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Spiroergometric and spirometric parameters in patients with multiple sclerosis: are there any links between these parameters and fatigue, depression, neurological impairment, disability, handicap and quality of life in multiple sclerosis?

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One-hundred and twelve patients with multiple sclerosis were selected as population-based sample and examined on impairment (Expanded Disability Status Scale), disability (Barthel Index), handicap (Environment Status Scale), the quality of life (Multiple Sclerosis Quality of Life), fatigue (Modified Fatigue Impact Scale), depression (Beck Depression Inventory Score), respiratory function (spirometric parameters on spirometry) and physical fitness (spiroergometric parameters on a bicycle ergometer).

The aim of the study was to examine and analyse (descriptive statistics) spiroergometric and spirometric parameters in patients with multiple sclerosis. Firstly, we tested the hypothesis whether spiroergometric and spirometric parameters are decreased and whether there are any correlations between these parameters and measures of impairment, depression, disability, handicap and quality of life. Secondly, we tested the hypothesis whether there is any correlation between a possible deconditioning and fatigue, and between a possible respiratory dysfunction and fatigue in multiple sclerosis.

It results from this study that many spiroergometric parameters in patients with multiple sclerosis are significantly lowered in comparison to the population norm. A link can be found between some spiroergometric parameters and neurological impairment, disability, handicap and quality of life. It is not possible to prove any correlation between spiroergometric parameters and depression. From the spirometric parameters, these are expiratory flows that are significantly lowered in MS patients. It is not possible to prove any correlation between spirometric parameters and fatigue, depression, neurological impairment, duration of the disease, disability, handicap and quality of life in multiple sclerosis.
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Key words: *fatigue; multiple sclerosis; spirometric and spiroergometric parameters*

Introduction

Excessive fatigue is one of the most disabling symptoms for 76–92% patients with multiple sclerosis (MS). Its perception varies widely from the common sense of lassitude and the loss of motivation to increasing muscle weakness associated with neurological disability.[1] There are primary causes (frontal lobe hypometabolism, autonomic dysfunction, conduction block in demyelinated central motor pathways, abnormal co-activaton of agonists and antagonists, mediators of inflammation), secondary causes (deconditioning, respiratory muscle weakness, pain) and other effects, such as physical, social and cultural environment, sleep disorders, physical health (medical comorbidity, iatrogenic causes) and psychological health (stress, depression), which contribute to the development of fatigue in multiple sclerosis.[2]

The aim of this work was to study two possible peripheral sources of fatigue-deconditioning (examined by spiroergometric parameters) and respiratory dysfunction (examined by spirometric parameters), and their correlation to fatigue.

The approach, which recommended the avoidance of physical activity because of thermosensitivity,[3,4] has changed. Presently, a regular workload with an adequate intensity is recommended.[1,5,6] Nevertheless, we suppose that physical fitness of patients without skilled training (with a professional supervisor) is already lowered in patients with a relatively mild neurological impairment. It is worsened according to the neurological impairment and the duration of disease. It has an impact on psychical status (depression) and it affects daily routine activities, social interaction and quality of life.

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The results of Kent-Braun *et al*.,[7] Miller *et al*.[8] and Sharma *et al*.[9] suggest that aerobic exercises and strengthening may be important to prevent secondary changes in muscles partially caused by deconditioning.[7–9] Petajan *et al*. and Schapiro *et al*.[1,5,6] add that aerobic exercises can improve fitness in MS. It is expected that deconditioning in MS increases weakness and fatigue,[3,10] but the studies have not confirmed any link between the subjective perception of fatigue and deconditioning. In this study, we attempt to find a correlation between spiroergometric parameters and fatigue.

It was described that, in multiple sclerosis, poor exercise tolerance is accompanied by dyspnoea.[11] In this work, we examined respiratory function by spirometric parameters and expected that they are already lowered in patients with a relatively mild neurological impairment, they are worsened according to the neurological impairment and the duration of disease, they have an impact on psychical status (depression) and they affect daily routine activities, social interaction and the quality of life.

Foglio *et al.*[11] and Smeltzer *et al*.[12] suggest that the potential peripheral source of fatigue is respiratory muscle weakness, but the studies have not confirmed any link between subjective perception of fatigue and respiratory muscle weakness in MS. In this work, we attempt to find a correlation between spirometric parameters and fatigue.

Methods

Choice and characteristics of the patients

One-hundred and twelve patients were examined from January 2002 to December 2003. The patients were chosen from 2500 patients of MS Centre at the Department of Neurology, 1st Medical Faculty, Charles University and VFN in Prague, randomly out of clinically stabilized outpatients with multiple sclerosis who came to regular medical examination (patients with MS without any complications regularly visit MS centre every six months) and signed the informed consent for the study (patients were informed on the aim and design of the study, on the course the examinations, on their safety/risks; patients were informed about their rights – to be informed, not to participate in the study, to withdraw their consent any time during the study, and on the confidentiality of their data).

