

# The effectiveness of whole-body cryotherapy and physical exercises on the psychological well-being of patients with multiple sclerosis: A comparative analysis

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## Abstract

**Background.** Due to the chronic character of multiple sclerosis (MS), non-pharmacological treatment can be applied. These therapies can be a good complementation to standard pharmacological treatment.

**Objectives.** The aim of the study was to evaluate the effectiveness of whole-body cryotherapy (WBC) and physical exercise training on the psychological and general well-being of patients with MS.

**Material and methods.** The study was carried out on 60 patients, who were divided into 3 groups: cryotherapy (Cryo), physical exercise training (Gym) and cryotherapy with physical exercise training (CryoGym). The Psychological General Well-Being Index, the Hospital Anxiety and Depression Scale and the Rivermead Mobility Index were used at 2 points in time: T1 – before the first therapy session and T2 – after 14 days of therapy.

**Results.** Statistically significant differences in the psychosocial well-being were found in the Gym and CryoGym group. Reduction of depressive symptoms and improved functional status was noted in Cryo group. The most significant improvement was observed in the group using WBC with exercise training (CryoGym).

**Conclusions.** Whole-body cryotherapy with physical exercise training was an effective therapy for patients with MS. The introduction of WBC into the standard physiotherapy protocol for patients with MS is fully justified.

**Key words:** multiple sclerosis, physical exercise, functional status, psychological well-being, whole-body cryotherapy

## Cite as

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## Introduction

Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system. It causes focal white matter injuries. The underlying mechanisms are still unclear, although the destruction of the immune system or myelin-producing cells failure caused by genetic and environmental factors are mainly considered. Demyelination of nerve fibers slows conduction by up to 20 times and may lead to a complete conduction block in advanced stages.<sup>1</sup>

The polymorphism, unpredictability, chronic nature, specificity of first symptoms and a varying episodic course of deterioration in MS all lead to feelings of powerlessness, helplessness, confusion, and loneliness among the patients. Existing studies point out the importance of patient self-perception in MS. They often have low self-esteem and self-acceptance as well as a negative self-rating. This is caused not only by the progressing impairment of movement, but also by the patients' emotional disorders and the inability to cope with the disease.<sup>2</sup>

Approximately 40% of patients develop depressive symptoms that require treatment with antidepressants. Perception of the health status is the principal predictor of depressive symptoms.<sup>3</sup> Research confirms that depressive disorders are usually mild in their early stages. Some reports indicate that the pathogenesis of depressive symptoms in MS may be organic. It has been shown that depression is more common in patients with lesions in the brain than in those with lesions in the spinal cord and cerebellum.<sup>4</sup>

The nature of the disease poses a challenge to doctors. The unpredictability of MS and a poor recovery prognosis make the planning and treatment process very difficult. It is, therefore, important to not only focus on the physical dysfunctions, but to maintain a balance between the physical and the psychological health of the patient. The positive attitude of the patients as well as their motivation and willingness to cooperate can positively influence the treatment process and their quality of life.

Physical exercise training is often used in the management of MS. Studies have shown that properly prescribed exercise programs can improve modifiable impairments in MS.<sup>5</sup> Exercise is generally safe and well-tolerated.<sup>6</sup>

Whole-body cryotherapy (WBC) can support and complement primary treatment and facilitate physical activity.<sup>7</sup> In recent years, the use of WBC has gained recognition as a treatment option. The physical, psychological and clinical effect of cryostimulation is unique and cannot be compared with any other body-cooling therapy.<sup>8</sup> Patients with MS subjected to cryogenic temperatures have shown an improvement in physical activity and experienced a reduction in spasticity and pain. Cryotherapy is a factor that improves the functional capacity of MS patients.<sup>9,10</sup> Whole-body cryotherapy was successfully used in patients with MS to improve psychological well-being, but there are

limited literature reports on the beneficial psychological effects of cryogenic temperatures.<sup>9,11</sup>

Therefore, the aim of the study was to evaluate the effectiveness of WBC and physical exercise training on the psychological and general well-being of patients with MS.

