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Effect of Whole-Body Cryotherapy on Biomechanical Parameters of Gait in Patients with Multiple Sclerosis - Controlled Randomised Studies

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Abstract

Purpose

Multiple sclerosis is a chronic, inflammatory, autoimmune disease of the central nervous system that results in motor disability. Whole-body cryotherapy is a particularly beneficial treatment in many cases. Unfortunately, there are no reports regarding the effects of isolated whole-body cryotherapy on gait improvement in patients with multiple sclerosis.

Study aim: The objective of the study was to evaluate the effect of a series of 10 and 20 whole-body therapy treatments on kinematic gait indices in individuals with multiple sclerosis.

Methods

Fifty-one patients with a multiple sclerosis diagnosis, age 23-65 years, completed the study. Patients were randomly assigned to a control group – no intervention, or an experimental group undergoing 20 whole-body cryotherapy procedures. The Timed 25-Foot Walk gait test (7.5 m), combined with real-time measurements of selected gait parameters, was used to assess locomotor performance. External gait images were recorded using two Casio recording devices.

Results

After 10 and 20 whole-body cryotherapy sessions, an increase was noted for preferred walking speed in the experimental group, however, these changes were not statistically significant. Simultaneously, a shorter gait cycle was observed on the side with greater spasticity after 20 whole-body cryotherapy sessions, as well as a shorter relative foot contact time on the same side, and increased relative foot swing duration in the experimental group. A negative correlation was found between gait velocity, step length and Expanded Disability Status Scale.

Conclusions

A series of 10 and 20 daily whole-body cryotherapy sessions slightly improved selected kinematic gait parameters in multiple sclerosis patients.

Keywords: Expanded Disability Status Scale, kinematic analysis, Ashworth Scale, multiple sclerosis, gait test

Introduction

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system (CNS), characterised by widespread damage to it, and resulting in diverse neurological

symptoms, such as sensory disturbances, pyramidal signs, dizziness, muscle spasticity, coordination disorders, visual disturbances, balance and gait disturbances. MS is the most common non-traumatic cause of disability in young adults [32].

Gait disturbances occur in approximately 70-85% of MS patients during the course of the disease, and after 15 years, up to 50% of patients require assistance with walking [9]. They impair patients' mobility and, consequently, their social and family relationships [14]. Gait disturbances in MS are not uniform, resulting from widespread damage to multiple structures of the brain and spinal cord caused by demyelinating or degenerative changes [16]. Damage to the cerebellum and cerebellar-spinal tracts is the cause of balance and motor coordination disorders, as well as ataxia. Damage to the posterior funiculi results in impaired proprioception, while damage to the upper motor neurons causes muscle weakness and spastically increased muscle tonus. Isolated symptoms of damage to individual structures or multifocal symptoms may occur. In progressive forms of MS, spinal cord damage most often occurs. This results from cumulative demyelinating lesions and increasing atrophy of the spinal cord and cerebellum, causing spastic paraparesis of the lower limbs, muscle weakness, as well as balance and gait disturbances [9,41], leading to shortened step length and slower gait speed [21].

As a result of the above-described changes, muscle spasticity develops, which may affect 40-90% of MS patients [3,41]. Reduced joint mobility (contractures), decreased gait stability and increased duration of double-support stabilisation are also observed [3]. Progression of gait disturbances - shortening the distance the patient can cover—is one of the basic symptoms of secondary progressive MS [10]. More and more often, MS patients are beginning to recognise the importance of walking, which is crucial for everyday functioning and maintaining independence [52].

Unfortunately, to date, there is no effective pharmacotherapy leading to the reversal of damage that has already taken place. Therefore, from the moment of diagnosis and at each stage, comprehensive rehabilitation should be implemented, the objective of which is to maintain the patient's optimal physical and mental fitness for as long as possible and to prevent adverse consequences of the disease. Comprehensive and systematic rehabilitation has a beneficial effect on quality of life among MS patients, extending their lifelong and professional fitness, as well as their independence [4,24]. In addition to kinesiotherapy, comprehensive rehabilitation of MS patients utilises various physical procedures to alleviate symptoms associated with the disease [15,27,49,50]. Among these procedures, whole-body cryotherapy (WBC) deserves special attention, as it is beneficial both in the subjective

assessment of MS patients and in clinical trials on these patients [24,26,39,57]. According to the latest position of an international group of experts, "WBC-related safety risks are within acceptable limits and can be proactively prevented by adhering to existing recommendations, contraindications, and commonsense guidelines" [19].

There are many reports in which it is noted that the use of WBC combined with subsequent kinesiotherapy provides many benefits for patients with multiple sclerosis, such as reduced muscle spasticity [25,28,51,54], increased muscle strength in the upper [23,39] and lower limbs, which ultimately results in reduced disability measured via the Expanded Disability Status Scale (EDSS) [25,27,54]. Improvement in balance and locomotion has also been observed - including gait and distance covered in a questionnaire survey [11], and a reduction in the time to walk a distance of 7.6 m in the Timed 25-Foot Walk (T25-FW) test [39]. In our previous study, we found improvement in the functional status of patients with multiple sclerosis, manifested by a significant reduction in EDSS values and decreased spasticity of the lower limb muscles, both on the sides with greater and less spasticity. Slight improvement in stability among patients with multiple sclerosis after 20 WBC treatments has also been noted [54].

