

## ORIGINAL ARTICLE

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**Respiratory muscle strength: Effects on functional capacity, quality of life and fatigue in women with multiple sclerosis****Ayla Fil Balkan, Yeliz Salci***Hacettepe University Faculty of Medicine, Department of Physical Therapy and Rehabilitation, Ankara, Turkey*

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**Abstract**

The aim of our study was to investigate the effect of respiratory muscle strength on functional capacity, fatigue and quality of life (QoL) in patients with multiple sclerosis (pwMS). Thirty-two fully ambulatory female pwMS were included in the study. The maximum expiratory pressure (MEP) and inspiratory pressure (MIP) were recorded for respiratory muscles strength. Functional capacity was assessed with the 6-Minute Walk Test (6MWT), fatigue with Fatigue Impact Scale and Fatigue Severity Scale, and QoL with the MSQoL-54. The partial correlation was made for removing the effect of age and examining the relationship between parameters. There were significant correlations between MIP and functional capacity, change in health, social function, sexual function and satisfaction sub-parameters of MSQoL-54 ( $\rho$ :0.579, -0.490, -0.545, -0.594, -0.585 respectively). MEP had also significant correlations with functional capacity, change in health, social function, sexual function and satisfaction ( $\rho$ :0.708, -0.490, -0.556, -0.608, -0.572 respectively). Conversely, no relation was found between respiratory muscle strength and fatigue. Respiratory muscle strength is an important factor that effects functional capacity and different QoL dimension such as sexual functions. It should be evaluated the earliest period in pwMS. However, fatigue is a multidimensional and complex phenomenon that cannot be simply associated with respiratory muscles strength.

**Keywords:** Multiple sclerosis; fatigue; walk test; respiration; quality of life**Introduction**

Multiple sclerosis (MS) is a chronic inflammatory and autoimmune disease characterized by demyelination and axonal degeneration of the central nervous system. It causes neurological signs and symptoms according to the affected area in the central nervous system. [1]. MS affects mostly the young and female population. It causes various problems such as ataxia, strength losses, muscle tone changes, cranial nerve and autonomic disorders, fatigue, respiratory problems, mood disorders and adversely affects the daily life activities and quality of life. [2].

Pulmonary dysfunctions appear to be most life-threatening findings among many symptoms. [3]. Deterioration in respiratory functions was previously associated with advanced and terminal course of disease in MS patients [4-5]. However, recent studies have reported that respiratory muscle strength has decreased from the early stages of the disease [6-8].

Functional capacity decreases in MS patients compared to healthy population [6]. There are controversial results on relationship between respiratory muscle strength and functional capacity. Ray et al. [9] found that there was no relationship between respiratory muscle strength and functional capacity in MS patients. Wetzel et al. [10] determined that there is a weak-to-moderate correlation between functional capacity and respiratory muscle strength.

Fatigue is a complex and multifactorial symptom in MS patients. It could be related to muscle weakness, balance disorders, depression and hypothalamic disorders. In previous studies, it has been investigated the effect of respiratory muscle strength on fatigue however the results are not clear [9, 11-12].

Quality of life tends to decrease in MS patients associated with disease severity as with many chronic diseases. In the literature, the number of studies carrying out the effect of respiratory muscle strength on quality of life is limited and the results are contradictory. While Muhtaroglu et al. reported that respiratory functions affect the quality of life in MS patients regardless of the level of disability [13], Ray et al. determined that there was no relationship between respiratory muscle strength and quality of life [9].

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Respiratory muscle strength is affected by age, gender and disability level [6, 14-16]. Although the effect of gender on respiratory function is known and MS is more common in women [17-18], these confounding factors are not controlled by carefully patient selection or by using suitable statistical method in studies. Our hypothesis is that the effects of respiratory muscle strength on functional capacity, fatigue and quality of life could be more effectively observed in MS by controlling the effect of age, gender and disability level. Therefore, the aim of this study is to investigate the effect of respiratory muscle strength on functional capacity, fatigue and quality of life in minimally effected women MS patients by controlling age.