## Material and methods

The study was carried out among patients diagnosed with MS. Participants were recruited by a neurologist. The study group included 60 patients, consecutively admitted to a neurologist, who met the following inclusion criteria: patient's written consent to participate in the study, physician's consent – no contraindications to participate in the study, especially no contraindications for the WBC (anemia, hypothyroidism, asthma, heart defects, impaired blood flow and heart rhythm, angina, untreated hypertension), MS in remission (at least 6 months since the last relapse), 0–6 points in the Expanded Disability Status Scale – EDSS (patient's independence in mobility and locomotion), and no other physiotherapy during the course of the study. The following exclusion criteria were also applied: progressive type of the disease, hemodynamic instability immediately prior to each WBC session, previous exposure to WBC, diagnosis and pharmacological treatment of mental disorders, and participation in any clinical test.

Participants were informed about the purpose of the study, the rules for participation and the possibility to withdraw at any stage of the study without consequences.

An approval from the Bioethics Committee of the University School of Physical Education in Wrocław was obtained.

Participants were randomly divided into 3 groups:

- Group 1 (CryoGym): 20 patients who had WBC and, immediately after leaving the cryo-chamber, participated in physical exercise training using the Thera-Band.
- Group 2 (Cryo): 20 patients who had WBC.
- Group 3 (Gym): 20 patients who participated in physical exercise training (resistance training using the Thera-Band).

Additionally, participants who had WBC were informed of the WBC procedure in the presence of a medical doctor. Hemodynamic parameters were analyzed in all the participants immediately prior to each WBC session. The cryotherapy chamber accommodated 5 patients at a time. They stayed in the vestibule with the physiotherapist for 30 s in order to adapt to the cryogenic temperature. Then, they entered the main chamber alone. The temperature was maintained at  $-110^{\circ}\text{C}$  during the first session and reached  $-160^{\circ}\text{C}$  on the last day of the study. The sessions were planned at a fixed time from Monday to Friday during a 2-week period. There were 10 sessions during one protocol.<sup>12,13</sup>

The physical exercise training (in groups 1 and 3), which aimed at strengthening muscles of the lower limbs, lasted

60 min per session. Each session began with a warm-up (10 min). It was followed by the main exercise (40 min of resistance exercises using the Thera-Band in closed kinetic chains) and a cool-down period to reduce the heart rate (10 min). Patients exercised in a lying position, gradually going to sit and standing position. Elastic bands with medium resistance (red) were used. The direction of the resistance was determined exactly. At 90° between the tape and the part of the body being trained, the resistance was maximal. Below the angle of 30° the resistance was minimal. Intensity in the range of a maximum of 8–15 repetitions was recommended. The number of sets was in the range 1–3. Exercises were performed to obtain a subjective feeling of fatigue (about 5–6 according to the 10-degree Borg scale). No pain reactions could occur during exercising. Rest periods between sets and exercises in the range of 2–4 min were recommended.<sup>14</sup>

Both forms of therapies (WBC and physical exercises) in all groups were carried out under the supervision of a medical doctor and a physiotherapist.

The study was conducted at 2 points in time: T1 – before initiating each of the 3 forms of therapy and T2 – 14 days after commencing the therapy and 2 days after finishing the last session, in order to minimize the impact of fatigue after exercise or euphoria and mood improvement immediately after leaving the cryochamber.

The structure of the 3 groups was similar and the characteristics of them are shown in Table 1.

The following research tools were used in the study: The Psychological General Well-Being Index (PGWBI) consists of 22 questions that assess the subjective psychological well-being and stress level of the patients within 6 subscales – anxiety, depression, positive well-being, self-control, general health, and vitality. The more points gained, the better the quality of life of a patient.<sup>15</sup>

The Hospital Anxiety and Depression Scale (HADS) consists of 2 independent subscales that assess anxiety (HADS-A) and depression (HADS-D). Each subscale consists of 7 items. Values 0–7 indicate normal levels of anxiety and depression, values 8–10 mean mild level of anxiety and depression, while values 11–21 suggest the probability of an anxiety or depressive disorder.<sup>16</sup>

The Rivermead Mobility Index (RMI) assesses patient’s mobility and locomotion. The more points gained, the better the functional state of a patient.<sup>17,18</sup>

### Statistical analysis

The following descriptive statistics were applied to the characteristics of the study group: mean, standard deviation, variables, numbers and percentages. The Shapiro–Wilk test was used to check for normal distribution