In clinical practice, WBC procedures in MS patients are used in conjunction with subsequent kinesiotherapy [28,51]. However, in the available literature, there are no reports regarding the effects of whole-body cryotherapy alone on locomotor performance and gait parameters in people with MS. Therefore, the aim of this study was to assess the effect of a series of 10 and 20 WBC procedures - without subsequent kinesiotherapy - on gait parameters in individuals with multiple sclerosis.

We hypothesised that whole-body cryotherapy alone, administered in a series of 10 and 20 treatments, would have a beneficial effect on the locomotor performance of patients with multiple sclerosis.

Methods

The research was conducted in compliance with the 1964 Declaration of Helsinki, and its later amendments, and the International Principles governing research on human beings and animals. The research protocol was approved by the Bioethics Committee of the District Medical Chamber in Kraków (No. 99/KBL/OIL/2019). All participants were provided with detailed written information regarding the purpose and course of the research, including the right to withdraw from participation at any time without giving justification. Subsequent to

this, the participants signed the "Informed Consent Form" and the "Personal Data Protection Form".

Experimental group

Initially, 76 patients with multiple sclerosis were enrolled in the programme. However, after considering contraindications to whole-body cryotherapy, 60 patients between the age of 23 and 65 were ultimately included in the intervention. The disease was diagnosed by a neurologist based on the McDonald diagnostic criteria, as modified by Thompson et al. [56].

The following inclusion criteria were used to qualify for the planned research:

- diagnosis of MS – primary and secondary progressive form of the disease;
- disease lasting at least two years from diagnosis;
- age above 18 and below 65;
- disability level of 3-6.5 points on Kurtzke's Expanded Disability Status Scale (EDSS);
- spasticity of 0-3.0 on the Modified Ashworth Scale (MAS);
- ability to walk independently and cooperate during examinations;
- no contraindications to cryochamber treatments [22];
- no use of whole-body cryotherapy treatments within the last six months preceding the examination.

The exclusion criteria for WBC procedures are described by Lubkowska [22]. The assessment of disability level (EDSS) and muscle tone in the lower limbs (MAS) was always performed by the same physician – a specialised neurologist.

The patients who participated in the study had primary (22%) and secondary progressive (78%) forms of MS, without relapses. Pharmacological treatment remained unchanged during the trial, and the patients' clinical condition was stable for the previous six months prior to the study. Forty percent of patients took MTX, 10% Dimethyl Fumarate, 10% Betaferon, 3% Fingolimod and 3% Natalizumab. As for Myorelaxants, 54% were on Baclofen and 19% took Sirdalud. Baclofen and Sirdalud were used as medications to reduce spasticity, and the dosage of these drugs was not changed during the study.

The patients ultimately qualified for the programme (n = 60) were randomly assigned to one of two groups: a control group (CG, n = 20) and an experimental group participating in 20 WBC treatments (EG, n = 40). Patients qualified for the project were assigned to the experimental or control group in the order of qualification, two subsequent patients were assigned to the experimental group, and the next patient was assigned to the control group.

For various reasons, nine individuals withdrew from the programme (two individuals in CG and seven individuals in EG). A total of 51 patients completed the study: 18 individuals in CG (female, n = 14; male, n = 4) and 33 individuals in EG (female, n = 23; male, n = 10).

