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Gait Analysis of Patients After Allogeneic Hematopoietic Cell Transplantation Reveals Impairments of Functional Performance

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Abstract

Background: After allogeneic hematopoietic cell transplantation (alloHCT), patients often report functional impairments like reduced gait speed and muscle weakness. These impairments can increase the risk of adverse health events similar to elderly populations. However, they have not been quantified in patients after alloHCT (PATs). **Methods:** We compared fear of falling (Falls Efficacy Scale–International) and temporal gait parameters recorded on a 10-m walkway at preferred and maximum gait speed and under dual-task walking of 16 PATs (aged 31-73 years) with 15 age-matched control participants (CONs) and 17 seniors (SENs, aged >73 years). **Results:** Groups' gait parameters especially differed during the maximum speed condition: PATs walked slower and required more steps/10 m than CONs. PATs exhibited greater stride, stance, and swing times than CONs. PATs' swing time was even longer than SENs'. The PATs' ability to accelerate their gait speed from preferred to fast was smaller compared with CONs'. PATs reported a greater fear of falling than CONs and SENs. **Conclusion:** Gait analysis of alloHCT patients has revealed impairments of functional performance. Patients presented a diminished ability to accelerate gait and extending steps possibly related to a notable strength deficit that impairs power-generation abilities from lower extremities. Furthermore, patients reported a greater fear of falling than control participants and even seniors. Slowing locomotion could be a risk-preventive safety strategy. Since functional disadvantages may put alloHCT patients at a higher risk of frailty, reinforcing appropriate physical exercises already during and after alloHCT could prevent adverse health events and reduce the risk of premature functional aging.

Keywords

gait analysis, fast gait speed, fear of falling, allogeneic hematopoietic cell transplantation, cancer survivors, functional impairment

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Background

Allogeneic hematopoietic cell transplantation (alloHCT) is the most intensive treatment known for patients with hematological malignancies. It is associated with diverse procedure- and therapy-induced side effects that can limit patients' physical and psychological functioning considerably.[1,2] Patients often experience significant weight loss and a change in body composition during hospitalization,[3,4] particularly muscle mass loss, resulting in substantial physical deconditioning.[5-7] In addition, neurotoxic medications can compromise neuromuscular output and thus functional performance.[8] Furthermore, chronic graft-versus-host disease is even known to worsen patients' functional status.[2,9]

All aforementioned factors substantially increase alloHCT survivors' frailty risk.[10] This is known to be strongly

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associated with elevated risk of injury or even mortality.[10] Despite rehabilitation programs, many patients complain about functional impairments like slowed gait speed or muscle weakness affecting their daily life and participation even in the long term.[1,11] However, these reports relied on patient-reported outcomes rather than objective measures.[1,10] Considering that physical function presents an acknowledged prognostic factor for the mortality of cancer survivors,[12,13] it would seem worthwhile to characterize those functional impairments in greater detail. An essential everyday task of prognostic value is gait.[13] Basically, preferred gait speed is a relevant parameter for daily physical function by reflecting demands on the neuromuscular and cardiopulmonary systems.[14,15] Moreover, a slower preferred or maximum gait speed may predict disability and even mortality.[12,14,16-18] Analyzing spatiotemporal gait parameters under different walking conditions (at preferred or maximum gait speed, under dual-tasking) additionally enables to infer power-generation abilities and gait stability.[19,20] Assessing variability in spatiotemporal gait parameters may suggest gait instability that is associated with a higher risk of falling.[21-23]

The prevalence of frailty among young alloHCT survivors corresponds to that in the elderly.[10] We know that anticancer therapies induce degradation processes resembling normal aging mechanisms in an intensity-dependent relation[24]: for example, patients with hematological malignancies are at particular risk for sarcopenia due to high-intensity treatment,[25] that is, a significant loss of muscle mass and function particularly characteristic of the elderly population.[26]