Examination

Fatigue, depression, impairment, disability, handicap and quality of life were examined by an independent examiner in all patients.

Impairment was examined by *Kurtzke's Expanded Disability Status Scale*[13] that assesses the neurological impact of multiple sclerosis using the Functional Systems (scale rates the function of eight major systems of the central nervous system – the pyramidal, cerebellar, brainstem, mental, spasticity, sensory, visual, bowel and bladder). The neurological impact is evaluated on a ten-item scale. The system rated disease severity from 0 (normal function) to 10 (death caused by multiple sclerosis).

Disability was examined by the test specially workout for this study. We evaluated the degree of independence in performing ten various self-care and mobility tasks (bowels, bladder, grooming, toilet use, feeding, transfer, mobility, dressing, stairs, bathing): The tasks in this test were accepted from Wade and Collin's version of *Barthel Index*. Data evaluation was performed in a slightly different way. Each answer was scored from 0 (dependent) to 10 (independent) on a three-item scale. Reachable maximal value on the scale is 100 and shows the best function of the person.

Handicap was examined by means of *Environment Status Scale*. This scale assesses work status, economic status, home, personal assistance, transportation, community assistance, social activity) and consists of seven items from 0 (no handicap) to 5 (significant handicap). The maximum value of the scale is 35 and shows the worst function of the person.

The quality of life was evaluated by *Multiple Sclerosis Quality of Life*.[14] This scale contains 54 items on physical function, role of physical and emotional limitations, pain, emotional well-being, energy, health perception, social function, cognitive function, health distress, overall quality of life, sexual function, health status and satisfaction with sexual function. The range of this scale is from 0 (the worst health state) to 100 (the best health state).

Fatigue was evaluated by *Modified Fatigue Impact Scale*.[2] This scale consists of 21 statements that describe how often fatigue has affected a person during last four weeks. Each statement is ranged from 0 (never) to 4 (almost, always). The maximum value of the scale is 84, which represents very frequent fatigue in the person.

Depression was evaluated using the *Beck Depression Inventory Score*.[15] This questionnaire is divided into thirteen categories and patients select a statement in each category which best fits their current feelings on the scale ranged from 0 (the best feelings) to 3 (the worst feelings). The maximum value of the total scale is 39 and shows the worst feeling of the person.

Spirometric parameters were obtained by flow/volume method; specialized SW application on the automatic analyser of respiratory gases Oxycon Delta, Jaeger/FRG.[16] The examination was executed under standard conditions.[17] The static and dynamic spirometric values (inspiratory vital capacity VC IN, expiratory vital capacity VC EX, expiratory reserve volume ERV, forced vital capacity FVC, forced expiratory volume in one second FEV 1, the proportion of forced expiratory volume in one second to maximal vital capacity FEV 1:Vcmax, peak expiratory flow PEF, mid-expiratory flows during the breathing out of the corresponding percentage of FVC MEF 75, MEF 50, MER 25) were examined at rest.

Spiroergometric parameters were obtained by spiroergometry on bicycle ergometer. The examination was executed under standard conditions[17] and it was carried out by means of the method called 'anaerobic threshold':[18] continuously increased load on the bicycle ergometer EL 800, Ergoline/FRG, in the intervals of one minute till the

subjective maximum of a patient, with the evaluation of the changes of respiratory gases and the calculation of selected parameters (maximal muscle performance Watt kg^{-1}, maximal heart rate HR min^{-1}, maximal pulmonary ventilation VE kg^{-1}, maximal metabolic equivalent MET, maximal respiratory exchange ratio RER, maximal oxygen uptake VO_2 kg^{-1}, maximal oxygen pulse VO_2 HR^{-1} kg^{-1}, maximal breath frequency BF min^{-1}, maximal expiratory volume tidal $V_T$ex, maximal oxygen ventilation equivalent EqO_2, maximal carbon dioxide ventilation equivalent $EqCO_2$) on the automatic analyser of respiratory gases Oxycon Delta, Jaeger/FRG. ECG curve was scanned by the electrodes Vacucar, Hormann/FRG, that were placed on the chest according to Wilson and on the limbs and back according to Mason and Likar.[19] The curve was continuously observed on the monitor OPD-3, Tesla/CZE, and written down every minute by ECG apparatus Bioset 3500 C, Hormann/FRG, with a built-in cardio tachometer. Blood pressure was examined indirectly by an auscultatory method at rest and while sitting on the bicycle ergometer before load, in three-minute intervals in the course of load, and, if possible, on the peak of load and in the first, third and fifth minute of recovery. At the end of testing, the patients evaluated the intensity of load according to Borg Scale.[20] If the patients met the method conditions, work tolerance, work capacity and anaerobic threshold were examined.