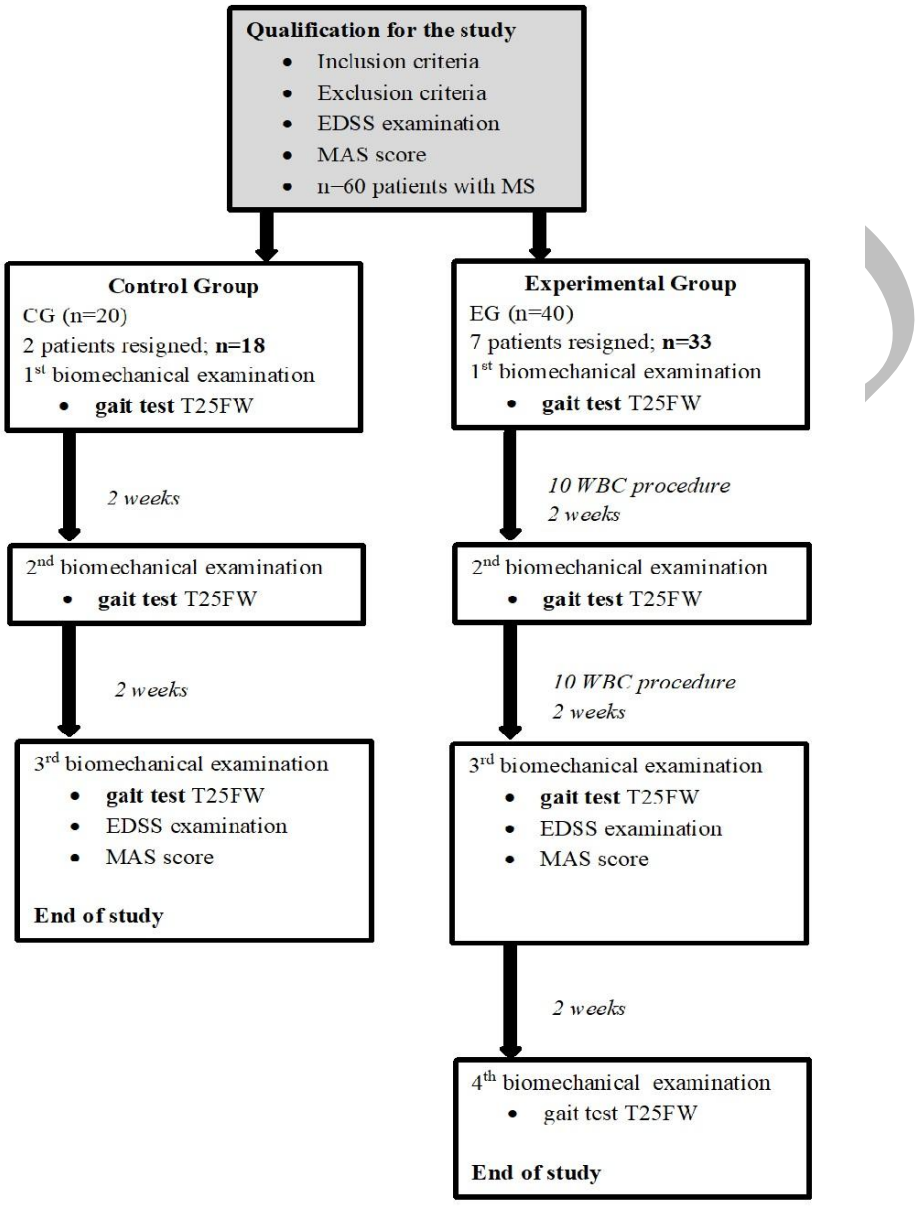

Fig.1. Block diagram of conducted study

Course of research

Locomotion assessment for the EG was conducted before cryotherapy application (Measurement 1), following 10 WBC procedures (Measurement 2), after 20 procedures (Measurement 3), and two weeks post WBC treatment course completion (Measurement 4). Measurements 2 and 3 were performed approximately 20-24 hours after the WBC procedure.

In the control group, locomotion examination was conducted similarly and adequately in time (three times) - measurements 1, 2 and 3 corresponded in time to measurements 1, 2 and 3 in the experimental group. During the measurements, the neurologist identified the sides of the body in terms of muscle spasticity (flexing and extending the limbs in the hip and knee joints) using the modified Ashworth Scale (MAS). The side with greater spasticity was designated as A1, while the side with less muscle spasticity was referred to as A0 (MAS_{A1} and MAS_{A0}, respectively).

The tests were always carried out in the morning (8.00-11.00 a.m.), in similar thermal conditions – the temperature in the laboratory during the tests was 20-22°C.

As part of patient preparation for the study, the skin of both lower limbs was marked with locations corresponding to the axes of rotation of the main lower limb joints: the hip, knee, and talocrural joint (marking stage). These markings were made so that they were clearly visible in the sagittal plane from the lateral side of the body (left and right). For this purpose, two strips of adhesive tape, approximately 10 cm long and 0.7 cm in width, were used. They were placed on the skin so that they intersected at the location of the individual joints of the lower limb. This marked the position of the superior border of the greater trochanter of the femur, the joint space above the fibular head, and the lateral malleolus, corresponding to the location of the joints (hip, knee and talocrural joints, respectively).

Examination of locomotion was conducted on a level platform, positioned 15 cm above the laboratory floor. This placement allowed for filming of the most distal parts of the lower limbs – the feet of the studied subjects. As is well known, specific gait phases are defined based on characteristic events: heel strike (HS) and toe-off (TO). To precisely define these events later on, the subjects walked barefoot or wore thin socks (Fig. 2).

Fig.2. Patient during gait recording

The length of the path along which the subjects walked was over 10 m, and the movement recording was analysed on a section corresponding to the locomotor performance test (T25-FW; i.e. approximately 7.5 m). The external image of the subjects' gait was recorded using two synchronised Casio recording devices (Exilim EX-FH25 Japan) in filming mode and at a frequency of 120 frames/s. They were placed on both sides of the platform along which the subjects moved.

In the T25-FW test, the subjects moved at the most comfortable, self-selected, preferred speed that their health and well-being allowed at the time.

Variables obtained in research

In this study, the sides were identified according to the level of spasticity assessed by the MAS. The side of the body with the lower score was designated A0 (less spastic), while the side of the body with the higher spasticity, as A1.

The recorded video footage, showing the subjects' gait over a distance of 7.5 m, was analysed using dedicated computer programs (MyoVideo; Noraxon USA and Skill Spector; Microsoft USA). Based on measurement data processing, the following values were determined:

- **v** – mean gait velocity [m/s];
- $\mathbf{t_{7.5}}$ – time to cover a 7.5 m distance [s];
- $\mathbf{l_{A1}}$ – average step length on the side of limb with greater spasticity (A1) [m];
- $\mathbf{l_{A0}}$ – average step length on side of the limb with less spasticity (A0) [m];
- $\mathbf{A1_{RoM}}$ – range of motion in knee joint of limb with greater spasticity during one gait cycle (A1) [deg];
- $\mathbf{A0_{RoM}}$ – range of motion in knee joint of limb with less spasticity during one gait cycle (A0) [deg].