Table 1. The characteristics of each studied subgroup

Variables	Total	Groups			Kruskal–Wallis/ Pearson's $\chi^2$
		Gym (n = 20)	Cryo (n = 20)	CryoGym (n = 20)	p-value
Age mean (SD)	49.4 (12.2)	53.3 (13.5)	45.8 (10.1)	48.8 (12.2)	0.1555
Body mass mean (SD)	70.0 (14.2)	71.7 (13.6)	68.6 (16.8)	69.6 (12.7)	0.6809
Height mean (SD)	166 (8.5)	164 (8.4)	167 (9.3)	167 (7.7)	0.3392
BMI mean (SD)	25.3 (4.0)	26.7 (4.1)	24.3 (4.1)	24.9 (3.6)	0.1449
Duration of disease from onset of symptoms [years] mean (SD)	20.3 (9.1)	21.1 (10.3)	17.9 (9.1)	24.3 (3.5)	0.5653
Gender, n [%]					0.1580
women	43 (100)	15 (35)	11 (26)	17 (39)	
men	16 (100)	5 (31)	8 (50)	3 (19)	
Marital status, n [%]					0.4400
married	42 (100)	14 (33)	13 (31)	15 (36)	
single/widow(er)	17 (100)	6 (35)	6 (35)	5 (30)	
Occupation, n [%]					0.4540
employed	25 (100)	7 (28)	10 (40)	8 (32)	
retired/disability pensioners	21 (100)	9 (42)	6 (29)	6 (29)	
unemployed	8 (100)	3 (37.5)	2 (25)	3 (37.5)	
EDSS mean (SD)	2.4 (1.9)	2.35 (1.9)	2.3 (1.7)	2.4 (2.1)	0.9992
Number of comorbidities mean (SD)	0.7 (0.8)	0.9 (0.9)	0.3 (0.5)	0.8 (0.8)	0.0940

SD – standard deviation; EDSS – Expanded Disability Status Scale.

of the data. The data was non-normally distributed; therefore, the Kruskal–Wallis and the  $\chi^2$  tests were used to compare the 3 groups. The effectiveness of the treatment was assessed by comparing variables measured at 2 time points (T1 and T2) and was determined with the Wilcoxon test. Statistical tests were verified at the 0.05 level of significance.

## Results

There were no differences among the groups in terms of age, gender, marital status, occupation, body mass, height, BMI, EDSS, number of comorbidities, and the duration of the disease from the onset of symptoms (Table 1). No side effects after using WBC or physical exercises were observed.

There were no differences between groups at baseline in the general well-being. After therapy a statistically

significant difference in the psychosocial well-being (between T1 and T2) was found in the Gym and CryoGym groups (Table 2).

There were also no differences between groups at baseline in the HADS, despite differences in the depressive subscale (HADS-D). A statistically significant reduction in the severity of anxiety symptoms between the T1 and T2 was found in the CryoGym group. Additionally, a significant reduction in depressive symptoms over a period of time was noted in the CryoGym and Cryo groups. Statistically significant differences were not noted in the remaining group (Table 3).

There were also no statistically significant differences between groups at baseline in the RMI. A statistically significant improvement in the functional status between the T1 and T2 was noted in the Cryo group (Table 4).

Results of the changes between T1 and T2 in different form of therapies among studied groups were summarized in Table 5.

**Table 2.** Comparison of the PGWBI between T1 and T2 in each group (Wilcoxon test) and between groups in T1 and T2 time point (Kruskal–Wallis test)

Groups	Baseline (T1)	Follow-up (T2)	Wilcoxon test	
	median (quartiles)	median (quartiles)	Z	p-value
Whole group	66.0 (49.0–78.0)	72.0 (61.0–85.0)	–4.604	0.0000
Gym	64.0 (50.2–77.7)	73.0 (58.0–90.0)	–2.417	0.0155
Cryo	71.0 (56.0–84.0)	77.0 (65.0–88.0)	–1.911	0.0561
CryoGim	67.0 (40.2–70.5)	70.5 (61.0–77.5)	–3.528	0.0004
Kruskal–Wallis test				
H	3.473	1.641		
p-value	0.1761	0.4402		

PGWBI – Psychological General Well-Being Index.