The aim of this study was to analyze alloHCT patients' gait under 3 conditions, that is, at preferred and maximum gait speed and under dual-task walking. Preferred gait speed is a reliable sign of vitality.[14,27] Maximum gait speed is known to predict disability,[12,18] while the concurrent execution of a cognitive task while walking has been shown to enhance gait variability,[28] especially in older compared with younger adults.[29,30] To quantify potential functional deficits, we compared patients' gait parameters with a group of age-matched healthy participants and normative values. We additionally aimed at comparing alloHCT patients' gait with a group of seniors to classify potential functional deteriorations. We hypothesized that, when compared with healthy control participants, alloHCT patients would display gait alterations similar to those characteristic of seniors. It is essential to identify the relevant functional disadvantages to promote improved and effective intervention strategies to reduce the risk for disability and adverse health events.

Methods

Study Design

We applied a 3-armed cross-sectional pilot study to evaluate gait differences between cancer patients after alloHCT (PATs), matched healthy control participants (CONs), and seniors (SENs).

Ethics

Our study was approved by the Ethics Committee of the University of Freiburg (102/12_140596), conducted according to the Declaration of Helsinki, and registered in the German Register of Clinical Trials.

Participants

We recruited 16 patients at the rehabilitation center Clinic of Tumorbiology, Freiburg, Germany, and 15 CONs. We also recruited 17 SENs who regularly perform moderate physical activity at a local sports club, Freiburg. Inclusion criteria for all groups were written informed consent and >18 years of age; for PATs, being after alloHCT (that is, after hospitalization due to alloHCT procedure) and currently during inpatient rehabilitation treatment including standard sports- and physiotherapy; for CONs, matched to patients' age, sex, weight, and height; for SENs, >70 years of age. Exclusion criteria for all groups were any neurodegenerative diseases and painful orthopedic problems, and for CONs and SENs, any cancer within the past year.

Setup and Measurements

All participants underwent detailed anamnesis including comorbidities, investigation of vibration sense, and fear of falling (Table 1). Subsequently, all participants underwent gait analysis under 3 conditions.

Vibration sense was determined on the first metacarpophalangeal joint, knuckle, and patella via the Rydel-Seiffer tuning fork with a graduating scale from 0 (no sensitivity) to 8 (highest sensitivity).

Fear of falling was evaluated by the Falls Efficacy Scale–International (FES-I), scored from 16 (no concern about falling) to 64 (very concerned about falling), showing high internal reliability and high test-retest reliability.[31,32]

For gait analysis, we used the wireless insole sensor-based gait analysis system OpenGo (Moticon ReGo AG, Munich, Germany) that has been shown to be valid and reliable for the measurement of temporal gait parameters during walking.[33] We recorded temporal gait parameters during 3 walking conditions on a 10-m walkway: (1) walking at preferred gait speed, (2) walking at maximum gait speed (fast condition: walking as fast as possible without running, meaning one or both feet always have ground contact), (3) walking at preferred gait speed while counting from 50 backward in steps of 2 (dual-task condition).[19,34] Participants walked wearing their own footwear (comfortable, closed, without heels), starting 2 m before and terminating their walk at least 2 m past the 10-m walkway.[19]

Table 1. Patient Characteristics.