Defining one gait cycle as the interval from placing the foot on the ground to the next placement of the same foot on the ground provided the basis for calculating the following variables:

- $\mathbf{T_CA0}$ – mean duration of one gait cycle for less spastic limb [s];
- $\mathbf{T_CA1}$ – mean duration of one gait cycle for limb with greater spasticity [s];
- $\mathbf{T_{STA}A0}$ – mean time of foot contact with ground of limb with less spasticity [s];
- $\mathbf{T_{STA}A1}$ – mean time of foot contact with ground of limb with greater spasticity [s];
- $\mathbf{T_{SWI}A0}$ – mean duration of transferring foot of limb with less spasticity [s];
- $\mathbf{T_{SWI}A1}$ – mean duration of transferring foot of limb with greater spasticity [s].

Methodology of whole-body cryotherapy treatments

Patients participated in 20 daily cryotherapy treatments in four, five-day series (Monday to Friday) in the afternoon. Treatments were performed in compliance with all necessary safety procedures at the Małopolska Cryotherapy Centre in Kraków, according to procedures described in [22], the study by Rymaszewska et al. [42], and detailed in the research by Staszkiewicz et al. [54]. WBC treatments were performed in the Bamet KN-1 cryochamber (Bamet, Wielka Wieś, Poland) cooled with liquid nitrogen. Oxygen content in the cryochamber was monitored using two sensors (EurOx.O2 G/E, Kraków, Poland) and remained between 21-22%. Humidity levels were also regulated.

Statistical analysis of results

Statistical analysis was performed using the IBM SPSS Statistics package and a Microsoft Excel spreadsheet.

The following descriptive statistics were used to describe the collected quantitative data:

- arithmetic mean (M), standard deviation (SD), minimum score (Min), maximum score (Max), 25^{th}, 50^{th} (median) and 75^{th} percentile values.

The following were used in the statistical analysis:

- Shapiro-Wilk test, evaluating the assumption regarding normality of distribution of the results. When the Shapiro-Wilk test results indicated that the distribution of the studied variables approximated a normal distribution, two-way MANOVA was used to examine the interaction between the repeated measures factor (measurement 1 vs. measurement 2 vs. measurement 3) and the between-group factor (control group vs. experimental group). To determine the effect size, partial eta squared (η^2_P) was calculated, with values > 0.01, 0.06 and 0.14 corresponding to small, medium and large effect sizes. If significant interactions were identified, the probability for post-hoc testing was calculated using the Bonferroni post-hoc test.
- When the assumptions for multivariate analysis of variance for dependent variables were not met, the Friedman test for dependent variables and the Dunn's *post-hoc* test with Bonferroni correction were used.
- Additionally, the Wilcoxon signed-rank test was used when only two measurements were performed.
- To examine differences between the groups depending on the distribution of variables, the Mann-Whitney U test and Student's *t*-test were used.
- To examine relationships between two variables, the decision was made to use Spearman's rho correlation coefficient [45].

In all analyses, effects for which the probability *p* value was less than the assumed significance level $\alpha = 0.05$ ($p<0.05$) were considered significant.

Results

Study participants and their characteristics

In Table 1, summarised are the data characterising the groups of studied patients in terms of age and disease duration, as well as the values of indicators describing body structure and the EDSS and MAS values on the side with less (A0) and greater (A1) spasticity.

Table 1. Characteristics of studied subjects at beginning of research procedure

		Control group (CG)	Experimental group (EG)
Age [years]	M ± SD	54.5 ± 7.2	49.9 ± 10.0
	Min-Max	39.0-65.0	23.0-64.0
Disease duration [years]	M ± SD	12.3 ± 5.2	13.7 ± 7.0
	Min-Max	6.0-27.0	2.0-39.0
Body mass [kg]	M ± SD	67.81 ± 8.13	66.80 ± 9.14
	Min-Max	58.0-91.0	55.0-90.0
Body height [cm]	M ± SD	166.1 ± 7.9	168.6 ± 7.5
	Min-Max	154.0-182.0	154.0-182.0
BMI [kg/m^2]	M ± SD	24.6 ± 3.0	23.6 ± 3.9
	Min-Max	19.6-32.2	18.1-32.3
EDSS	M ± SD	4.75 ± 1.1	4.82 ± 1.1
	Min-Max	3.0-6.5	3.0-6.5
MAS_{A0}	M ± SD	1.11 ± 0.3	1.23 ± 0.5
	Min-Max	1.0-2.0	0.0-3.00
MAS_{A1}	M ± SD	1.86 ± 0.8	2.14 ± 0.7
	Min-Max	0.0-3.0	1.0-3.0

No statistically significant differences were observed between the groups for any of the variables described here ($p > 0.05$).

Disease duration ranged from 6 to 27 years in the CG and from 2 to 39 years in the EG. The disability status (EDSS) was similar in both groups (ranging from 3.0 to 6.5), and no between-group differences were observed at baseline. After 20 WBC procedures, the EDSS in the experimental group decreased from 4.82 to 4.48 ± 1.1 ($p < 0.05$), while the EDSS in the CG remained unchanged. MAS_{A0} and MAS_{A1} values did not differ significantly between the control and experimental groups ($p > 0.05$) at baseline. After 20 WBC procedures in the EG, there was a reduction in lower limb muscle spasticity—on the A0 side (MAS_{A0}) from 1.23 ± 0.5 to 0.97 ± 0.3 ($p < 0.05$), and on the A1 side (MAS_{A1}) from 2.14 ± 0.7 to 1.55 ± 0.8 ($p < 0.05$), while in the CG, no statistically significant changes in lower limb spasticity were noted ($p > 0.5$).