**Table 3.** Comparison of the HADS between T1 and T2 in each group (Wilcoxon test) and between groups in T1 and T2 time point (Kruskal–Wallis test)

HADS	Groups	Baseline (T1)	Follow-up (T2)	Wilcoxon test	
		median (quartiles)	median (quartiles)	Z	p-value
HADS-A	whole group	7.0 (4.0–10.0)	6.0 (4.0–7.0)	–2.920	0.0035
	Gym	5.5 (4.0–8.0)	5.5 (2.0–9.5)	–0.970	0.3320
	Cryo	7.0 (4.0–8.0)	5.0 (4.0–7.0)	–1.499	0.1336
	CryoGym	9.0 (5.0–13.0)	6.0 (5.0–7.0)	–2.556	0.0106
	Kruskal–Wallis test				
	H	5.504	1.485		
	p-value	0.0638	0.4759		
HADS-D	whole group	5.0 (3.0–8.0)	4.0 (2.0–6.0)	–3.031	0.0024
	Gym	4.0 (3.0–7.0)	4.0 (2.0–6.7)	–0.724	0.4691
	Cryo	4.0 (2.0–6.0)	4.0 (1.0–5.0)	–2.045	0.0409
	CryoGym	7.0 (5.0–11.0)	6.0 (4.0–7.0)	–2.485	0.0128
	Kruskal–Wallis test				
	H	6.288	3.998		
	p-value	0.0431	0.1354		

HADS-A – Hospital Anxiety and Depression Scale-Anxiety, HADS-D – Hospital Anxiety and Depression Scale-Depression.

## Discussion

Multiple sclerosis is a specific chronic disease which causes gradual physical status decline, emotional burden, poor overall well-being, and depression.

The analysis of the results showed that cryogenic temperatures have a large impact on mental and physical health, especially in improving patients' mood. The same results were noted in studies conducted by Rymaszewska et al. Cryostimulation led to an immediate improvement in the somatic and mental well-being and caused psychomotor relaxation in patients.<sup>19,20</sup> Authors emphasized that this can be partially explained by a significant increase in the concentration of beta-endorphins and testosterone in the hypothalamus-pituitary-adrenal axis.<sup>21</sup> It is established that MS has to be dealt with on both physical and psychological levels, so the planning and implementation of physiotherapy programs can be complemented by cryotherapy in order to be more effective.<sup>22</sup> This was also observed in the present study. Whole-body cryotherapy significantly reduced the perceived symptoms of depression and improved the patients' functional status. Short-term exposure to extremely low temperatures induces numerous neurotransmitter changes in the central nervous system.<sup>21</sup> The alleviation of depressive symptoms under

**Table 4.** Comparison of the (RMI) between T1 and T2 in each group (Wilcoxon test) and between groups in T1 and T2 time point (Kruskal–Wallis test)

Groups		Baseline (T1)	Follow-up (T2)	Wilcoxon test	
		median (quartiles)	median (quartiles)	Z	p-value
RMI	whole group	14.0 (11.0–15.0)	14.0 (13.0–15.0)	-3.254	0.0011
	Gym	12.0 (10.0–14.0)	13.5 (11.0–14.0)	-1.890	0.0587
	Cryo	14.0 (12.0–15.0)	15.0 (13.0–15.0)	-2.366	0.0180
	CryoGym	14.0 (12.2–15.0)	14.0 (13.0–15.0)	-1.750	0.0800
	Kruskal–Wallis test				
	H	2.097	1.905		
	p-value	0.3504	0.3858		

RMI – Rivermead Mobility Index.

**Table 5.** Summary of the results of the applied different forms of therapies in the studied groups

Variables	Groups		
	Gym	Cryo	CryoGym
PGWBI	0.0155	0.0561	0.0004
HADS-A	0.3320	0.1336	0.0285
HADS-D	0.4691	0.0409	0.0128
RMI	0.0587	0.0180	0.0800

PGWBI – Psychological General Well-Being Index; HADS-A – Hospital Anxiety and Depression Scale-Anxiety; HADS-D – Hospital Anxiety and Depression Scale-Depression; RMI – Rivermead Mobility Index.