	PATs (n = 16), Median (IQR)	CONs (n = 15), Median (IQR)	SENs (n = 17), Median (IQR)	*P*
Male:female (n)	8:8	7:8	11:6	
Age (years)	56 (52-61)	58 (49-62)	76 (75-79)[a]	.000
Height (cm)	176 (170-182)	173 (168-179)	170 (166-177)	NS
Weight (kg)	83 (63-89)	78 (64-90)	79 (65-83)	NS
BMI (kg/m^2)	25 (21-29)	25 (22-28)	27 (23-30)	NS
FES-I (points 16-64)	21 (18-34)	16 (16-17)[a]	17 (16-17)[a]	.001
Vibration sense (score 0-8)				
Metatarsophalangeal	6.2 (5.2-6.5)	6.5 (5.8-6.9)	5.8 (3.1-7.2)	NS
Ankle	6.0 (4.8-6.2)	6.4 (5.8-6.9)	5.8 (1.8-6.6)	NS
Patella	6.3 (5.3-6.7)	6.8 (6.3-7.0)	6.1 (3.1-6.9)	NS
Comorbidities, n (%)				
Orthopedic:				
Lower extremities	4 (25)	2 (14)	9 (53)	
Spine	2 (13)	0 (0)	2 (12)	
Polyneuropathy	4 (25)	0 (0)	0 (0)	
Stroke	0 (0)	0 (0)	2 (12)	
Seizures	1 (6)	0 (0)	0 (0)	
Heart disease	3 (19)	0 (0)	8 (47)	
PAOD	1 (6)	0 (0)	0 (0)	
Pulmonary disease[b]	1 (6)	1 (7)	1 (6)	
Diabetes mellitus	1 (6)	0 (0)	0 (0)	
Neurotoxic agents[c] (n)	2.0 (1.0-2.8)			
Weeks after alloHCT	30.9 (11.5-61.1)			
GvHD grade, n (%)				
0	5 (31)			
II	7 (44)			
III	4 (25)			
Corticosteroid therapy[c], n (%)				
Pre alloHCT	16 (100)			
Post alloHCT	5 (31)			
Ongoing	7 (44)			

Abbreviations: PATs, patients; IQR, interquartile range; CONs, control participants; SENs, seniors; NS, not significant; BMI, body mass index; FES-I, Falls Efficacy Scale–International; PAOD, peripheral arterial occlusive disease; alloHCT, allogeneic hematopoietic cell transplantation; GvHD, graft-versus-host disease.

[a]Indicate a significant difference to PAT.

[b]Chronic obstructive pulmonary disease, asthma, pulmonary embolism.

[c]Received within the alloHCT schedule.

Our analysis system consists of ultrathin and flexible insoles of different sizes fitting various shoe sizes. Each insole integrates 13 capacitive pressure sensors recording at a 50-Hz sampling rate. Sensor data were downloaded for further processing. Additionally, participants were filmed while walking, and the recorded videos were synchronized with sensor data. The analysis software Beaker (Moticon ReGo AG) illustrated time-dependent ground reaction forces for each insole and displayed synchronized videos.

Data Processing

A custom software written in Python programming language was used to reliably identify the initial (foot-strikes) and last contacts (foot-offs) of every footfall from our gait data (see Figure 1A). Data acquired from 1 sole and 1 measurement are considered 1 data set. Each data set was analyzed independently.

To detect steps, the force values from all sensors of each sole were added together for each time point. This 1-dimensional data set (force over time) was then smoothened using a Gaussian filter of width (ie, standard deviation) 0.033 × sampling rate (Hz). From the smoothened data, we identified steps via the argrelmin(. . .) function from the Scipy signal library. These minima represent the time points when the foot is lifted between 2 steps. In this analysis, 1 step is considered as the initiation of the lifted state, making a foot-strike, then taking the foot-off, and then back to the lifted

