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Wpływ rehabilitacji oddechowej na nasilenie zmęczenia ocenianego według *Fatigue Severity Scale* u pacjentów z chorobą płuc

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Abstract

Introduction: Fatigue is a known symptom of advanced lung disease and impacts quality of life and psychological health. Many of these patients undergo pulmonary rehabilitation as part of their therapy. Understanding the effect of pulmonary rehabilitation on fatigue in these patients is important, as one may be able to design more focused rehabilitation programs.

The aim of this study is to evaluate the effect of pulmonary rehabilitation on fatigue as measured by the Fatigue Severity Scale (FSS) in patients with advanced lung disease.

Material and methods: Patients were enrolled in a standardized 6 week pulmonary rehabilitation program. They were asked to complete questionnaires to evaluate their self-reported fatigue (FSS), and depression as measured by Geriatric Depression Scale (GDS). The GDS is a self-reported assessment tool used to identify depression in patients. The FSS is a validated instrument that indicates a perception of fatigue that might require medical intervention. Participants completed questionnaires both at baseline and after completing the standardized pulmonary rehabilitation program. Data was analyzed in Statistical Analysis System (SAS). The change in FSS was evaluated using the Wilcoxon signed-rank test. P-values < 0.05 were considered statistically significant.

Results: 21 patients (12 females; 9 males; mean age 64.3 ± 11.2 yrs) were considered for the study. Pre-pulmonary rehabilitation FSS scores ranged from 1.6 to 6.7 (mean score of 4.6 ± 1.7). Post pulmonary rehabilitation FSS scores ranged 1.0 to 6.2 (mean score of 3.9 ± 1.6). The median pre-rehabilitation FSS was 5.3 (inter quartile range; Q1–Q3: 3.0–6.1), and median post rehabilitation FSS was 3.9 (inter quartile range; Q1–Q3: 2.6–5.1). There was a significant decrease in FSS scores after completing pulmonary rehabilitation program ($p < 0.0208$). There was a decrease in GDS (pre-rehabilitation, mean: 5.5 ± 3.6; post-rehabilitation, mean: 4.2 ± 2.9), but this decrease was not statistically significant. The change in GDS correlated with the change in FSS (Spearman Correlation Coefficient 0.525, $p < 0.0146$).

Conclusions: Patients with advanced lung disease reported a measurable component of fatigue. Participating in pulmonary rehabilitation resulted in significant improvement in patient's self-reported fatigue severity. Further studies are necessary to evaluate and design interventions to improve fatigue in in the setting of advanced lung disease.

Key words: pulmonary rehabilitation, fatigue, depression, screening tools, COPD, interstitial lung disease

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Streszczenie

Wstęp: Zmęczenie jest dobrze znanym objawem zaawansowanej choroby płuc. Ma ona znaczący wpływ na jakość życia i zdrowie psychiczne pacjenta, dlatego wielu pacjentów w ramach terapii przechodzi rehabilitację oddechową. Aby stworzyć nowe ukierunkowane programy rehabilitacyjne bardzo istotne jest zrozumienie wpływu rehabilitacji oddechowej na nasilenie duszności u tych chorych.

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Celem pracy jest ocena wpływu rehabilitacji oddechowej na nasilenie zmęczenia mierzonego za pomocą *Fatigue Severity Scale* (FSS) u pacjentów z zaawansowaną chorobą płuc.

Materiał i metody: Pacjenci zakwalifikowani do standardowego 6-tygodniowego programu rehabilitacyjnego byli proszeni o dokładne wypełnienie 2 ankiet przed rehabilitacją i po jej zakończeniu: ankiety FSS, która jest cennym narzędziem pozwalającym na ocenę zmęczenia pod kątem potrzeby interwencji medycznej, oraz ankiety *Geriatric Depression Scale* (GDS), która jest narzędziem używanym do oceny nasilenia depresji przez samych pacjentów. Dane przeanalizowano za pomocą programu Statistical Analysis System (SAS). Zmienne wartości FSS oceniono przy użyciu testu Wilcoxona dla par obserwacji. Wartości $p < 0{,}05$ uznano za istotne statystycznie.