Statistical analysis

All measured spiroergometric values as well as all the measured spirometric values were compared with the Czech population norm[21] determined by standard examination of extensive group (3762 probands) of healthy population and allow comparison in terms of age and gender.

In some cases, the data did not satisfy the normality assumptions. Often the data were not distributed symmetrically, either. To describe the data, besides the average value and the standard deviation, also the median value and the quartile range were used (see Tables 1 and 2). The latter mentioned were displayed in Box-Plots (see Figures 1 and 2).

For testing the hypotheses, we preferred the nonparametric tests. Testing whether the standardized values are equal to 100 was carried out with the help of the one-sample Wilcoxon test (see Table 2). The independence of parameters was tested by means of Spearman's correlation coefficient (see Tables 3 and 4).

Considering the number of performed comparisons it is appropriate to apply the Bonferroni correction for multiple comparisons. Each difference was considered statistically significant if the level of the test significance was lower or equal to 0.05 divided by the number of performed tests in the batch (k). Using this approach the overall significance level $P_{overall}$ of the whole batch of tests is lower or equal to 0.05. For a high number of comparisons, the Bonferroni correction is very strict. That is why we also mention the differences significant at the 5% level of significance for single comparison. Nevertheless, such results should be validated by further research.

Results

Characteristics of the patients

The study examined 112 patients, comprising 29 men (25.89%) and 83 women (74.11%). Seventy-nine patients (70.54%) had relapsing–remitting MS, 24 patients (21.43%) had primary progressive MS and nine patients (8.04%) had secondary progressive MS. Further basic anthropometrical parameters and data characterizing the disease are shown in Table 1.

Descriptive statistics

Spiroergometric and spirometric parameters The patients determined maximal load on the Borg scale at a lower degree than healthy untrained subjects (average rating of perceived exertion was 14.15). Load was limited by multiple sclerosis (76.19% of patients ended the test because of sudden limb muscle weakness). The patients were not, at the end of the test, fully charged concerning cardio-respiratory and metabolic categories. That is why it is not possible to consider the last phase of the examination as maximal, but only as peak.

The majority of spiroergometric and spirometric parameters in MS patients is lowered in comparison to the norm. The significantly lowered parameters are: muscle performance, heart rate, pulmonary ventilation, metabolic equivalent, oxygen uptake, breath frequency, peak expiratory flow, mid-expiratory flows during the breathing out of

Table 1 Basic anthropometrical parameters and data characterizing the disease in the examined patients

	Mean	*SD*	*Median*	*Lower quartile*	*Upper quartile*
Impairment (EDSS)	3.07	1.68	3.00	2.00	4.00
Disability (BI)	96.82	5.73	100.00	95.00	100.00
Handicap (ESS)	4.03	4.97	2.00	0.00	6.50
Quality of life-physical (MSQOLp)	55.77	15.39	56.46	45.79	66.72
Quality of life-mental (MSQOLm)	63.56	20.11	65.85	49.95	80.42
Depression (BDI)	7.15	4.94	6.00	3.75	10.00
Fatigue (MFIS)	38.85	16.20	38.00	28.50	49.25
Duration of the disease	8.79	6.46	7.00	4.00	12.00
Age	36.44	9.52	35.00	28.00	44.00
Height	171.35	8.29	170.00	165.00	178.00
Weight	65.84	13.01	63.00	57.00	73.00

Table 2 Descriptive statistics of spiroergometric and spirometric parameters in relation to the norm

	Mean	*SD*	*Median*	*Lower quartile*	*Upper quartile*	P *value*
(Wilcoxon test)						
Watt kg^{-1}	53.34	20.84	52.57	37.11	69.03	*** <0.0001
HR min^{-1}	82.63	13.20	84.60	72.76	91.11	*** <0.0001
VE kg^{-1}	75.09	26.43	73.75	53.19	87.96	*** <0.0001
MET	64.39	38.69	56.14	35.83	86.09	*** <0.0001
RER	99.11	12.51	97.27	92.73	104.55	0.1122
VO_2 kg^{-1}	81.77	23.05	80.24	64.43	96.87	*** <0.0001
VO_2 HR^{-1}	99.22	26.41	98.15	80.39	114.66	0.5303
BF min^{-1}	84.87	21.15	82.05	68.29	95.12	*** <0.0001
$V_T$ex	95.14	31.82	96.01	69.72	118.11	0.1485
EqO_2	104.46	28.13	99.10	84.19	116.92	0.5415
$EqCO_2$	109.62	23.81	106.67	93.98	117.83	***0.0003
VC IN	96.40	16.62	96.40	86.40	105.00	*0.0231
VC EX	99.61	13.67	98.10	90.60	109.60	0.7033
ERV	101.69	44.42	101.30	71.55	129.00	0.9916
FVC	100.53	16.76	100.30	91.70	110.90	0.5275
FEV 1	103.10	16.43	103.30	95.30	112.10	*0.0076
FEV 1:Vcmax	104.92	7.46	105.80	100.70	109.90	*** <0.0001
PEF	85.67	18.80	84.70	75.80	96.80	*** <0.0001
MEF 75	91.77	18.26	93.90	81.50	101.60	*** <0.0001
MEF 50	92.63	22.40	89.60	78.60	107.70	***0.0005
MEF 25	92.30	29.56	90.30	72.60	113.90	*0.0057