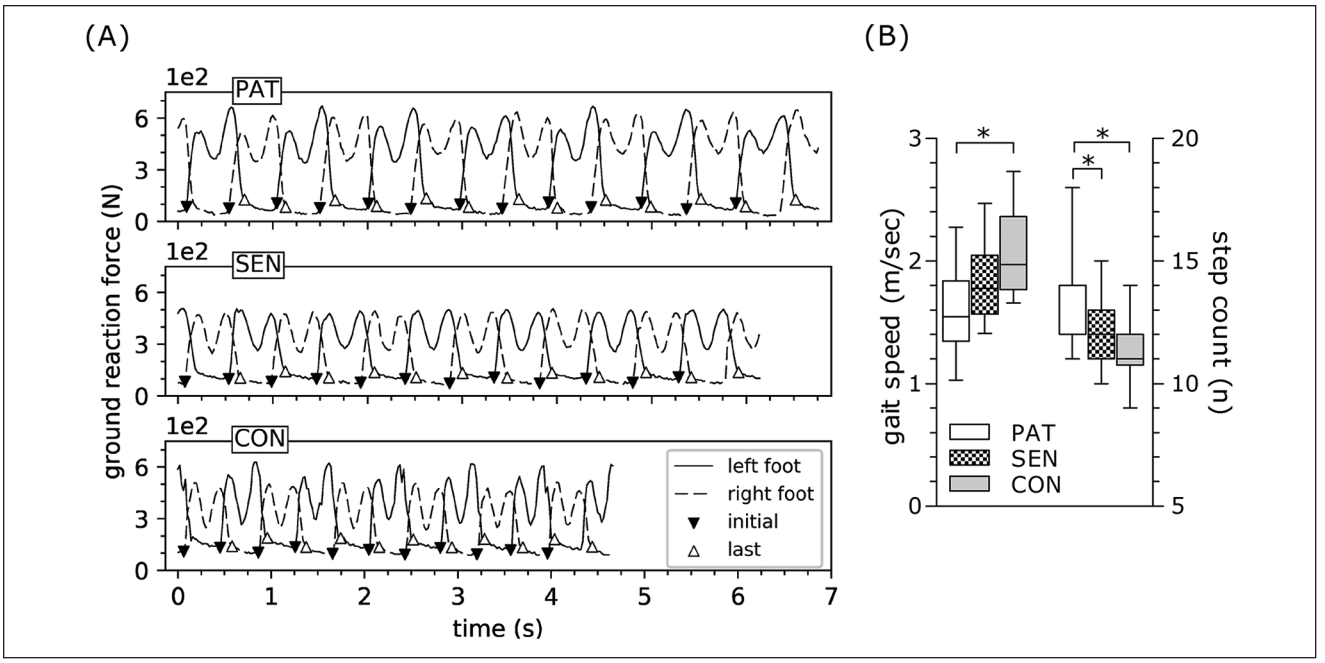

Figure 1. Fast walking condition. (A) Time-dependent ground reaction forces of left and right footfalls during 1 representative gait cycle of PATs (alloHCT patient), SENs (senior), and CONs (healthy control participants), respectively, within 10 m. ▲▼ mark initial and last contacts of each footfall. (B) Distribution of gait speed (left *y*-axis) and step count (right *y*-axis) for PAT, SEN, and CON. Box-and-whisker plots show the lower quartile (25th percentile), median (50th percentile), upper quartile (75th percentile), and degree of dispersion as 95% confidence interval. *Indicates a significant difference between groups (*$P < .05$).

state. Additionally, heuristics were applied to reduce the probability of erroneous step detection.

To precisely differentiate the foot-strikes and foot-offs from the steps, we conducted the following analysis for each step: the smoothened data were linearly interpolated by a factor of 60. An individual threshold was defined at 15% from its lowest to highest load value for each interpolated step. The time points where the data passed above and below this threshold were defined as the foot-strike and foot-off, respectively. The consistency of the foot-strikes and foot-offs was checked for a pair of data sets (left and right foot) by verifying their order: foot-strike left, foot-off right, foot-strike right, foot-off left, and so forth repetitively (except at the beginning and end of the data set). Foot-strikes with missing corresponding foot-offs at the end of the measurement were ignored. The same was done for foot-offs with missing corresponding foot-strikes at the beginning of the measurement.

The step count was accumulated from the detected foot-strikes and foot-offs, and temporal gait parameters gait speed (m/s), cadence (steps/min), stride time (seconds), stance time (seconds), and swing time (seconds) were calculated subsequently.[20] We also calculated the mean value, standard deviation (SD), and coefficients of variation (CV as SD/mean × 100) of each of these parameters (except gait speed and cadence) for each pair of data sets. Furthermore, the relative increase (%) from preferred to maximum gait speed was computed.