Assessment of locomotor efficiency

The data in Table 2 indicate that at the beginning of the experiment (measurement 1), there were no statistically significant differences in gait performance over a distance of 7.5 m between patients in the experimental group and the control ($p > 0.05$).

During each measurement, patients in the CG achieved a mean gait speed (v) slightly exceeding 0.5 m/s. At the same time, this variable was slightly higher in patients in the EG in

subsequent measurements (measurements 2 to 4). The mean time to cover the target distance (7.5 m) in the CG ranged from 14.5 s to 19.4 s, while in the EG, these ranges were from 14.6 s to 16.6 s. The shortest time to comfortably cover 7.5 m was recorded in the EG after 20 WBC treatments (14.62 s). However, this duration returned to baseline values two weeks after the completion of the treatments. Nonetheless, these changes were not statistically significant. No statistically significant differences were noted between the values of the variables recorded in the EG and CG for any of the measurements.

Table 2. Descriptive statistics of gait speed (v) and time to cover distance of 7.5 m ($t_{7.5}$) in control and experimental groups at subsequent measurement sessions

		Control Group (CG)			**Experimental Group (EG)**			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
v [m/s]	M ± SD	0.57 ± 0.22	0.59 ± 0.2	0.51 ± 0.25	0.58 ± 0.23	0.61 ± 0.23	0.62 ± 0.23	0.64 ± 0.23
	Min-Max	0.24-0.83	0.28-0.9	0.17-0.9	0.17-1.0	0.14-1.05	0.17-0.97	0.07-0.97
$t_{7.5}$ [s]	M ± SD	15.8 ± 7.5	14.5 ± 5.8	19.4 ± 11.8	16.2 ± 9.8	15.4 ± 10.75	14.6 ± 8.1	16.6 ± 19.1
	Min-Max	9.1-31.2	8.4-26.5	8.3-44.4	7.5-44.4	7.2-54.5	7.8-43.0	7.7-107.1

In Table 3, the step lengths of patients from both groups walking the 7.5 m distance during consecutive measurements are presented. The results of the analyses did not indicate any statistically significant change in step length (on either side of the body) across the studied groups during the study period ($p > 0.05$). There were also no statistically significant differences between the side with less spasticity and that with its greater size ($p > 0.05$).

Table 3. Characteristics of step length achieved by limbs with different degrees of spasticity in patient groups during subsequent measurements (l_{A1}, l_{A0})

		Control Group (CG)			Experimental Group (EG)			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
l_{A1} [m]	M ± SD	0.38 ± 0.16	0.39 ± 0.12	0.34 ± 0.16	0.41 ± 0.16	0.41 ± 0.14	0.40 ± 0.13	0.43 ± .14
	Min - Max	0.07-0.57	0.16-0.56	0.03-0.58	0.03-0.67	0.05-0.65	0.11-0.59	0.03-0.66
l_{A0} [m]	M ± SD	0.36 ± 0.15	0.38 ± 0.10	0.35 ± 0.14	0.40 ± 0.13	0.40 ± 0.14	0.42 ± 0.12	0.41 ± 0.14
	Min - Max	0.14-0.60	0.22-0.54	0.14-0.57	0.14-0.62	0.07-0.66	0.21-0.65	0.05-0.65

In Table 4, presented are changes in knee joint mobility in subsequent measurements for gait performed at preferred speed over a distance of 7.5 m. The results demonstrated that in the experimental group (EG), on the side with greater spasticity, the $A1_{RoM}$ value fell within a narrow range of 38.2-39.8 degrees, whereas on the side with lesser spasticity ($A0_{RoM}$), the knee range of motion slightly exceeded 40 degrees. No statistically significant changes in knee range of motion during gait were observed in individual measurements after 10 and 20 WBC treatments ($p > 0.05$). There were also no significant differences between the values of the variable described for either side of the body ($A0_{RoM}$ and $A1_{RoM}$) or between the studied groups.

Table 4. Descriptive statistics of knee joint range of motion in subjects during 7.5 m walking in subsequent measurement sessions on more and less spastic sides ($A1_{RoM}$ vs. $A0_{RoM}$)

		Control Group (CG)			Experimental Group (EG)			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
$A1_{RoM}$ [deg.]	M ± SD	41.0 ± 13.72	39.1 ± 14.21	34.0 ± 17.02	39.8 ± 27.41	38.5 ± 13.42	38.2 ± 12.8	38.2 ± 13.09
	Min-Max	7.0-63.0	12.0-67.0	8.5-54.0	10.0-58.0	11.0-64.0	5.0-57.0	8.0-63.0
$A0_{RoM}$ [deg.]	M ± SD	39.9 ± 12.18	40.5 ± 9.92	33.9 ± 18.78	39.1 ± 16.36	41.4 ± 11.73	40.6 ± 11.88	42.8 ± 11.52
	Min-Max	17.0-55.0	25.0-57.0	21.0-55.0	16.0-58.0	14.0-61.0	17.0-62.0	18.0-63.0

The numerical data presented in Table 5 enable analysis of changes in the duration of one gait cycle during the locomotion test conducted in both groups of patients. These values indicate that in the experimental group, cryotherapy treatments promoted shortening of the gait cycle on the side with greater spasticity. In the control group, no significant changes were observed in individual measurements.

