton training in patients with chronic SCI leads to significant functional improvements in the 10MWTsss and 6MinWT results and in WISCI II scores following HAL-supported treadmill training. The declared aim of the neurologically controlled exoskeleton training is patients' functional improvement, leading to increased patient mobility when not wearing the exoskeleton.

The voluntary drive and the normalized motion assistance attained using a neurologically controlled exoskeleton induce muscle hypertrophy. Neuronal activity and repeated executions of specific tasks promote learning and lead to reinstatement or restructuring of appropriate proprioceptive feedback. Locomotor training restores spinal reflex circuits, promotes presynaptic inhibition, and normalizes contraction and coordination of agonistic and antagonistic muscles—especially in the impaired legs. Furthermore, HAL locomotor training has been shown to renew S1 and M1 representations of impaired lower extremities; this is probably related to recruitment and more effective use of the remaining afferent pathways and corticospinal tracts.[17,32] As recommended in the literature, locomotor training performed using a neurologically controlled HAL exoskeleton is a perfect combination of task relation and high repetition.[18,31]

Negative predictors like older age or lesion level, as described in the literature, seem to be less important or nonsignificant in terms of the extent of functional improvement following intensive training using the neurologically controlled HAL exoskeleton in patients with chronic iSCI or cSCI.

The present study is strengthened by its large sample size of participants who underwent HAL-assisted BWSTT. Compared with other single-center clinical trials focusing on locomotor training following SCI in humans it is, to our knowledge, one of the largest trials worldwide.[12,23] The intervention was of high intensity, with daily training (5 times/week) over a 12-week period (mean 58.78 sessions).

Despite a large number of participants, the study was limited by small patient numbers in the 4 subgroups. Although lacking a control group, the baseline assessments of the study cohort can be interpreted as a control group in this pre- and postintervention study design.[20] We did not document any type of further physical therapy or medication. Study participants were asked not to modify their physical therapy, unsupervised training program, or antispasticity medication during the intervention. Otherwise the possibility could not be excluded that changes in therapeutic regimens might have had an influence on HAL-related functional outcomes.

Conclusions

Treadmill training using the neurologically controlled HAL exoskeleton in chronic iSCI or cSCI leads to significant functional improvements in the 10MWTsss and 6MinWT results and in the WISCI II score when not wearing the exoskeleton as a supportive device. A time reduction of 47% in the 10MWTsss and an extension of 50% in gait endurance can be expected. The therapy leads to a reduction of needed walking assistance in roughly 44% of patients. Besides short-distance gait speed in the 10MWTsss, age > 50 years does not influence the training-related functional outcomes. Furthermore, an iSCI of the thoracic spine including spastic motor behavior is a nonsignificant negative predictor for the functional outcome following the above-mentioned HAL-associated training paradigm. The HAL exoskeleton is not a walking aid for use during daily activities, but is a temporary training tool to improve functional mobility without the device.

The baseline assessments of patients with chronic SCI are suitable as a control group in a pre- and postintervention study. To clarify these promising results against the odds in the literature, future investigation is needed.

Acknowledgments

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Disclosures

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Conception and design: Grasmücke, Jansen, Meindl, Schildhauer, Aach. Acquisition of data: Grasmücke, Zieriacks, Jansen, Sczesny-Kaiser, Aach. Analysis and interpretation of data: Grasmücke, Zieriacks, Wessling, Aach. Drafting the article: Grasmücke, Schildhauer, Aach. Critically revising the article: Grasmücke, Fisahn, Wessling, Meindl, Schildhauer, Aach. Reviewed submitted version of manuscript: Aach. Approved the final version of the manuscript on behalf of all authors: Grasmücke. Statistical analysis: Grasmücke, Wessling. Administrative/technical/material support: Grasmücke, Zieriacks, Schildhauer. Study supervision: Grasmücke, Schildhauer, Aach.

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