## Materials and Methods

### Patients

Patients who were admitted to Hacettepe University Department of Neurology were included in the study. Ethical approval for the present study was obtained from Hacettepe University Non-Interventional Clinical Research Ethics Board. The inclusion criteria were: a) female sex b) diagnosed with multiple sclerosis c) Mini Mental State Test score >25 d) to be full ambulatory (Expanded Disability Status Scale-EDSS ≤ 4.5). Patients who had another neurological, psychiatric, neuromuscular, systemic or cardiovascular system disease and had attack within 3 months were excluded.

### Outcomes Measurements

The degree of disability was measured with Expanded Disability Status Scale (EDSS), respiratory muscle strength with mouth pressure device and functional capacity with 6 Minute Walk Test (6MWT). Fatigue were evaluated with Fatigue Severity Scale (FSS) and Fatigue Impact Scale (FIS) and quality of life with Multiple Sclerosis Quality of Life Questionnaire (MSQoL-54). The EDSS score was determined by the neurologist. Other assessments were performed by physiotherapists with at least ten years of experience.

EDSS is the most widely used scale to evaluate disability level and to monitor disease progression in MS patients. Its score ranges from 0 to 10 (0= neurologically normal and 10= death due to MS). EDSS scores 1.0–4.5 refer to patients with MS who are fully ambulatory, and scores 5.0–9.5 are defined by impairment to ambulation [19].

Respiratory muscle strength (MIP and MEP) depends on the abdominal muscle strength, auxiliary respiratory muscles, the elasticity of the lungs and of the thoracic cage [7]. In this study, MIP and MEP were assessed with the portable electronic mouth pressure device (Micro MPM, Micro Medical Ltd, Kent, England). In addition, normative values ( $MIP = 104 - 0.51 \times \text{age}$  and  $MEP = 170 - 0.53 \times \text{age}$ ) were calculated using the formula developed by Black and Hyatt [20]. Predicted values of MEP and MIP were determined by using normative and real values. Respiratory muscles were considered as weak if they were less than 80% of predicted MIP and MEP values [21-22].

6MWT is reliable and valid test used to evaluate functional capacity in MS patients [23]. In present study, The American

Thoracic Society guidelines were followed for the test. 6MWT was performed in a 30-m hallway and turnaround points were identified. The total distance covered in 6 minutes were recorded in meters [24].

Fatigue was assessed by FSS and FIS which are self-reported scales. FSS includes nine items scored on a seven-point scale from 1 (strongly disagree) to 7 (strongly agree). The higher score indicates greater fatigue severity. The FIS consists of 40 items scored from 0 (no problem) to 4 (extreme problem) on a five-point Likert scale. High scores indicate more functional limitations caused by fatigue [25-26].

Quality of life was evaluated with the Turkish version of MSQOL-54. This questionnaire contains fifty-four items consisting of twelve subsections and two additional single-item measures. These subsections were physical function, role limitation due to physical problems, role limitation due to emotional problems, pain, emotional well-being, energy, health perceptions, social function, cognitive function, health distress, sexual function, and overall quality of life. The single item measures are change in health and satisfaction with sexual function. Individuals are asked to answer each item by choosing one of the numbers (1,2,3...). There are two summary scores at the end of the MSQOL-54 test. These are physical health and mental health scores [27].

### Statistical analysis

Statistical analysis of the data was performed with Statistical Package for Social Sciences (SPSS) Version 17 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics (mean, standard deviation and median) were calculated for participant characteristics, respiratory muscle strength (including percent predicted values), functional capacity, fatigue and quality of life. Frequency counts and percentages were calculated for disease severity, marital status and type of MS. Non parametric partial correlations to remove the effect of age were computed between the respiratory muscle strength and fatigue, 6MWT and quality of life, with tests of significance to determine that "r" was not equal to zero. Strength of the positive and negative correlation was defined very weak (0.00–0.19), weak (0.20–0.39), moderate (0.40–0.59), strong (0.60–0.79) and very strong (0.80–1.0) [28]. Significance coefficient (p value) was accepted as 0.05.

## Results

As shown in Table 1, the study included 32 women patients aged 18 to 58 years. Their EDSS scores ranged from 1 to 4. Twenty-nine (90.6%) patients had relapsing remitting MS and three (9.4%) patients had primer progressive MS (Table 1).