* $P < 0.05$, ** $P < 0.001$, *** $P_{\text{overall}} < 0.05$.
Comment: The relative values of spiroergometric and spirometric parameters were received in the follow way: The absolute values of spiroergometric and spirometric parameters of each patient were compared with average value of the same age and gender healthy untrained population. Then the relative values were statistically analysed using described descriptive statistic methods.

the corresponding 50 and 75% of forced vital capacity. The values of oxygen and carbon dioxide ventilation equivalents are increased at lowered oxygen transport capacity. The proportion of forced expiratory volume in one second to vital capacity is significantly increased (Table 2, Figures 1 and 2).

After Bonferroni correction, the statistically significant (at the overall significance level $P_{\text{overall}} = 0.05$) non-zero correlations are correlations between: neurological impairment and muscle performance (Figure 3), neurological impairment and heart rate, neurological impairment and pulmonary ventilation, neurological impairment and metabolic equivalent, neurological impairment and oxygen uptake, neurological impairment and oxygen pulse and neurological impairment and expiratory volume tidal. Also correlations between disability and muscle

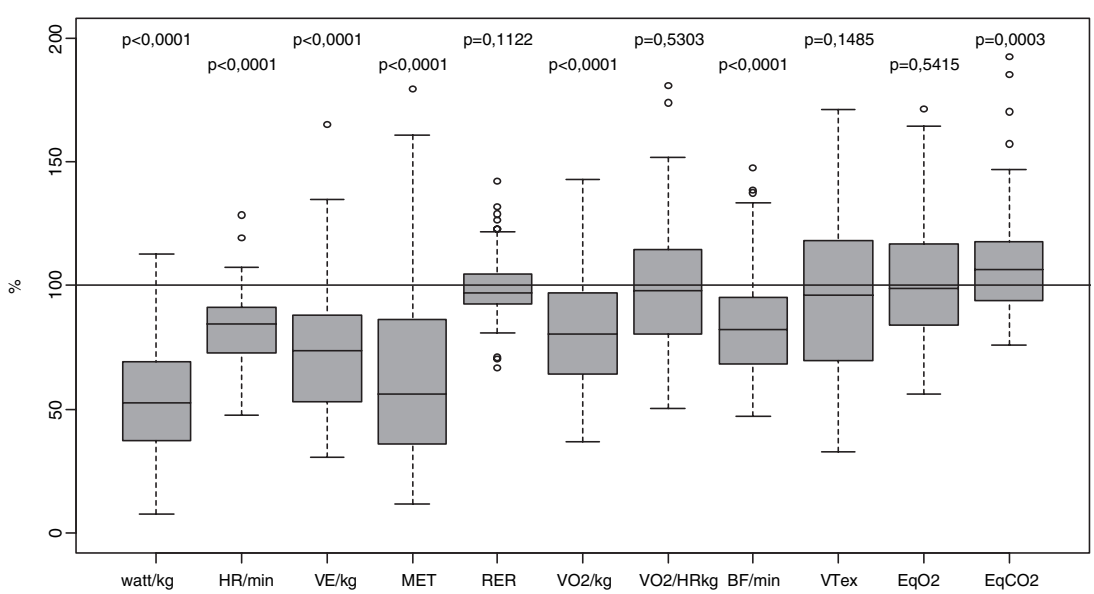

Figure 1 *Spiroergometric parameters in relation to the norm. The difference was considered statistically significant for* $P < 0.002$, thus significant at the overall significance level $P_{\text{overall}} < 0.05$.