In the EG, the duration of one gait cycle was reduced by 5.8% in measurement 2 (after 10 WBC treatments) and by 7.3% in measurement 3 (after 20 WBC treatments) compared to measurement 1. In measurement 4 (two weeks after the completion of the WBC treatment cycle), this time increased again but remained 2.9% shorter compared to measurement 1. On the side with less spasticity (A0), no statistically significant changes were observed after WBC treatments.

In the control group, no statistically significant changes were observed in the duration of one gait cycle for individual measurements, either on the side with greater or less spasticity ($p > 0.05$).

Table 5. Descriptive statistics regarding duration of gait cycle over distance of 7.5 m in studied patient groups

		Control Group (CG)			**Experimental Group (EG)**			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
T_{CA1} [s]	M ± SD	1.47 ± 0.45	1.37 ± 0.29	1.51 ± 0.44	1.47 ± 0.36	**1.35[a]** ± 0.24	**1.31[b]** ± 0.28	**1.38[cd]** ± 0.30
	Min - Max	0.83-2.83	0.98-2.1	1.1-2.86	1.06-2.86	0.94-1.91	0.76-2.08	0.93-2.39
T_{CA0} [s]	M ± SD	1.42 ± 0.46	1.39 ± 0.34	1.45 ± 0.43	1.44 ± 0.35	1.37 ± 0.28	1.32 ± 0.24	1.37 ± 0.31
	Min - Max	0.73-2.93	0.94-2.18	1.09-2.76	1.03-2.76	0.9-2.13	0.98-1.9	0.95-2.37

[a] measurement 1 vs. measurement 2; [b] measurement 1 vs. measurement 3; [c] measurement 1 vs. measurement 4;
[d] measurement 3 vs. measurement 4 - $p < 0.05$
side A0 vs. A1 - $p < 0.05$

In Table 6, the changes are summarised regarding the duration of the lower limb contact phase (T_{STA}) and swing phase (T_{SWI}) during the locomotion test performed in patients from both groups.

Based on the Friedman test results, in the experimental group, the foot contact time on the side with higher spasticity (first three measurements) was reduced (by 4.5% in

measurement 2 and 12% in measurement 3; $p < 0.05$). However, in measurement 4 (two weeks after the completion of cryotherapy), higher values of foot contact time were recorded, similar to those from the second measurement. The mean swing time on A1 side also decreased after 10 WBC treatments, but unfortunately increased two weeks after ending the WBC treatments. No statistically significant changes were observed on the side with lower spasticity ($p > 0.05$).

Table 6. Descriptive characteristics of foot contact time with ground and its transfer in both groups of patients for 7.5 m gait distance

		Control Group (CG)			Experimental Group (EG)			
		Measurement 1	Measurement 2	Measurement 3	Measurement 1	Measurement 2	Measurement 3	Measurement 4
$T_{STA}A1$ [s]	P_{25}	0.84	0.75	0.79	0.84	0.75	0.76	0.79
	median	0.88	0.84	1.00	0.96	**0.89** [a]	**0.85** [b]	**0.89** [c]
	P_{75}	1.20	1.03	1.20	1.18	1.08	0.97	1.03
$T_{STA}A0$ [s]	P_{25}	0.79	0.80	0.78	0.82	0.81	0.73	0.77
	median	0.89	0.87	0.93	0.97	0.92	0.87	0.88
	P_{75}	1.06	1.08	1.22	1.15	1.10	1.04	1.09
$T_{SWI}A1$ [s]	P_{25}	0.34	0.35	0.36	0.38	0.36	0.38	0.38
	median	0.41	0.44	0.43	0.42	**0.40**[d]	0.42	**0.43** [d]
	P_{75}	0.46	0.49	0.49	0.47	0.44	0.43	0.48
$T_{SWI}A0$ [s]	P_{25}	0.38	0.33	0.33	0.38	0.36	0.37	0.38
	median	0.41	0.41	0.40	0.42	0.40	0.40	0.42
	P_{75}	0.50	0.44	0.49	0.48	0.43	0.44	0.43

[a] measurement 1 vs. measurement 2; [b] measurement 1 vs. measurement 3; [c] measurement 1 vs. measurement 4;
[d] measurement 2 vs. measurement 4 - $p < 0.05$

A negative correlation was found between gait velocity, step length and EDSS value.

The results of Spearman's rho test examining the relationships between selected gait indices and the results of the EDSS and Ashworth scales (MAS) obtained in the first measurement, independently for both groups, indicated statistically significant relationships between EDSS and: mean gait speed (CG: rs = -0.721; $p = 0.002$; EG: rs = -0.565; $p = 0.002$), duration of gait (CG: rs = 0.721; $p = 0.002$; EG: rs = 0.565; $p = 0.002$), step length achieved by the limb with less spasticity (CG: rs = -0.636; $p = 0.008$; EG: rs = -0.400; $p = 0.039$) and the duration of one gait cycle performed by the limb with greater spasticity (CG: rs = 0.592; $p = 0.016$; EG: rs = 0.424; $p = 0.027$).