Velocity-dependent parameters, that is, step count, cadence, stride, stance, and swing time, were normalized to the gait speed of the appropriate walking condition for statistical analysis.

Statistics

Differences between groups were assessed by nonparametric analysis (Kruskal-Wallis analysis of variance) as the assumption of normal distribution (Shapiro-Wilk test) was not satisfied. The level of significance was set to $P = .05$. *P* values of post hoc comparisons were corrected by the Bonferroni's procedure. Bivariate correlations were calculated according to Spearman ρ to display the relationship between gait parameters and fear of falling. All statistical analyses were conducted using IBM SPSS Version 22 software (SPSS Inc, Chicago, IL). Group data are presented as median and interquartile range (Table 2). Graphics were created by using Prism 5 Version 5.03 (GraphPad Software, Inc, La Jolla, CA).

Results

The comparative groups PATs and age-matched CONs exhibited similar anthropometric parameters. Vibration sense did not differ between groups. Concerning FES-I, PATs reported

Table 2. Gait Parameters of Patients After alloHCT (PATs), Matched Healthy Control Participants (CONs), and Seniors (SENs)[a].

		PATs, Median (IQR)	CONs, Median (IQR)	SENs, Median (IQR)		Correlation (r)[b] Between Gait Parameters and FES-I
Trial	Parameter	n = 14	n = 12	n = 16	*P*	n = 43
Preferred	Gait speed (m/s)	1.16 (1.03-1.27)	1.16 (1.11-1.50)	1.20 (1.10-1.30)	ns	−.257
	Cadence (step/min)[a]	103.1 (96.5-109.2)	104.9 (97.2-110.7)	109.0 (101.5-113.3)	ns	−.155
	Steps (n/10 m)[a]	15.0 (14.0-16.0)	14.5 (13.0-15.0)	15.0 (14.0-15.8)	ns	.301
	Stride time (seconds)[a]	1.14 (1.10-1.22)	1.12 (1.06-1.20)	1.09 (1.03-1.14)	ns	.163
	Stance time (seconds)[a]	0.73 (0.70-0.77)	0.71 (0.68-0.76)	0.70 (0.67-0.76)	ns	.146
	Swing time (seconds)[a]	0.41 (0.40-0.45)	0.42 (0.37-0.43)	0.38 (0.36-0.41)	ns	.165
	Stride time (%CV)	1.81 (1.34-2.12)	1.63 (1.40-1.81)	1.84 (1.55-2.61)	ns	.151
	Stance time (%CV)	2.04 (1.78-3.79)	2.60 (2.03-3.19)	2.71 (2.07-3.36)	ns	−.150
	Swing time (%CV)	3.39 (3.27-5.63)	3.25 (2.77-4.57)	4.09 (3.27-5.37)	ns	.073
	Gait speed increase (%)	31.2 (24.07-51.0)	57.1 (37.3-88.0)[c]	51.5 (42.3-67.3)	.044	−.423**
		n = 16	n = 13	n = 17		n = 47
Fast	Gait speed (m/s)	1.54 (1.35-1.84)	1.88 (1.76-2.37)[c]	1.78 (1.57-2.05)	.010	−.514**
	Cadence (step/min)[a]	121.1 (111.5-129.7)	135.2 (124.7-154.9)	131.9 (123.9-138.0)	ns	−.332*
	Steps (n/10 m)[a]	12.0 (12.0-14.0)	11.0 (10.0-12.0)[c]	12.0 (11.0-13.0)	.018	.588**
	Stride time (seconds)[a]	0.97 (0.91-1.05)	0.87 (0.76-0.93)[c]	0.88 (0.85-0.94)	.004	.370*
	Stance time (seconds)[a]	0.61 (0.58-0.66)	0.54 (0.48-0.60)[c]	0.58 (0.54-0.60)	.004	.371*
	Swing time (seconds)[a]	0.36 (0.34-0.38)	0.33 (0.29-0.34)[c]	0.33 (0.30-0.35)[c]	.005	.325*
	Stride time (%CV)	1.84 (1.21-2.25)	1.74 (1.45-2.30)	1.86 (1.43-2.48)	ns	.064
	Stance time (%CV)	2.10 (1.78-2.82)	2.85 (2.10-3.75)	2.82 (2.41-4.06)	ns	−.174
	Swing time (%CV)	3.82 (2.91-4.64)	4.11 (2.39-4.85)	4.51 (3.36-6.10)	ns	.008
		n = 15	n = 12	n = 15		n = 43
Dual task	Gait speed (m/s)	1.12 (0.93-1.29)	1.37 (1.23-1.61)[c]	1.29 (1.05-1.50)	.039	−.504**
	Cadence (step/min)[a]	104.4 (86.5-106.5)	109.4 (98.9-114.7)	113.7 (100.4-117.3)	ns	−.339*
	Steps (n/10 m)[a]	15.0 (13.0-16.0)	13.0 (12.0-14.0)	13.0 (13.0-15.0)	ns	.431**
	Stride time (seconds)[a]	1.14 (1.10-1.36)	1.07 (1.02-1.18)	1.03 (1.00-1.18)	ns	.345*
	Stance time (seconds)[a]	0.72 (0.70-0.84)	0.68 (0.63-0.74)	0.66 (0.64-0.74)	ns	.331*
	Swing time (seconds)[a]	0.42 (0.39-0.53)	0.40 (0.37-0.43)	0.38 (0.36-0.45)	ns	.301
	Stride time (%CV)	2.45 (2.08-3.44)	2.56 (1.25-4.54)	2.30 (1.85-4.25)	ns	.069
	Stance time (%CV)	3.63 (2.56-4.31)	3.15 (2.19-4.75)	3.57 (2.92-4.63)	ns	.064
	Swing time (%CV)	4.88 (3.66-6.14)	3.59 (3.07-7.04)	4.88 (3.90-6.44)	ns	.212