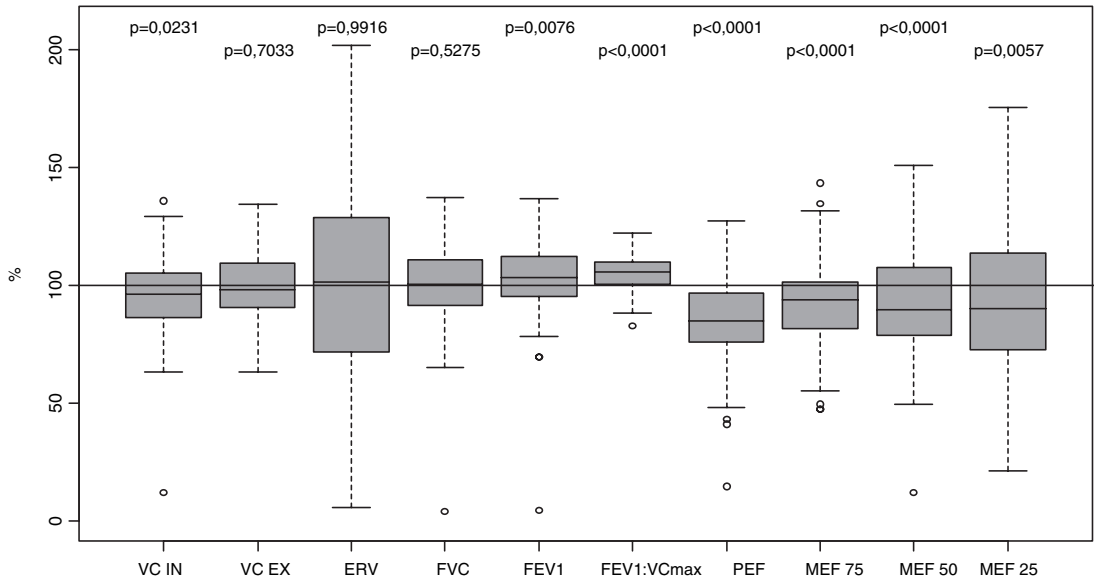

Figure 2 *Spirometric parameters in relation to the norm. The difference was considered statistically significant for* $P < 0.002$, thus significant at the overall significance level $P_{\text{overall}} < 0.05$.

performance, disability and pulmonary ventilation, disability and metabolic equivalent, disability and oxygen uptake and disability and expiratory volume tidal. As well as correlation between handicap and pulmonary ventilation, and correlation between quality of life (physical) and muscle performance. For achieved correlations, see Table 3.

Considering Bonferroni correction, it is not possible to prove any correlation between spiroergometric and spirometric parameters and the duration of disease. Nevertheless, at the significance level of $P = 0.001$ for a single comparison, it is possible to prove the connection between metabolic equivalent and the duration of disease ($r = -0.33$) and between muscle performance and the duration of disease ($r = -0.32$). It is also possible to confirm the relation between expiratory volume tidal and the duration of disease ($r = -0.28$), between the duration and the heart rate ($r = -0.23$) and between duration and pulmonary ventilation ($r = -0.24$) at the significance level $P = 0.05$ for a single comparison (Tables 3 and 4). Nevertheless, the possible clinical significance of the latter mentioned relations would need to be validated by a further research.

Considering Bonferroni correction, there is no statistical significance of correlation between spirometric parameters and neurological impairment, we also cannot prove any correlation between spirometric parameters and the duration of disease, and it is not possible to confirm any significant influence of spirometric parameters on disability, on handicap, or on the quality of life. Nevertheless, at the significance level $P = 0.05$ for a single comparison it is possible to prove the connection between expiratory vital capacity and disability ($r = 0.24$), and between expiratory reserve volume and disability ($r = 0.28$, see Table 4). However, the clinical significance of these relations is also questionable.

Table 3 Correlation between spiroergometric and clinical parameters (Spearman's correlation coefficients)

	MFIS	*BDI*	*EDSS*	*Duration of disease*	*BI*	*ESS*	*MSQOLp*	*MSQOLm*
Watt kg^{-1}	* −0.28	−0.08	*** −0.59	** −0.32	***0.59	** −0.37	***0.43	0.03
HR min^{-1}	−0.16	−0.11	*** −0.47	* −0.23	*0.25	* −0.31	*0.34	0.17
VE kg^{-1}	−0.19	−0.15	*** −0.54	* −0.24	***0.43	*** −0.40	*0.31	0.10
MET	* −0.23	−0.11	*** −0.48	** −0.33	***0.47	* −0.33	*0.27	−0.04
RER	−0.04	−0.10	−0.02	0.02	0.03	−0.05	−0.05	0.01
VO_2 kg^{-1}	−0.20	−0.07	*** −0.46	−0.18	***0.40	* −0.27	*0.32	0.07
VO_2 HR^{-1}	−0.21	−0.04	*** −0.35	−0.10	**0.39	* −0.22	*0.23	−0.04
BF min^{-1}	−0.19	−0.18	−0.05	0.01	−0.03	−0.08	0.12	0.12
$V_T$ex	−0.15	−0.06	*** −0.52	* −0.28	***0.52	** −0.39	*0.24	0.05
EqO_2	−0.14	−0.20	* −0.23	−0.10	0.13	* −0.30	0.06	0.08
$EqCO_2$	−0.16	−0.20	* −0.23	−0.15	0.11	** −0.37	0.06	0.07

* $P < 0.05$, ** $P < 0.001$, *** $P_{\text{overall}} < 0.05$.
The difference considered statistically significant for $P < 0.05/88$, thus significant at the overall significance level $P_{\text{overall}} < 0.05$.