The mean of MIP values was  $67.33 \pm 24.83$  cmH<sub>2</sub>O (median: 65 cmH<sub>2</sub>O). Predicted MIP % value was calculated as  $77.85 \pm 33.02$  (median: 72.85). The mean of MEP values was  $82.90 \pm 26.91$  cmH<sub>2</sub>O (median: 86.50 cmH<sub>2</sub>O) and the predicted MEP% value was  $53.53 \pm 19.79$  (median: 56.46). It was observed that the MEP% and MIP% values of our patients were low (<80%). FSS score was  $42.22 \pm 17.16$  point and FIS score  $58.19 \pm 39.74$  (Table 1).

In our study, there was a moderate correlation between MIP and

functional capacity evaluated by 6MWT (Rho: 0.579,  $p = 0.002$ ). In addition, 6MWT had strong correlation with MEP (Rho: 0.708,  $p = 0.0001$ ). However, respiratory muscle strength (MIP and MEP) was not related to fatigue. Similarly, there was no relationship between fatigue and functional capacity (Table 2).

Total the quality of life score and the values of all sub-parameters were slightly to moderately decreased (Table 3).

The relationship was found between respiratory muscle strength (MIP and MEP) and sub-parameters of MSQoL-54. MIP and MEP mildly to moderately correlated with social function, sexual function, change in health and sexual satisfaction. In addition, there was a relation between MEP and emotional well-being and health perception (Rho: -0.406,  $p = 0.044$  and Rho: -0.450,  $p = 0.024$ , respectively) (Table 4).

**Table 1.** Demographic and clinical features of patients

	X±SD
Age (year)	36.97±11.00
BMI (kg/m <sup>2</sup> )	23.31±3.97
MS duration (year)	8.35±5.44
<b>Respiratory Muscle Strength</b>	
MIP (cmH <sub>2</sub> O)	67.33±24.83
MEP(cmH <sub>2</sub> O)	82.90±26.91
MIP%	77.85±33.02
MEP%	53.53±19.79
6MWT (m)	520.51±70.35
<b>Fatigue</b>	
FSS	42.22±17.16
FIS	58.19±39.74
	(%) N
<b>MS type</b>	
RRMS	(90.6) 29
PPMS	(9.4) 3
<b>Marital status</b>	
Single	(25) 8
Married	(75) 24
<b>EDSS score</b>	
1-2,5	(53.1) 17
3-4	(46.9) 15

X±SD: Mean ± standard deviation, BMI: Body Mass Index, kg / m<sup>2</sup>: Kilogram / Square meter, N: Number of patients, %: Percentage, m: Meter, cmH<sub>2</sub>O: Centimeter water, MIP: Maximal Inspiratory Pressure, MEP: Maximal Expiratory Pressure, MIP%: predicted MIP values MEP%: predicted MEP values, 6MWT: Six Minute Walk Test, FSS: Fatigue Severity Scale, FIS: Fatigue Impact Scale, MS: Multiple Sclerosis, RRMS: Relapsing Remitting Multiple Sclerosis, PPMS: Primary Progressive Multiple Sclerosis, EDSS: Extended Disability Status Scale, MSQoL-54: Multiple Sclerosis Quality of Life Scale-54

**Table 2.** The relationship between respiratory muscle strength, functional capacity and fatigue

	MIP	MEP	6MWT	FSS	FIS
<b>MIP</b>	1				
R		0.898	0.579	0.245	0.171
p		0.0001	0.002	0.238	0.415
<b>MEP</b>		1			
R			0.708	0.262	0.260
p			0.0001	0.207	0.209
<b>6MWT</b>			1		
R				0.293	
p				0.155	
<b>FSS</b>				1	
R					0.928
p					0.0001
<b>FIS</b>					1
R					
p					

R: Spearman Correlation Coefficient, p: Level of Significance, MIP: Maximal Inspiratory Pressure, MEP: Maximal Expiratory Pressure, 6MWT: Six Minute Walk Test, FSS: Fatigue Severity Scale, FIS: Fatigue Impact Scale

