A short-term exercise program in patients with multiple sclerosis: is body mass index important?

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Obesity is a health problem that can exacerbate the symptoms of multiple sclerosis (MS). In the current study, we aimed to investigate the effectiveness of a short-term exercise program on fatigue, depression, anxiety, and walking performance in normal-weight and overweight patients with MS (PwMS). Sixty-two PwMS were divided into groups according to their BMI (BMI normal/ BMI high). Also, they were all included in the exercise program. The participants took a moderate-intensity walking program 5 days a week for 4 weeks, including 30 min between 5 min of warm-up and 5 min of cooling periods. Also, patients underwent breathing, posture, flexibility, and stretching exercises for 4 weeks. Fatigue, depression, anxiety, 6-minute walking test (6MWT), and BMI were measured before and after the 4 weeks. After the exercise program, there were statistically significant improvements in fatigue, depression, anxiety, and the 6MWT. However, no relation could be detected between the examined variables and BMI. All patients participated effectively in the exercise program, regardless of BMI. The results obtained from this study support that a short-term exercise program is an effective therapeutic intervention, unrelated to BMI, in improving fatigue, depression, anxiety, and walking performance in PwMS. ***International Journal of Rehabilitation Research*** **44: 138–143 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.**

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Introduction

Multiple sclerosis (MS) is a chronic, autoimmune, demyelinating, inflammatory, and neurodegenerative disease [1,2]. The recent studies show that exercise training and rehabilitation increase the performance of the patients with MS (PwMS) on their physical and mental health, and social roles. It can be included as the standard treatment in MS [3–5].

Depressive disorders occur in 16–54% of patients living with MS [6]. In the literature, modest evidence exists for the benefits of the antidepressant drug and cognitive behavioral therapy (CBT) in MS; however, there are some problems such as drug side effects and limited accessibility to CBT [7]. On the other hand, some studies emphasized the positive influence of exercise in patients with a major depressive disorder or depressive symptoms [8]. However, studies in PwMS have shown that depressive symptoms are an obstacle to participation in exercise programs [9]. Also, physical inactivity is common in PwMS. This situation can contribute to physical and mental comorbidities, including high depressive symptoms. In this sense, a cycle occurs between physical activity and depressive symptoms. When people are depressed, their physical activities decrease and as their physical activities decrease, they become more depressed. Cross-sectional studies provided evidence of an inverse relationship between physical activity and depressive symptoms in PwMS [10].

Cohort studies on fatigue prevalence and incidence in MS show that more than 50% of PwMS experience symptoms of fatigue at least once a week [11]. The pre-existing severe fatigue levels in PwMS delay the participation of patients in high-intensity exercise programs with the anxiety of increased fatigue, and accordingly, the possibility of an increase in physical activity decreases [12]. The prevalence and impact of fatigue and depression emphasize the importance of managing these symptoms in PwMS [13].

An international epidemiological study reported that 22.5% of PwMS were overweight. Also, 19.4% of them were obese [14]. Studies have shown the prevalence of overweight in PwMS, and these findings may be a significant variable in the development and management of MS [14–17]. Also, it has been reported that obesity is associated with an increased risk of MS [15–17]. Also, high levels of obesity have been observed at the beginning of MS in adults and have been associated with a faster progression of disability [18,19]. In this study, we aimed to evaluate how physical characteristics will affect exercise program results based on BMI.