Table 4 Correlation between spirometric and clinical parameters (Spearman's correlation coefficients)

	MFIS	*BDI*	*EDSS*	*Duration of disease*	*BI*	*ESS*	*MSQOLp*	*MSQOLm*
VC IN	0.12	0.10	−0.09	0.01	0.18	−0.15	0.08	0.00
VC EX	0.18	0.11	−0.15	−0.07	*0.24	−0.10	0.09	−0.03
ERV	0.14	0.06	−0.18	−0.14	*0.28	−0.09	0.11	0.05
FVC	0.20	0.11	−0.10	−0.01	0.20	−0.12	0.07	−0.05
FEV 1	0.20	0.15	−0.11	0.03	0.12	−0.08	0.00	−0.04
FEV 1:Vcmax	0.07	0.11	0.01	0.05	−0.2	0.08	−0.20	−0.01
PEF	−0.08	0.06	−0.12	0.01	0.07	−0.16	0.05	0.07
MEF 75	−0.04	0.05	−0.11	0.03	0.03	−0.12	0.05	0.09
MEF 50	0.06	0.09	−0.12	0.00	0.00	−0.06	0.00	−0.04
MEF 25	0.17	0.11	−0.03	−0.02	−0.07	0.11	−0.14	−0.05

* $P < 0.05$.
No statistically significant difference at $P < 0.05/80$.

Fatigue and depression

Considering the number of performed comparisons, we did not prove any statistically significant connection between spiroergometric parameters and fatigue, nor between these parameters and depression. Similarly, no connection was shown between spirometric parameters and fatigue, nor between spirometric parameters and depression (see Tables 3 and 4). When not considering the Bonferroni correction, only the correlation between muscle performance and fatigue ($r = -0.28$) and between metabolic equivalent and fatigue ($r = -0.23$) can be shown to be statistically significant. Nevertheless, the significance needs further validation.

When studying fatigue more closely, we confirmed a significant correlation between fatigue and handicap ($r = 0.45$), fatigue and depression ($r = 0.58$) and between fatigue and quality of life ($r = -0.54$ for physical and $r = -0.53$ for mental quality of life). Significance of correlation between fatigue and neurological impairment ($r = 0.29$) is questionable, for our data it can be confirmed at significance level $P = 0.05$ only when not considering the number of comparisons (for better illustration of the relationship, see Figure 4). No correlation can be proved between fatigue and duration of the disease, or between fatigue and age.

Discussion

Spiroergometric parameters in MS

Previous studies have examined various functional parameters, while the majority of them did not take into consideration the categories of age, sex, weight and neurological impairment. They also used different methods for spiroergometric examination and, therefore, the results are not mutually comparable. Nevertheless, results from the previous studies indicate that physical conditioning of MS patients is low.[1,5,6,11,22,23,24,25] This was further confirmed by this study when all possible spiroergometric parameters were examined. The large number of

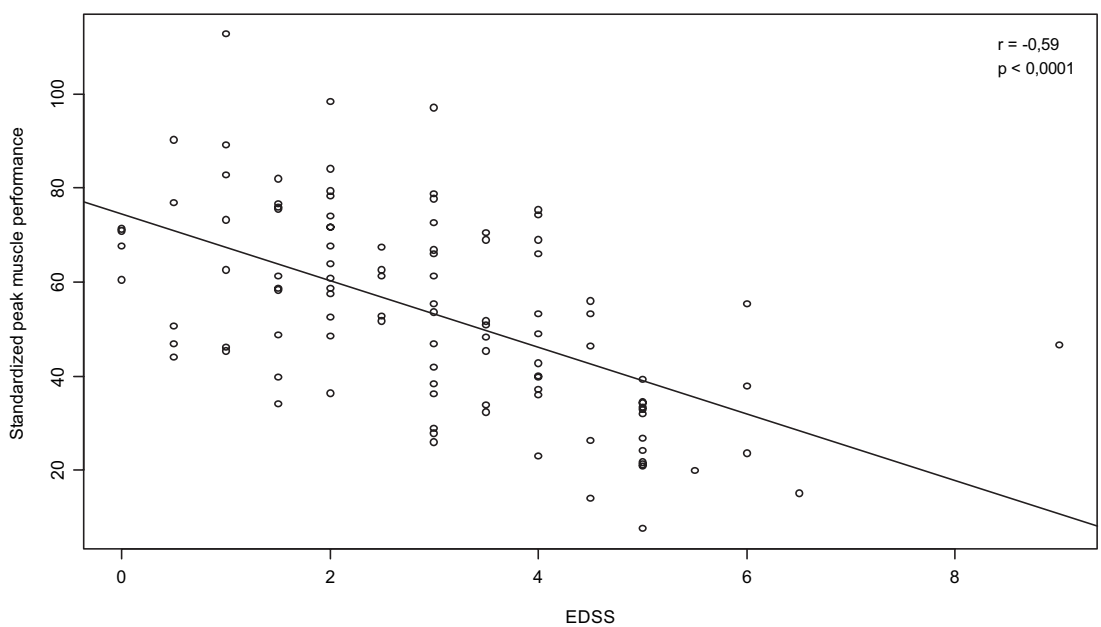

Figure 3 *Relationship between the neurological impairment and peak muscle performance.*