Wyniki: Do badania włączono 21 pacjentów (12 kobiet i 9 mężczyzn, średnia wieku 64,3 ± 11,2 roku). Wyniki FSS przed rehabilitacją wynosiły od 1,6 do 6,7 (średni wynik na poziomie 4,6 ± 1,7), a po rehabilitacji od 1,0 do 6,2 (średni wynik na poziomie 3,9 ± 1,6). Mediana FSS przed rehabilitacją wynosiła 5,3 (przedział międzykwartylowy; Q1–Q3: 3,0–6,1), po rehabilitacji wyniosła 3,9 (przedział międzykwartylowy; Q1–Q3: 2,6–5,1). Wykazano istotnie statystycznie niższy wynik w FSS po zakończeniu programu rehabilitacji oddechowej ($p < 0{,}0208$; test Wilcoxona dla par obserwacji). Wykazano również niższy wynik w GDS po rehabilitacji, ale nie był on istotny statystycznie (średnia przed rehabilitacją: 5,5 ± 3,6; średnia po rehabilitacji: 4,2 ± 2,9). Zmiany w GDS korelowały ze zmianami w FSS (współczynnik korelacji rang Spearmana 0,525, $p < 0{,}0146$).

Wnioski: U chorych z zaawansowaną chorobą płuc nasilenie zmęczenia można przedstawić za pomocą mierzalnych danych. U pacjentów, którzy przeszli program rehabilitacji oddechowej, stwierdzono istotną poprawę w postaci zmniejszenia nasilenia zmęczenia. Potrzebne są dalsze badania, aby oceniać nowe metody leczenia, które pozwolą zmniejszyć dolegliwości towarzyszące zaawansowanym chorobom płuc.

Słowa kluczowe: rehabilitacja oddechowa, zmęczenie, depresja, narzędzia przesiewowe, POChP, choroby śródmiąższowe płuc

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Introduction

Fatigue is defined as extreme, persistent tiredness and mental, physical weakness or exhaustion [1]. It is a known symptom of advanced lung diseases that impacts quality of life and psychological health [2]. There is a general impression that features of fatigue manifest as underlying depression [3] however, each differ and may represent different aspects of underlying psychological impairment. Measurement of fatigue has been utilized in many neurological [4] and rheumatological [5] disorders but has yet to gain popularity in pulmonary medicine.

Patients with advanced lung disease such as chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD) and other debilitating pulmonary conditions face symptomatology consistent with oxygen deprivation, including dyspnea, cough, wheezing and exercise intolerance. These patients regularly undergo pulmonary rehabilitation as part of their therapy [2, 6]. Rational for using pulmonary rehabilitation as an adjuvant to pharmacotherapy is well established [7]. However, understanding the effects of pulmonary rehabilitation on fatigue in these patients is not well studied but is very important, as one may be able to design more structured rehabilitation programs targeting fatigue improvement as well as exercise capacity which set the basis for this study. We decided to study the effects of pulmonary rehabilitation on fatigue as measured by the Fatigue Severity Scale (FSS) in patients with advanced lung disease.

Pulmonary rehabilitation

The American Thoracic Society and the European Respiratory Society (ATS/ERS) have defined pulmonary rehabilitation (PR) as an "evidence based, multidisciplinary and comprehensive intervention for patient with chronic respiratory diseases who are symptomatic and often have decreased daily life activities" [7]. The principal purpose of PR programs is to improve function, disease related symptoms, optimize functional capacity and an overall improvement in quality of life (QoL). Pulmonary rehabilitation has become a staple of therapy in advanced lung disease including COPD [8], idiopathic pulmonary fibrosis [9] and pulmonary hypertension [10] amongst others. It is also well known that participation in a pulmonary rehabilitation program reduces the number of future exacerbations in COPD patients [11].

The PR program at our center is certified by the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) and is designed towards adult patients with chronic lung disease or patients preparing/recovering from lung surgery. The program consists of an exercise and education component with 3 sessions weekly over a period of 6–8 weeks. Following the completion of the 6–8 week program, maintenance sessions are also available for patients to participate. The rehab facility at our site is equipped with exercise equipment such as treadmill, upper/ /lower body recumbent stepper (NuStep® Inc., Ann Arbor MI USA), arm ergometers and free weights. In addition, safety equipments available include: ECG monitoring, pulse oximetry, blood pressure monitoring and supplemental oxygen. The education component consists of bi-weekly educational lecture series that comprise of breathing techniques along with stress and relaxation exercises. As part of our PR program all patients are asked to fill out quality of life, fatigue and sleep questionnaires before and after completion of the program.

Measuring fatigue and depression

As there is a general impression that features of fatigue manifest as underlying depression [3] it is important to define and quantitatively measure these two separate domains. To better understand and quantify fatigue severity many scales have been developed [12]. The most commonly used fatigue scale is the Fatigue Severity Scale (FSS) developed by Krupp et al. [4]. The FSS is a 9 question validated instrument that indicates a perception of fatigue that might require medical intervention [4] and is scored using a 7-point Likert scale where a score of 7 is associated with greater amounts of fatigue. The sum of responses is taken and divided by number of items for the scale score. The mean score for normal individuals on the FSS is 2.3 ± 0.7 [13].