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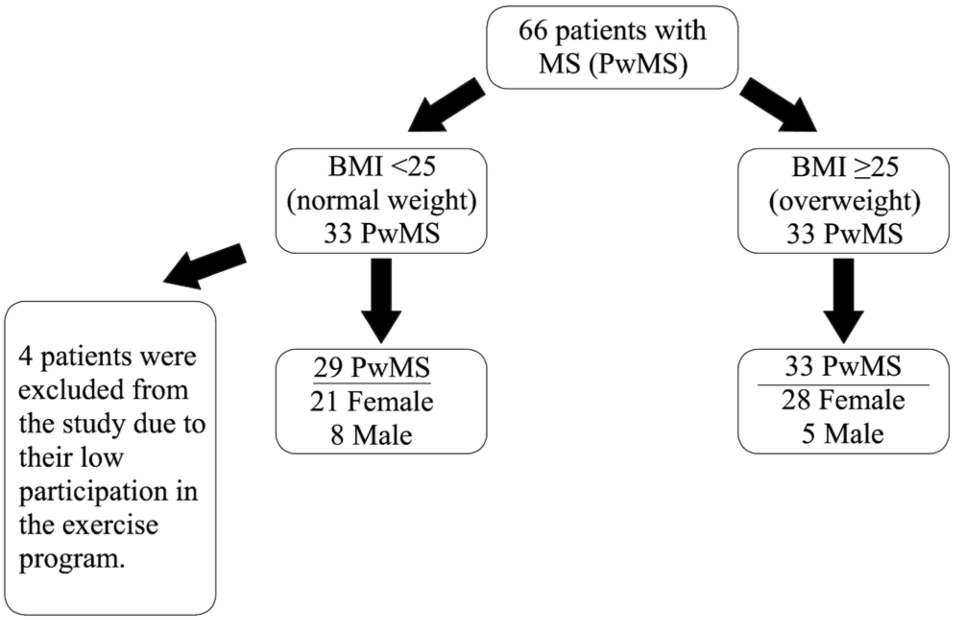
Fig. 1



Flowchart of subject included.

In the current study, we put forward two hypotheses. First, the 4-week short-term exercise program will have a positive effect on fatigue, depression, anxiety, and walking performance in PwMS. Second, these changes will be more beneficial in patients with normal weight compared to those with overweight.

Methods

Patients who were admitted to the physical medicine and rehabilitation (PMR) outpatient clinic between November 2019 and February 2020, who was diagnosed with MS, and who volunteered to participate in the study were included in the study. PwMS who applied to the Physical Therapy and Rehabilitation (PMR) outpatient clinic between November 2019 and February 2020 were included in the study.

The sample group was composed of patients aged 18–65 years, with an EDSS score of 5 and below, who were clinically and laboratory-stable (no drug changes in the last 6 months), and were not exercising regularly. Patients with progressive neurological diseases other than MS, chronic diseases (i.e. kidney diseases, cardiopulmonary diseases), orthopedically limited patients, and patients who have been exercising regularly for the past 6 months were not included in the sample group. In addition, patients with cognitive and mental disabilities, psychotic disorders, bipolar affective disorders, and anxiety or depression requiring medical treatment were referred to the psychiatrist and were not included in the sample group.

Before evaluations, the patients were given verbal and written information on the nature of the study. All procedures were conducted by the relevant principles of the Helsinki Declaration. Also, approval of the study was obtained from the University of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (Number 76/11, Date: 25 November 2019).

The participants were divided into two groups as BMI < 25 kg/m^2 (normal weight) and BMI > 25 kg/m^2 (overweight). The patients were given an exercise program 5 days a week for 4 weeks. A moderate-paced gait program with 60–80% of the maximum heart rate was recommended for 30 min between the 5-min warm-up and cool-down periods. Also, patients underwent breathing, posture, flexibility, and stretching exercises twice a day for 4 weeks.

Sixty-six patients were given a 4-week exercise program. The exercise program was given to the patients as a checklist. Also, patients were phoned once a week. Patients were motivated to continue the exercises. During the study, four patients were excluded because they did not follow the exercise program. Thus, the analyses were evaluated on 62 patients (Fig. 1).