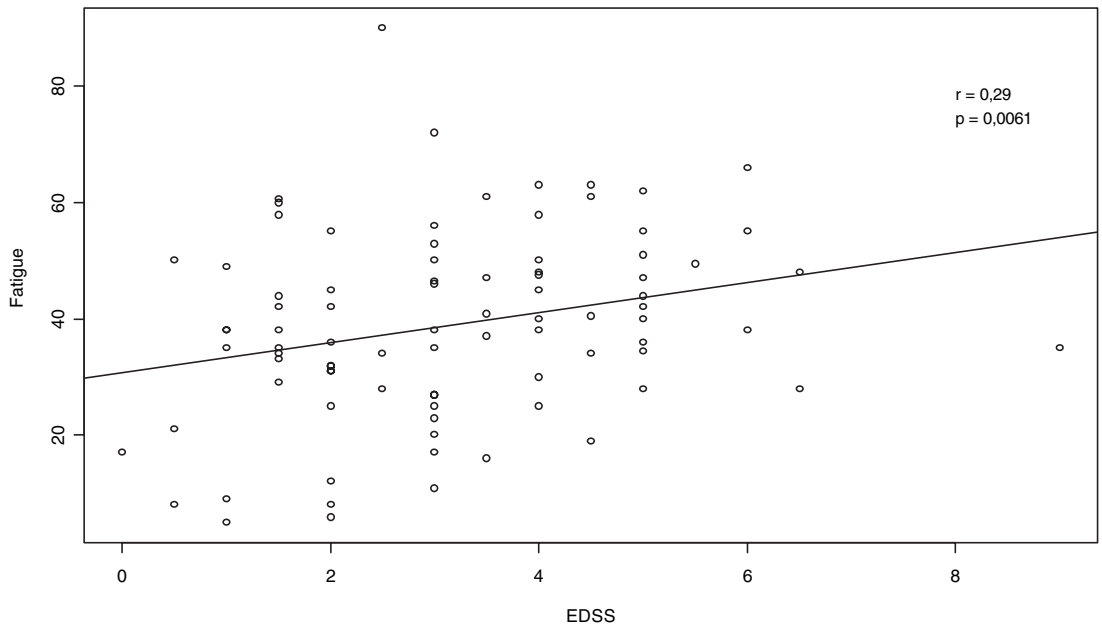

Figure 4 *Relationship between the neurological impairment and fatigue.*

examined parameters made it difficult to interpret the results. On the other hand, it was shown that a physical condition should be ideally estimated in the complexity (the parameters have a variable influence on each other according to subject variability) and at each point in time. No coefficient characterising a physical condition exists. It is possible to evaluate a physical condition based on muscle performance, heart rate, respiratory exchange ratio, pulmonary ventilation and oxygen uptake or only based on oxygen uptake.[17] However, this was not the aim of this study.

We found the lowered ability of MS patients to achieve maximum physical condition and we explain it by impaired coordination (the execution of big rhythmical movements is impossible), by the emergence of sudden muscle weakness of extremities (76.19% of the patients ended the test because of this reason) and by the lack of motivation to perform as well as possible (e.g. in comparison to sportsmen). We agree with Ponichtera-Mulcare *et al*.[23] that it is more suitable to speak about the achievement of the peak than of the maximum.

The authors who monitored cardiorespiratory fitness in MS patients discovered that it is already lowered in patients with a mild neurological impairment,[5,22,23] but not in patients with minimal neurological impairment.[22] Muscle performance decreases in relation to the neurological impairment.[5,22] The parameters of maximal oxygen uptake and of maximal heart rate significantly change with the duration of the disease.[11] Heart rate at rest is altered significantly with neurological impairment.[11] Foglio *et al*.[11] proved greater dependence of maximal muscle performance on inspiratory muscle function than on the neurological impairment. Our study also proved that functional parameters of the patients are lowered already at the onset of the disease. The majority of spiroergometric parameters are significantly lowered with neurological impairment. Lowered physical fitness significantly influences MS patients in activities of daily living and social interaction as well as impairing their quality of life.