extremely low temperatures may be associated with an increase in catecholamine levels in areas of noradrenergic neuron clusters. The results of studies conducted by Zagrobelny also support the noradrenergic “antidepressant” mechanism of action of WBC.<sup>23</sup> Studies indicate that in this process, hypothalamic structures are activated, and endogenous catecholamines, ACTH, cortisol, and beta-endorphins are released.<sup>21</sup> This can also explain the improved functional status of patients in our study. Patients felt an improvement in their physical performance after 10 days of a 3-minute WBC sessions. Low depression symptoms, good sleep and lower fatigue have an influence on physical well-being, motivation for life and contribute to a more active lifestyle. Such data can be used by physiotherapists working with patients with MS. The patient’s approach and confidence in the used method may impact the patients’ motivation and further rehabilitation process. Another result of cryogenic temperatures exposition is the sudden decrease of temperature of the skin and subcutaneous tissues. The temperature of muscles also decreases (although slower). Reducing pain is connected with reducing nerve conduction velocity, inhibiting nociceptors (responsible for the pain sensation), blocking C fibers (neurons responsible for pain sensations conduction) and reducing the release of pain mediators.<sup>24–26</sup> This effect is most likely achieved by slowing down nerve conduction and reducing the responsiveness of peripheral sensory-motor endings, including muscular tone receptors (the Golgi apparatus in the tendons and neuromuscular

spindles in the muscles) as well as partial blockade of the motor plate and  $\gamma$ -motoneurons.<sup>26,27</sup> Therefore, it seems important to look for links between reducing pain (analgesic effect of WBC) and a more effective kinesiotherapy and increased motivation for exercise, which translates into improved psychophysical efficiency of MS patients.<sup>28</sup>

Physical activity, including exercise training, is safe and also very important for people with MS. Now, there is also evidence that at least some of the disability that occurs after MS is due to secondary

deconditioning resulting from a sedentary lifestyle adopted because of the MS symptoms and not CNS damage alone.<sup>29</sup> Therefore, physical activity is necessary for maintaining well functional status and health in people with MS.<sup>30</sup> Maintaining physical function, increased social participation and feelings of self-management and control are the most commonly identified perceived beneficial consequences of physical activity and exercising.<sup>5</sup> People with MS participating in regular physical activity have favorable scores in fatigue, depression and quality of life, when compared to MS patients who do not participate in regular physical activity.<sup>31</sup>

The mechanism of the influence of physical activities on depression is especially essential, as it is based on psychological (“faith in yourself” and the conception of distracters) and biological (for example  $\beta$ -endorphin and thermogenic theory) theories.<sup>32,33</sup>

A lot of researchers found exercising to be beneficial and presented the advantages of regular physical activity on the patient psychological well-being.<sup>5,29,34–37</sup> The same results were noted in our study. We observed significant improvement in psychological well-being in the group with exercise training.

But the most significant improvement was noted in the group using WBC with exercise training (Cryo-Gym). Whole-body cryotherapy with exercise training significantly reduced anxiety levels and depressive symptoms in patients with MS. Connection physical exercises and WBC was the most effective therapy in the presented study.

Disability, fatigue, depression, and anxiety are strongly and negatively associated with the perceived physical and mental health. A study by Szilasiova et al. demonstrates that anxiety and depression are the strongest predictors of mental health and are crucial in clinical practice.<sup>38</sup> Therefore, it is important to choose a rehabilitation program that will affect both the physical and psychological well-being of the patients.

Cross-sectional study analyses suggest that people who exercise regularly are less likely to develop depression.<sup>39</sup> This is also reflected in other studies which show that regular physical activity is positively associated with

a reduction in depressive symptoms and an increase in the quality of life of those patients.<sup>40,41</sup> Hence, combining physical activity and cryogenic temperatures seems to be the most effective method of improving the condition of patients with MS. The results of our study support this concept.

The present study has certain limitations, which include the size of the groups. The instrument used to measure symptoms of depression is a screening instrument and does not provide a medical diagnosis. The study certainly needs to be continued and confirmed on a larger group, and study tools should be supplemented with biochemical measurements.

## Conclusions

In the presented study, WBC improved the psychophysical well-being of patients with MS. The use of WBC reduced anxiety and depressive symptoms in studied patients with MS, particularly when combined with physical exercise training. The introduction of WBC into the standard physiotherapy protocol for patients with MS is fully justified.

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