Neurological examinations of all patients, the 6-minute walking test (6MWT), Fatigue Severity Scale (FSS), Beck Depression Inventory (BDI), and Beck Anxiety Inventory (BAI) were evaluated at the beginning of the exercise program and the end of the 4-week exercise program. To prevent observer bias, a single common result

Table 1 Demographic data of BMI normal and BMI high groups

	BMI normal (n = 29)	BMI high (n = 33)	*P*-value
Age mean ± SD	41.3 ± (9.9)	43.5 ± (9.5)	0.421
Years of education mean ± SD	9.0 ± (4.3)	8.7 ± (4.4)	0.737
Sex n (%)			
Female	21 (72.4%)	28 (84.8%)	0.234
Male	8 (27.6 %)	5 (15.2%)	
Disease duration	8.0 ± (6.5)	9.21 ± (6.7)	0.384
BMI mean ± SD	21.6 ± (2.5)	30.3 ± (4.2)	0.000*

Table 2 Comparison of data before and after treatment in BMI normal group (n = 29)

Scale	BT (mean ± SD)	AT (mean ± SD)	*P*-value
6MWT (m)	378.3 ± 181.0	417.2 ± 181.2	0.000*
BDI	14.2 ± 8.3	11.8 ± 7.7	0.000*
BAI	12.5 ± 7.3	9.9 ± 6.9	0.013*
FSS	21.9 ± 11.4	16.8 ± 10.3	0.000*

AT, after treatment; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BT, before treatment; FSS, Fatigue Severity Scale; max, maximum; min, minimum; 6MWT, 6-minute walking test.*$P < 0.05$.

was created after physical examination and measurements were performed by two different experts.

Measurements

Sociodemographic data form

This form was prepared by the research team to obtain information of the participants such as age, sex, BMI, years of education, type of MS, duration of the disease, therapies they received before, and whether there is a concomitant disease.

Fatigue Severity Scale

The FSS is designed for MS patients and patients with chronic fatigue syndrome [20]. The validity and reliability of the Turkish version of FSS have been tested by Gencay *et al.* [21]. The survey consists of nine questions: each question is evaluated on a scale from 1 (representing minimum fatigue) to 7 (representing maximum fatigue). The lower the total score, the less fatigue is considered.

Beck Depression Inventory

It was developed by Beck *et al.* in 1961 and consists of a 21-item self-report scale that evaluates emotional, somatic, and cognitive symptoms. It was revised in 1984 by Beck. High scores are associated with high depressive complaints. It was revised by Beck in 1984. The Turkish validity and reliability study was conducted by Hisli [22].

Beck Anxiety Inventory

It is a self-report scale developed by Beck *et al.* in 1988, consisting of 21 items. High scores are associated with high anxiety. The Turkish validity and reliability study of the scale was conducted by Ulusoy *et al.* [23].

6-minute walking test

The 6MWT has been implemented as a measurement of mobility [24]. 6MWT is a simple test that does not require equipment and experience. Patients are asked to walk the longest possible distance for 6 min, preferably in a 30-m long corridor. The average walking distance in healthy people is about 400–700 m.

Statistical analysis

SPSS 15.0 for Windows Evaluation Version (statistical package for the social sciences) was used to evaluate data with the statistical package program. Sociodemographic data of patients with nominal characteristics are shown as a percentage. Numerical variables are shown with mean and SD, while categorical variables are represented by numbers and percentages. Changes before and after treatment were examined separately for both groups, paired-sample *t*-test was used. Two sample *t*-tests were used to evaluate the difference between groups. While evaluating the change in measurements, the changes between the beginning and the end of the treatment were taken as percentages. Since high scores in 6MWT showed a positive change, the scale was evaluated by multiplying the coefficient of variation (−1). Pearson's correlation was used to examine the correlation in the change of parameters in all patient groups. *P*-value <0.05 was considered statistically significant in the interpretation of all results.

Results

Sixty-six PwMS were given a 4-week exercise program. Compliance with the program was checked from the checklist given to the patients. Four patients were excluded due to their low participation (less than 4 days per week) in the exercise program. Sixty-two patients with relapsing-remitting MS were included in the study. The exercise program was well-tolerated by both overweight and normal-weight MS patients and no adverse events were reported by the participants.