**Table 3.** MSQoL-54 total score and sub-parameter scores

SUB-PARAMETER	X±SD
Physical Health	74.06±18.37
Role limitations due to physical problems	56.25±43.53
Role Limitation Due to Emotional Problems	56.25±43.54
Pain	64.06±22.80
Emotional Well-being	56.12±17.98
Energy	43.62±22.26
Health Perceptions	50.46±21.03
Social Function	75.78±18.12
Cognitive Function	58.90±23.88
Health Distress	56.25±26.91
Sexual Function	75.26±24.55
Change in Health	55.46±25.18
Satisfaction with sexual function	68.75±33.60
Overall quality of life	59.32±16.14
Mental Health Composite	57.16±19.56
Physical Health Composite	61.31±18.08

X±SD: Mean ± standard deviation

**Table 4.** The relationship between respiratory muscle strength and quality of life

	PH	PRL	ERL	PAIN	EWB	EN	HP	SF	CF	HD	SEF	CH	SSF	OQL
<b>MIP</b>														
<b>R</b>	0.292	0.076	-0.089	-0.043	-0.332	-0.272	-0.384	-0.545	-0.227	-0.198	-0.594	-0.490	-0.585	-0.201
<b>p</b>	0.156	0.717	0.673	0.838	0.105	0.188	0.058	0.005	0.276	0.342	0.002	0.013	0.002	0.336
<b>MEP</b>														
<b>R</b>	0.252	-0.043	-0.197	-0.106	-0.406	-0.311	-0.450	-0.556	-0.286	-0.251	-0.608	-0.494	-0.572	-0.297
<b>p</b>	0.225	0.837	0.349	0.614	0.044	0.130	0.024	0.004	0.165	0.226	0.001	0.012	0.003	0.150

R: Spearman Correlation Coefficient, p: Level of Significance, MIP: Maximal Inspiratory Pressure, MEP: Maximal Expiratory Pressure, PF: Physical Function, PRL: Role Limitations Due to Physical Problems, ERL: Role Limitations Due to Emotional Problems, EWB: Emotional Well-being, EN: Energy, HP: Health Perceptions, SF: Social Function, CF: Cognitive Function, HD: Health Distress, SEF: Sexual Function, CH: Change in Health, SSF: Satisfaction with Sexual Function, OQL: Overall Quality of Life

## Discussion

In the present study, it was demonstrated that respiratory muscle strength decreased in female MS patients with mild to moderate disability, was related to functional capacity and different dimension of quality of life such as sexual function. However, no relationship has been shown between fatigue and respiratory muscle strength.

Respiratory muscles weakness has been demonstrated in MS patients from the early course of disease regardless of the degree of disability in previous studies [6]. Altıntaş et al. reported respiratory dysfunction in patients with minimal disability even without respiratory symptoms and findings [7]. According to the present study's results, MS patients with minimal disability had lower respiratory muscle strength than expected values. These results are compatible to prior studies although this study was conducted on female patients unlike other studies. We also observed MEP% values lower than MIP% values. Normal expiration performed passively while forced expiration needs muscle activity. Auxiliary respiratory muscles and abdominal muscles weakness can decrease the MEP values [29]. The lower MEP values may be attributed to the progressive ascending muscle weakness in MS patients. Additionally, later influence of inspiratory muscles and diaphragm [6, 30-31] causes low MIP values which is relatively higher than MEP values.

Savcı et al. reported that there was no relationship between functional capacity and respiratory functions [32]. Similarly, Ray et al. found that respiratory strength does not affect functional capacity [9]. However, Whetzel et al. reported a relationship between respiratory muscles strength and walking distance [10]. Functional capacity was assessed with 6MWT in the present study and we demonstrated from moderate to strong correlation between 6MWT and respiratory muscles strength. These inconsistent results may arise due to factors such as differences in subjects' age and disability level selected, in statistical methods used in the studies. It was known that age affects MIP and MEP values [20]. Ray and colleagues' study population's age was higher than our study. With increasing age, confounding factors such as disability level [33] may affect the functional capacity and more severe problems may mask the minimal effect of respiratory muscle strength. Additionally, the studies by Savcı et al. [32] and Ray et al. [9] included patients with EDSS scores in the range of 1-6.5 while the present study included fully ambulatory patients with

EDSS scores 1- 4. Statistical analysis differences may also lead to controversial results in addition to demographic differences. Neither the studies by Savcı et al. nor that of Ray et al. remove the confounding effect of age on the relationship between functional capacity and respiratory muscle strength. In the present study partial correlation was performed to remove the effect of age in a similar way of the study of Whetzel et al. [10] and our results compatible with their results. As a result, it should consider that removing effect of age allows more reliable results to be obtained.