Abbreviations: IQR, interquartile range; *r*, correlation coefficient; FES-I, Falls Efficacy Scale–International; ns, not significant; CV, coefficient of variation.
[a]The parameters cadence, steps, stride, stance, and swing time have been normalized to gait speed of the appropriate walking condition for statistical analysis. *P* values refer to differences of the normalized data.
[b]Spearman ρ.
[c]Indicate a significant difference to PAT.
*$P < .05$; **$P < .01$.

a significantly greater fear of falling than CONs and SENs (Table 1).

We analyzed 130 out of 141 pairs of data sets (Table 2) due to failures during recording via the soles.

Preferred Gait Speed

All groups displayed a similar preferred gait speed and step count within the 10-m walkway. Furthermore, all temporal gait parameters were similar in all groups (Table 2).

Fast Condition

The fast condition (Table 2) revealed greater group difference than walking at preferred gait speed (see Figure 1B). Gait speed and step count differed significantly between PATs and CONs: PATs walked slower and needed more steps to walk 10 m than CONs. PATs revealed the largest temporal gait parameters versus CONs (stride time, stance time, and swing time) and even SENs (swing time). Groups did not differ in their gait variability.

Furthermore, the CONs' ability to accelerate their gait speed from preferred to fast was significantly greater compared with PATs (Table 1).

Dual-Task Condition

As with fast walking, during the dual-task condition (Table 2), PATs walked significantly slower than CONs. All the other temporal parameters and their variability did not differ between groups.

Correlations (Table 2) between gait parameters and reported fear of falling revealed no relationship between FES-I results and gait parameters at the preferred gait speed. However, during the fast and dual-task condition, we detected negative correlations for gait speed and cadence. The level of FES-I also correlated with step count, stride time, stance time, and swing time (only fast condition). Furthermore, we observed a negative relationship between FES-I level and the ability to increase gait speed.