Similar correlations were demonstrated after 20 WBC procedures; in none of the cases were statistically significant differences found between the strength of correlation coefficients in the studied groups ($p > 0.05$).

However, two additional statistically significant correlations were noted in the experimental group, which were not found in the control group: between the EDSS and relative ground contact time (rs = 0.401; $p = 0.038$) and transfer (rs = -0.401; $p = 0.038$) on the side with less spasticity and relative transfer time. Moreover, in the experimental group, a number of significant correlations were found between the Ashworth scale values on the side with less spasticity and: mean gait velocity over the distance of 7.5 metres (rs = -0.454; $p = 0.017$), gait duration over the distance of 7.5 metres (rs = 0.454; $p = 0.017$), step length achieved by the limb on the side with less (rs = -0.418; $p = 0.030$) and greater (rs = -0.400; $p = 0.039$) spasticity, and the duration of one gait cycle performed by the lower limb on the side with less (rs = 0.436; $p = 0.023$) and larger spasticity (rs = 0.409; $p = 0.034$).

Discussion

The aim of this study was to assess the effect of a series of whole-body cryotherapy (WBC) treatments on improving the locomotion of patients with multiple sclerosis.

Although gait disturbances in MS patients pose a significant challenge for this group, the majority of studies in which the effects of WBC on their locomotion are examined do not include assessment regarding the outcomes of objective laboratory methods. Therefore, the aim of this study was to assess changes in gait parameters following the application of 10 and 20 WBC treatments in patients with MS (experimental group – EG) and to compare them with gait parameters in MS patients from the control group who did not participate in cryochamber

treatments. The T25-FW was used for locomotion examination, during which movement was recorded (video) using two Casio recording devices (Exilim EX-FH25). Based on the analysis of the available literature, it can be concluded that this was the first comprehensive study conducted in order to evaluate the results of whole-body cryotherapy treatments using objective biomechanical gait analysis.

Gait is a complex motor activity, but it is commonly assumed to be performed automatically and essentially without conscious awareness [20,48]. Sheridan and Hausdorff [47] also emphasise the role of cognitive and executive functions, as well as attention as components of motor control. Gait quality is influenced by factors such as general health, motor control, muscle and musculoskeletal condition, sensory and perceptual functions, exercise capacity, activity level, cognitive state, motivation and mental health, as well as the environmental conditions in which the activity takes place. A consequence regarding the influence of such a large number of variables on gait is its velocity [30].

When assessing gait quality and efficiency, the following gait parameters are most often taken into account: 1) gait speed, 2) step length, 3) duration of the stance and swing phases, 4) variability of time-space gait indices, and 5) range of motion in the hip, knee and ankle joints [40]. In our research, gait velocity, step length, duration of individual gait phases and range of motion in the knee joints were assessed and analysed.

The obtained results demonstrated that the mean gait velocity over a distance of 7.5 m (v), and consequently, the time to cover this distance ($t_{7.5}$), did not differ significantly between the studied groups. It is worth emphasising that the values of these variables were almost identical in both patient groups for the first measurement, although the time to walk the intended distance was slightly longer in the experimental group. In subsequent measurements, after 10 and 20 cryotherapy sessions (measurements 2 and 3), a trend towards increased gait speed was evident in the EG, and the lowest mean gait duration to cover a distance of 7.5 m was recorded after 20 cryotherapy sessions. Unfortunately, this positive effect of cryotherapy was no longer visible two weeks after completing the cryotherapy sessions (measurement 4).

Similar to the results of the current study, a lack of improvement in the time required to cover a distance of 7.6 m after 20 whole-body cryotherapy sessions was noted in a study involving 25 patients with MS [23]. Radecka et al. [39] reported significant improvement in the T25-FW test after 20 WBC sessions in a study involving 114 patients with MS. However, the level of disability in this group was within the EDSS range of 0-3, which was significantly lower than the level observed in our study. Furthermore, in the cited studies, patients who

underwent cryotherapy participated in 15-minute kinesiotherapy sessions that included locomotion exercises.

In another study, involving 23 patients with MS who underwent whole-body cryotherapy twice a day for 14 days, as well as group and individual kinesiotherapy, questionnaire results indicated improved locomotion in straight-line walking and stair climbing among 65% of patients and increased distance covered without rest in almost 60% of the participants [11].

Gait quality, including gait velocity, is of great importance to patients. According to Andrews et al. [1], the mean walking speed required to cross a city street is approximately 1.32 m/s, while the speed required to safely cross intersections with traffic lights ranges from 0.21 to 0.89 m/s (mean 0.49 m/s). Similar, although slightly higher, values were reported by Salbach et al. [43]. According to these authors, the necessary speed to safely cross traffic lights range from 0.44 to 1.32 m/s. Patients in our research fall within the lower range of these values, therefore rehabilitation aimed at improving these values is recommended.

In our study, a reduction in the gait cycle duration on the side with greater spasticity was also observed in the experimental group after 10 and 20 treatments, which persisted two weeks after the treatment. In the EG, the foot contact time on the side with greater spasticity (the first three measurements) was also reduced (by 4.5% in measurement 2 and 12% in measurement 3; $p < 0.05$). However, in measurement 4 (two weeks after the completion of cryotherapy), higher foot contact time values were noted, similar to those from the second measurement. No statistically significant changes were observed on the less spastic side ($p > 0.05$). These effects may be the result of reduced spasticity on this side due to the WBC treatments.