Among the participants, there were 13 (21%) men and 49 (79%) women, and the mean age of all patients was 42.5 (±9.7) years. The mean disease duration was 8.7 (±6.6) years and the mean education period of the patients was 8.8 (±4.3) years. When the data of all participants are examined, 6MWT was 396.5 (±165.3) before treatment and 425.2 (±162.3) after treatment. BDI was 14.4 (±8.1) before treatment and decreased to 11.9 (±7.7) after treatment. BAI was 14.7 (±8.6) before treatment and 11.2 (±8.0) after treatment. FSS before treatment was 22.8 (±10.6) and 17.8 (±10.3) after treatment. The participants were divided into two groups as BMI < 25 kg/m^2 (normal) and BMI > 25 kg/m^2 (high). The demographic data of the groups with normal BMI and high BMI are given in Table 1.

When the participants were divided into two groups according to their BMI, there was no significant difference between the groups in terms of age, years of education, sex, and disease duration.

In both patient groups, 6MWT, BDI, BAI, FSS data were evaluated with the Wilcoxon signed ranked test, and

Table 3 Comparison of data before and after treatment in BMI high group (n = 33)

Scale	BT (mean ± SD)	AT (mean ± SD)	*P*-value
6MWT (m)	412.4 ± 151.3	432.1 ± 146.1	0.000*
BDI	14.5 ± 8.0	11.9 ± 7.9	0.000*
BAI	16.6 ± 9.3	12.4 ± 8.8	0.000*
FSS	24.2 ± 9.9	18.6 ± 10.3	0.000*

AT, after treatment; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BT, before treatment; FSS, Fatigue Severity Scale; min, minimum; max, maximum; 6MWT, 6-minute walking test.*$P < 0.05$.

Table 4 Scale changes between groups

Scale	BMI normal (mean ± SD)	BMI high (mean ± SD)	*P* value
6MWT change (m)	38.9 ± 38.2	21.2 ± 36.7	0.067
BDI change	2.4 ± 2.1	2.6 ± 3.7	0.805
BAI change	2.6 ± 5.3	4.2 ± 4.3	0.186
FSS change	4.5 ± 4.2	5.5 ± 6.8	0.467

BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; FSS, Fatigue Severity Scale; max, maximum; min, minimum; 6MWT, 6-minute walking test.

there was a significant difference between before and after treatment values (Tables 2 and 3).

Changes in the before and after treatment scales between the groups were evaluated with the Mann–Whitney U test, and there was no significant difference in all four scales (Table 4).

The correlation between the change values in the scales was investigated by Pearson Correlation and it was found that FSS correlated with the BDI (r: 0.488, *P*: 0.000) and BAI (r: 0.347, *P*: 0.006). Also, the change of BDI was correlated with the change of BAI (r: 0.332, *P*: 0.008).

Discussion

Previous studies have found that exercise programs have several benefits. These include enhancing skeletal muscle capacity and function, increasing walking speed and physical fitness, disease modification, increasing tolerance to fatigue and alleviating or improving psychological indicators such as anxiety and depression [4,11,25–28]. In our study, we aimed to evaluate the positive effects of exercise on functional capacity, fatigue, anxiety, and depression in PwMS. Also, we aimed to evaluate the relationship between the effects of exercise and BMI. In a 5-year study examining the relationship between disability and BMI, BMI is an important determinant of the progression of disability [29]. Obesity and overweight in MS patients are associated with many factors such as fatigue, depression, low aerobic capacity, cardiovascular disease risk, insulin resistance, blood lipid problems, and it is an important determinant for quality of life [16,18]. Body composition and weight status may be one of the factors that can limit the positive effect of exercise training on fatigue and depression in PwMS. There is limited information in the literature on the effects of exercise in overweight PwMS. Therefore, it is important to clarify the effects of exercise in overweight patients.

Our results show that the exercise program has similar benefits on fatigue, depression, anxiety, and 6MWT in overweight and normal-weight PwMS, and supports previous studies reporting the positive effects of exercise training on fatigue and depression in PwMS [11,25,30–32]. Exercise has been shown to improve walking performance, which is low in MS, by increasing aerobic capacity and muscle strength [4,26,28,33]. We evaluated walking performance in PwMS with 6MWT and found significant improvement in both groups after the exercise program.