Discussion

The present study first quantifies alloHCT patients' gait abilities in comparison to a group of CONs and SENs. It was this study's aim to quantify the functional deficits that may exacerbate alloHCT patients' risk for adverse health events. Our comparison to healthy participants revealed significant differences in maximum gait speed: patients walked more slowly and took shorter steps than control participants. Furthermore, the patients' fast gait performance more closely resembled that of seniors than of control participants. This analogy may reveal comparable alterations in joint work due to degradation processes induced by patients' treatment or aging, respectively. These processes may result in similar compensation strategies for avoiding risk, for example, falls and injuries.

Assessing gait speed is an acknowledged method to predict health risks in terms of disability, falls, or mortality.[27,35] In particular, a preferred gait speed slower than 0.8 m/s indicates a higher risk for falls, immobility, and early mortality.[13,35] None of our participants walked slower than 0.8 m/s under any of the 3 test conditions. Regarding preferred gait speed, we detected no relevant group differences. The patients' and, surprisingly, the control participants' preferred gait speed (median 1.16 m/s) lay at the lower end of normative values (1.10-1.39 m/s).[36,37] However, control participants presented a greater interquartile range than patients (0.39 m/s vs 0.24 m/s). The patients' range was rather similar to the gait speed of individuals aged 20 years and older.[20,34] Surprisingly, our seniors walked even faster than control participants, as their preferred gait speed (median 1.20 m/s) lay at the upper end of their normal age-adjusted range (1.12-1.22 m/s),[20,38] assuming a healthy aging process. However, note that the seniors included in this study were physically active. Concerning the fast condition, the maximum gait speed of the control group (median = 1.88 m/s) and of seniors (median = 1.78 m/s) corresponded to reference values.[34,36,37] In contrast, our patients walked significantly slower (median = 1.54 m/s) and took more steps, indicating shorter step length, than age-matched control participants. Furthermore, our patients exhibited longer temporal parameters, that is, stride, stance, and swing time, during fast walking. Slowing gait could be a safety strategy to compensate for reductions in muscle strength and function. Vice versa, deficits of neuromuscular function might inhibit patients' ability to increase their gait speed to an age-appropriate maximum level.

The main differences between groups occurred during the fast walking condition. Patients did not reach the maximum speed level of control participants, which might be a result of reduced power-generation abilities. In general, walking faster requires altered joint kinetics to accelerate the body's propulsion. Degeneration processes such as aging can modify this alteration: for example, an age-associated strength decrease may lead to a distal-to-proximal (ankle to hip) shift of joint work[39-41] that can affect locomotor ability.[42,43] Naturally, the neuromuscular system's aging implies a continuous functional decline caused by time-dependent, accumulated cellular damage[44,45] that results in age-related loss of muscle mass and function. This loss is strongly related to physical disability,[46,47] functional impairments,[48] and even mortality,[49] whereby the loss of strength contributes proportionally more to predicting disability than does muscle mass.[50,51] Impairment of functional performance is also prevalent in cancer survivors, depending on treatment intensity rather than age, which is why alloHCT patients carry a particularly high risk for being affected.[25]

Generally, anticancer treatment induces degradation processes that can impair functional performance and increase the risk for premature aging.[24] Furthermore, the lengthy therapies combined with long periods of hospitalization that often accompany alloHCT cause inactivity extending to immobility. There is ample evidence that long-term bedrest or inactivity promotes muscle mass loss, especially in the lower body's weight-bearing, antigravity muscles—the more distal, the more pronounced.[52-54] This degradation process can lead to considerable functional consequences.[55-57] Concerning alloHCT, our patients might not have recovered from the physical decline they experienced during alloHCT, even when some of their alloHCTs dated back several months. We assume that a disease- and therapy-related change in body composition, that is, muscle mass loss, plus inactivity have impaired neuromuscular function and resulted in weaker lower body muscle strength and power output.[2,7] These factors have thus quantifiably limited patients' maximum gait speed and step length. As mentioned above, slowing locomotion can be interpreted as a risk-preventive