Studies investigating the relationship between fatigue and respiratory muscle strength in MS patients are limited, and the results are contradictory. Ray et al. reported a weak to moderate relationship between fatigue and respiratory muscle strength [9]. Taveira et al. divided MS patients into two group according to fatigue level using modified FIS. They reported that there was no difference in respiratory muscle strength (MIP and MEP) between the two groups [12]. Similarly, we observed that fatigue was not associated with respiratory muscle strength. Fatigue in MS is a multifactorial and has a complex pathophysiology that cannot be explained by a single factor [34-35]. Ray et al. and Taverira et al. evaluated fatigue using Modified FIS, not FIS and FSS. Ray et al.'s study included methodological differences with our study in terms of age, gender and EDSS score while the study of Taverira et al. was more similar to our study in terms of age and EDSS. These factors like age, gender and disease severity might have affected our results. The degree of disability also is related to fatigue [35]. We might not have found a relationship between fatigue and respiratory muscle strength due to including patients with a low level of disability.

The QoL is a multidimensional symptom like fatigue and it can be affected in MS patients as well as in all chronic diseases [36]. In present study, QoL of the patients was investigated with MSQoL-54, which is specific to MS, and it was observed that respiratory muscle strength interacted with its sub-parameters. In previous studies, it is seen that there is little emphasis on the direct relationship between respiratory muscle strength and quality of life. To our knowledge, there are a few studies on this subject in the literature. Muhtaroglu et al. evaluated the quality of life with SF-36, from which MSQoL-54 was developed. They showed that there was a relationship between QoL (physical function, physical role limitation, social function, emotional role limitation and energy sub-parameters) and respiratory muscle strength [13]. Köseoğlu et al. did not evaluate respiratory muscle strength but reported



a relationship between pulmonary function tests and QoL [11]. Silverman et al. also investigated the relationship of respiratory muscle strength on QoL but evaluated it from the perspective of swallowing [37]. In our study, we found that the sub-parameters of QoL (emotional well-being, health perception, social function and health change) were related to respiratory muscle strength. In addition, there was the interaction between respiratory muscle strength and sexual function/satisfaction sub-parameters.

Sexual dysfunction which is common even in patients with minimal disability, is one of the most common problems in MS patients [38]. In Turkey, 59.3% of women with MS have sexual problems [39] and it may affect the mental state of patients more than disease severity [40]. To our knowledge, the present study is the first research showing the relationship between respiratory muscle strength and poor quality of life caused by sexual dysfunction. Najafidoulatabad et al. [41] investigated the effect of yoga on sexual dysfunction in MS patients. They have implemented a program that also included breathing yoga (pranamaya) and reported that patients' sexual dysfunctions decreased and quality of life improved. The researches reporting that pranamaya increased respiratory function [42-43], and our results suggested that sexual dysfunction in MS patients may be related to respiratory muscle strength. Further investigation of this relationship is warranted, and the results will contribute the MS literature by improving the training programs aimed ameliorating the quality of life of patients.

Our results showed that respiratory muscle strength in MS patients decreased in the early stages of the disease even if there were no symptoms related to respiratory problems, and this decrease affected the functional capacity and quality of life in many ways.

The present study had some limitations. Firstly, the number of patients was limited and the majority of patients had relapsing remitting type MS. Therefore, our study results may not represent the general MS population. Secondly, the presence of sexual dysfunction was not evaluated with any scale and was inferentially determined according to the values of a sub-parameter in the MSQoL-54.

As a result, respiratory muscle strength decreases from the earliest period in MS patients and affects functional capacity. At the same time, weakness of these muscles negatively affects different dimensions of the quality of life. Therefore, it may be beneficial to evaluate respiratory muscle strength at early stage and if necessary to add exercises improving respiratory function in treatment programs for management MS. In addition, the present study demonstrated that respiratory muscle strength affects the quality of life related to sexual function. We think that the relationship between these functions should be investigated in more comprehensive studies.

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#### Competing interests

*The authors declare that they have no competing interest.*

#### Financial Disclosure

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#### Ethical approval

*Ethical approval for the present study was obtained from Hacettepe University Non-Interventional Clinical Research Ethics Board.*

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