In the current study, we observed that exercise had beneficial effects in PwMS but we found that BMI was not effective on changes in fatigue and depression as a result of exercise training. Doctors sometimes have low expectations for overweight people to adapt or benefit from exercise programs [34]. In our study, we revealed that this is a bias in terms of MS disease and their benefit from exercise.

Some studies have reported that exercise training does not effect on body composition, but changes in resting heart rate, insulin resistance, and body fat percentage [18,35]. In another study, it was reported that both BMI and body fat percentage decreased significantly after aerobic interval exercise training [26]. In our study, no significant weight loss or BMI change was found with exercise training. This may be because the exercise program was completed in only 4 weeks. It may be possible to lose significant weight by continuing a long-term exercise program [36]. It should be kept in mind that exercise training together with diet modification can provide more weight loss.

As in this study, it has been shown in the literature that exercise has positive effects on depression and anxiety in PwMS [6,25,37,38]. These results emphasize the importance of exercise therapy for the management of depression in MS, given the limited evidence supporting the success of traditional therapies for high depressive symptoms among PwMS, including CBT and pharmacotherapy [6,39].

The relationship between depressive symptoms and fatigue in PwMS has been consistently shown in previous studies [40,41]. In our study, we found a relationship between fatigue, depression, and anxiety scores in the correlation analysis. Given the relationship between fatigue and depression, improvement in one symptom can have positive consequences for other symptoms. For this reason, it has been reported that depressive symptoms can improve fatigue and vice versa [42]. In this sense, interventions that target clusters of symptoms rather than targeting a single symptom may be more beneficial.

Although it is thought that the items of the Beck Depression Scale related to somatic complaints may overlap with MS symptoms, studies have reported that this overlap does not affect the consistency of the scale negatively and that the original version of the scale should be used in PwMS [43,44]. In our study, we used the BDI and BAI scales in their original form. However, we did not use BDI and BAI to diagnose depression and anxiety disorder. These scales are self-report scales and can be used to evaluate the complaints of individuals. In addition to this, unlike many studies in the literature, having a psychiatrist in our research team has been beneficial both to avoid possible diagnosis and to interpret the symptomatology more appropriately. Further, no additional psychiatric treatment intervention (pharmacological or nonpharmacological) was applied to the patients in the study group.

Thus, while we confirmed one of our two hypotheses that we established, we could not confirm the other. In other words, the exercise program had a positive effect on fatigue, depression, anxiety, and walking performance in PwMS. However, we could not find any difference in these changes between normal and overweight people. The fact that we did not find any difference related to BMI in our results may increase the importance of our short-term exercise program.

Our study has some limitations. First, there is a need for studies with larger participant groups. Besides, we did not observe significant weight changes that could have an impact on our results. The reason for this may be due to the implementation of a short exercise program such as 4 weeks and during the training program, a decrease in adipose tissue and an increase in muscle tissue can occur simultaneously. Therefore, a significant weight change may not be observed. Long-term exercise programs can provide more precise and complementary results. Also, in the study, no long-term follow-up could show the lasting effect of exercise. Finally, the absence of a control group in the study also limits the success of the study. Compliance with the exercise program and the results obtained are related to the basal capacity of the participant. Comparison between MS and healthy controls in terms of both physical and psychological values would have caused erroneous results. Therefore, we did not use the healthy control group.

Conclusion

In this study, it was found that the exercise program was effective in improving MS fatigue and psychological symptoms and increasing walking performance. However, BMI was not related to the results of the exercise program. We argue that the expectation of benefit from treatment based on body weight consists of a bias. People with MS benefit from exercise, and contrary to our estimates, it gives positive results regardless of BMI.

Clinicians may recommend PwMS to participate in exercise training to prevent or alleviate symptoms of depression. We think that exercise will become more important, especially in the case of drug side effects or when the conditions for CBT are not suitable. Future studies should focus clinically on PwMS and depression, investigating the effectiveness of exercise compared to other empirically supported antidepressant treatments, including cognitive-behavioral therapy and pharmacotherapy.

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Conflicts of interest

There are no conflicts of interest.

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