Multiple sclerosis influences basic physiologic response to load[28] by demyelinating processes.[27,29] However, it is probably caused by deconditioning in consequence of the lack of physical activities.[26] The restriction of physical (often also of social) activities in MS patients was confirmed.[26,30] It could be primarily caused by muscle weakness and fatigue,[3,4,10] but it can be partially caused by the recommendations of specialists to avoid physical activities. However, the positive impact of regular workload with an adequate intensity on muscle tissue, ligamentous and skeleton structure, cardiorespiratory and metabolic processes, function of the central nervous system (production, regulation and maintenance of motor programs), mood, general well-being, etc., in the healthy population[31,32] as well as in MS patients[1,5,6,22–24,33] has been already confirmed. Insufficient activity in MS patients is linked to muscle changes that occur independently of the CNS damage (lowered oxidative capacity, lowered muscle dynamic properties, increased muscle fatigue, impaired metabolic response of muscles to load, impaired excitation–contraction coupling).[7,8,30] Increasing fatigue at load is therefore probably caused by an imbalance between the increased metabolic need of MS patients and their lowered supply by cardiorespiratory systems.[26]

The possible relationship between spiroergometric parameters and fatigue is inferred indirectly from the effect of aerobic training.[1,5,30] The above-mentioned studies describe that the improvement of physical fitness simultaneously decreases fatigue and increases abilities to execute activities of daily living. In our study, we did not prove any relationship between lowered spiroergometric parameters and fatigue at the overall significance

level. $P_{overall} = 0.05$, however, the independent evaluation of individual correlations showed a significant relationship ($P < 0.05$) between muscle performance and fatigue, and between metabolic equivalent and fatigue. Nevertheless, the significance of these relationships needs further validation. We did not confirm the hypothesis that lowered spiroergometric parameters increase fatigue in MS patients.

Spirometric parameters in MS

This study evaluated respiratory functions in patients with a relatively mild neurological impairment. We perceived as important to understand respiratory functions in MS in the stage of the disease without complications (for example pneumonia, aspiration pneumonia etc.). According to Tantucci *et al*.,[34] several abnormalities can be found also in the clinically stable patients with the moderate to severe neurological impairment. Grasso *et al*.[35] claim that the development of respiratory dysfunction is not influenced only by the duration of the disease and the neurological impairment, but also by cerebellar dysfunction (respiratory dysfunction can therefore occur also in patients with the mild neurological impairment).

The results of this study are in accordance with the studies showing that pulmonary functions (inspiratory and expiratory vital capacities, expiratory reserve volume, forced vital capacity, forced expiratory volume in one second) in MS patients are not usually affected but in the advanced stages of the disease, while respiratory muscles are affected already in the early stages of the disease.[11,12,36–39]

The proportion of forced expiratory volume in one second and vital capacity of patients in our study is increased. We explain this phenomenon by the fact that the first second of breathing out in MS patients is less influenced than the whole expiration. This ratio is not dependent on the neurological impairment (see Refs.[11,12,35] and the results of this study).

Peak expiratory flow and mid-expiratory flows of the corresponding percentage of forced vital capacity in this study are significantly lowered. In our opinion, the significant decrease of these parameters gives evidence of the weakness of expiratory muscles. The studies monitoring respiratory dysfunctions in MS patients evaluate the weakness of expiratory muscles by means of maximal volitional minute ventilation or by means of maximal inspiratory and expiratory pressure.[11,12,33–35]

In comparison to the parameters evaluating pulmonary functions, the respiratory muscle function is impaired already in MS patients with the moderate neurological impairment. Maximal expiratory pressure is lowered already in outpatients, while maximal inspiratory pressure in wheelchair-bound or in bedridden patients.[12,34,35] The respiratory muscles weakness increases with the neurological impairment[11,12,33–35] and the duration of the disease.[34] This study proved that the decrease of expiratory flows occurs already in patients with a relatively mild neurological impairment, however, we did not succeed in proving a statistically significant dependency on the neurological impairment. It is also assumed that respiratory impairment in MS patients may aggravate fatigue.[11,12,35] However, this study did not confirm that lowered expiratory flows in MS patients could contribute to the development of fatigue.

Conclusion

There is a lot of practical information resulting from this cross-sectional study in MS patients.

First, the results concerning lowered physical condition of patients with mild neurological impairment show that deconditioning in multiple sclerosis is a serious problem, because it affects daily routine activities, social interaction and quality of life. These results point at the necessity to deal with multiple sclerosis more comprehensively and to include a regular, well-timed and controlled prevention of deconditioning into the treatment plan.

Secondly, the results concerning lower expiratory flows show that a respiratory dysfunction occurs already in MS patients with mild neurological impairment. Although, this dysfunction has not got any impact on clinical parameters examined in this study, we assume that there is necessary to influence it to prevent respiratory complications described in advanced stages of the disease.

Thirdly, the results concerning correlation between fatigue and handicap and quality of life emphasize the importance of influencing fatigue in patients with multiple sclerosis.

This study contributes to better understanding of physical fitness, respiratory function and fatigue in multiple sclerosis and could be a base for preparing a comprehensive program for people with multiple sclerosis. However, clinical implications from the results should be verified in further prospective research studies.

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