Reducing gait cycle duration promotes increases gait speed. This interdependence of variables stems directly from the fact that increased gait velocity can be achieved by lengthening steps or increasing their frequency, or by utilising both mechanisms [53]. This mechanism undoubtedly also applies to pathological gait, including that in patients with MS, as evidenced in the data presented by Benedetti et al. [3]. In numerous studies, strong correlations have been demonstrated between EDSS scores and kinematic values of gait indices [5,18,24]. Both tools complement each other by combining a qualitative comparison of the neurological status of MS patients, assessment of disease progression and monitoring the effectiveness of medications with quantitative gait analysis; therefore, they are increasingly being incorporated into MS diagnostics [2,3].

In the first measurement, the mean values of the gait cycle duration, both on the side with greater and less spasticity (T_CA1 and T_CA0, respectively), did not differ between the two studied groups. In the experimental group, after 10 and 20 cryochamber treatments, the duration of one gait cycle was shorter on the more spastic side compared to the baseline value, and it was still shorter during the fourth measurement, performed two weeks after the completion of the treatments. Due to the fact that the gait cycle duration affects gait speed, shortening one gait cycle on the side with greater spasticity could have contributed to increased gait velocity and a shorter time to cover a distance of 7.5 m in patients in this group. These values can serve as a group characterisation, allowing, for example, gait symmetry assessment, the significance of which was emphasized by, among others, Coca-Tapia et al. [5]. It should be noted that symmetry understood in the context of muscle work during gait showed an increasing tendency in the case of EG in the present study.

Comparing the results of our research regarding the main kinematic parameters of gait with data from the literature is very difficult, even when contrasting the results of studies conducted using identical measurement methodology employing the same functional gait test (Timed 25-Foot Walk Test, 7.5-metre gait test). A wide range of functional gait tests are currently used in medical and physiotherapy practice, differing in duration, speed and the method of covering the given distance. Analysis of the literature indicates that short test distances are used in patients with MS, 4 metres [12], 7.5 metres (so-called "25 feet") [14,18,29], and 10 metres [7]. However, the measurement distance can sometimes be extended to 100 or even 500 metres [33]. Occasionally, the start phase is not included in the research protocol, and measurements are taken when the subject is already moving at a certain speed [34]. The speed at which the subjects move varies in individual trials: from preferred, onto forced and slightly higher [6], reaching maximum speed [34]. In gait studies on MS patients, a time criterion is also used, and measurements are conducted in trials lasting two [18] or six minutes [13,38], using traditional surfaces and treadmills [17,55]. These differences make it difficult to accurately compare the results obtained in the research.

Human gait is inextricably linked to its so-called determinants, characterised and discussed in detail in a now classic work [44]. In this article, it is demonstrated that the efficiency of locomotion and its energy cost depend on the course of movement at each level of the biokinematic chain, which is the lower limb. Therefore, mobility in the hip, knee and upper ankle joints, as well as in the pelvis, is crucial. In our study, only knee joint mobility measurements were included.

Perry and Burnfield [31] found that the range of motion of the knee joint in healthy individuals ranged from 50 to 60 degrees, although this value was influenced by the speed of movement. Our results ($A0_{RoM}$, $A1_{RoM}$ approximately 40°) did not fall within this range, but as is well known, the gait of MS patients generally resembled pathological gait patterns rather than physiological ones. Its significant individual differences, as well as our research methodology, did not provide a satisfactory basis for analysing angular changes in other joints of the lower limb. Therefore, the image of changes in temporal and spatial indicators was supplemented only by angular changes in the knee joint. Thus, it is unattainable to determine the impact of the treatments and procedures the patients underwent on the effective mobility of the other joints. Consequently, it is not possible to determine whether the beneficial changes in gait in the EG were due to improved functional status of the joints located above or below the knee. It can be assumed that such improvement may have taken place, but a clear answer could only be given in the case of additional studies focused on this aspect of locomotion in patients with MS.

Benedetti et al. [3] estimated the mean range of motion in the knee joint during gait in patients with MS. The average was found to be 46 degrees, which is slightly higher than in the present study. However, it should be noted that the gait speed in their study was approximately 1 m/s, which is significantly higher than in our measurements. Furthermore, the patients in the cited study were significantly younger and had an EDSS of 0, without spasticity. In the studies by Filli et al. and Severini et al. [8,46], the angular values recorded in the knee joint of patients with comparable EDSS were closer to the results obtained in our research.

Comparative analyses of the results obtained in subsequent measurements during natural, preferred walking a distance of 7.5 m did not show statistically significant differences in knee joint mobility ($A0_{RoM}$, $A1_{RoM}$) between the CG and EG, which indicates no improvement in this respect under the influence of cryotherapy treatments.

Conclusions

A series of 10 and 20 daily WBC sessions improved selected kinematic gait parameters in MS patients (slightly increased gait velocity, shorter time to cover the distance of 7.5 m, statistically significant reduction in gait cycle duration, and shorter foot-to-ground contact time in the limb with greater muscle spasticity). This could be due to normalisation of muscle tone symmetry on the contralateral sides of the body and favourable balance of tonus in the

antagonistic muscles of the lower limbs. It is possible that the results could be improved by the use of targeted kinesiotherapy after WBC sessions in MS patients.

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