safety strategy,[58] which may reflect patients' greater fear of falling. Considering that functional impairments limit autonomy, raise the risk of adverse health events, and are associated with shorter survival in cancer survivors,[59] improving patients' physical capacity should be a key objective in their long-term rehabilitation. It is well known that even weak patients or frail old people can substantially enhance their physical function when they do specific exercises.[60,61]

The dual-task condition revealed only group differences in gait speed as patients walked slower than control participants. Performing a cognitive task while walking may interfere with the cognitive resources needed to establish a regular gait pattern.[62] Wide gait variability, especially under the dual-task condition, may indicate cognitive impairments, as the tasks compete with each other by challenging the cognitive system.[62] Since our patient group did not differ from control participants and seniors, particularly in their gait variability, we assume that the alloHCT procedure did not lead to persistent considerable cognitive impairments. However, neurocognitive dysfunctions after alloHCT are known, and considering that the age of alloHCT recipients is rising,[63] we propose focusing especially on these factors when investigating older patients. Furthermore, spatial gait parameter analyses could yield additional information about step width, a relevant parameter for interpreting gait stability.[22,23,64] The analysis system we applied could only record temporal parameters, but the flexible and mobile use of wireless sensor–based insoles is a comfortable means of assessing gait under field conditions, for example, on an irregular surface.[65]

Limitations and Future Perspectives

Our study implies some methodological limitations. As discussed above, the analysis system could not cover all gait dimensions. Furthermore, the seniors' group presented a relative high performance level, patients were at various phases after alloHCT procedure, and sample size was small. For future work, a greater sample size would allow subgroup analysis in order to attribute functional deficits to specific alloHCT-related side effects. Furthermore, the comparative groups, that is, healthy control participants or seniors, should be representative for their age-appropriate cohort, and the patients' group should be more homogeneous. Moreover, a longitudinal approach would reveal intervention effects on gait abilities of alloHCT patients and provide greater information about underlying adaptation mechanisms relevant for patients' functional status. We propose including an exercise intervention and a long-term follow-up to detect adverse health events, as well as further physical performance tests and patient-reported outcomes in a randomized controlled trial.

Conclusions

The present study revealed functional deficits of alloHCT patients via gait analysis. While patients' performance at preferred gait speed lay in the range of normative values, their ability to accelerate gait and extending steps was diminished. Furthermore, patients reported a greater fear of falling than control participants and even seniors. Thus, slowing locomotion could be a risk-preventive safety strategy. Furthermore, we assume that patients suffer from a notable strength deficit that may impair their power-generation abilities from lower extremities. These functional disadvantages may put alloHCT patients at a higher risk of frailty.[10,12] We, therefore, strongly recommend that appropriate physical exercises be routinely integrated[66] already during hospitalization and that the physical rehabilitation of alloHCT patients be reinforced with the goal of minimizing functional impairments and thus health risks over the long term.

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Authors' Note

The data that support the findings of this study are available from the corresponding author on reasonable request.

Author Contributions

SK and AW designed the study and supervised the measurements. SK provided assistance in data analysis, interpreted the data, and drafted the manuscript. ES and IDW recruited participants, collected and analyzed data, and participated in data interpretation. PvO wrote the software for data processing and drafted the manuscript. AW participated in data interpretation. AG and HB participated in the study's design and revised the manuscript. HB prepared patients' medical history. All authors made contributions to the article, are in agreement with the content, and have read the final manuscript.

Declaration of Conflicting Interests

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Ethical Approval

Ethics approval was given by the Ethics Committee of the University of Freiburg (102/12_140596).

Informed Consent

Every participant signed a written informed consent prior to inclusion.

Trial Registration

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