In addition to fatigue, depression symptomatology was also evaluated using the Geriatric Depression Scale (GDS). The GDS short form is a self reported assessment tool which was used to identify depression in patients; a score greater than 5 is considered suggestive of depression [14, 15].

The GDS is a self-reported depression scale developed in 1982, specifically for the geriatric population (> 60 years) with time frame of "past week" [15]. It is used for screening depression in elderly population and therefore distinguishing dementia from depression in patients aged 65–85 [14]. Items in the scale address cognitive and affective domains while somatic domains are not addressed [14]. While the scale was originally developed as 30-item scale, the GDS has been modified (15 questions) and validated [16]. Both versions of the scale, GDS are answered in a "yes" or "no" fashion with 1 point assigned to items answered "yes" [14]. A GDS ≥ 11 is considered a sign for possible depression [14]. A 5 item GDS is also found to be equally effective as compared to 15 item GDS with a sensitivity of 0.94 and specificity of 0.81 respectively [16].

Material and methods

We conducted a retrospective review of data collected on 21 patients with diagnosis of advanced lung disease who participated in the North Shore — Long Island Jewish Health System PR program. For the purposes of the study, COPD and IPF were defined using the standards established by the American Thoracic Society [9, 17]. At the time of the enrollment in PR, all patients were clinically stable, and all were receiving optimal medical therapy. All participants completed fatigue and depression questionnaires both at baseline and after completing the standardized pulmonary rehabilitation program. Institutional Review Board approval was obtained. Data was analyzed using SAS (Cary, NC USA). The change in FSS was evaluated using the Wilcoxon signed-rank test. A p-value of ≤ 0.05 was considered statistically significant.

All patients underwent complete pulmonary function testing with body plethysmography (Care Fusion, Palm Springs, CA). From the spirometry tracing, FEV_1, FVC, and FEV_1/FVC were calculated according to American Thoracic Society recommendations [18]. The results were expressed as absolute values and as percentages of the predicted value [19]. In addition lung volumes and diffusion capacity of carbon monoxide (DLco) was conducted. Reference values used for spirometry were from National Health and Nutrition Examination Survey (NHANES) III and DLco was calculated using Burrows formula. As part of standard of care, patients with ILD/IPF underwent a six minute walk test (6MWT) in accordance with ATS guidelines [20].

Results

Twenty one patients (12 females; 9 males; mean age 64.5 ± 10.9 yrs: 15 COPD, 5 ILD/IPF, 1 other; Tab. 1) were considered for the study. For all patients oxygen saturation ranged between 88 and 98 percent. Out of 21 patients 5 were on oxygen therapy. Overall pulmonary function testing in COPD patients displayed a reduced FEV_1/FVC ratio (0.58 ± 0.15) and increased residual volume (3.09 ± 1.04; Tab. 2). Patients with ILD/IPF showed a characteristically reduced diffusion capacity (DLCO) (14.32 ± 7.22) and slightly reduced total lung capacity (64.8 ± 13.84; Tab. 3). Mean distance on 6MWT for these patients was 320 meters.

At baseline, pre-pulmonary rehabilitation FSS scores ranged from 1.6 to 6.7 [median score 5.3 25th percentile (Q1)–75th percentile (Q3): 3.0–6.1; mean score ± standard deviation: 4.6 ± 1.7] and post-rehabilitation FSS scores ranged 1.0 to 6.2 (median score 3.9; Q1–Q3: 2.6–5.1; mean score of 3.9 ± 1.6). The change in FSS score after pulmonary rehabilitation was statistically significant ($p < 0.0208$, Wilcoxon signed-rank test; Fig. 1). The COPD cohort had a pre-PR FSS score of 4.4 ± 1.7 and a post-PR FSS score of 4.1 ± 1.6 while the ILD/IPF cohort had a pre-PR FSS score of 5.0 ± 1.8 and a post-PR FSS score of 3.5 ± 1.8.

GDS scores at baseline, pre-rehabilitation showed a median score 4.0 (Q1–Q3: 3.0–9.0; mean 5.5 ± 3.6) and a post-rehabilitation the median score of 4.0 (Q1–Q3: 2.0–6.0; mean 4.2 ± 2.9). Though there was improvement, the change was not statistically significant ($p < 0.1492$, Wilcoxon signed-rank; Fig. 2). However, the change in GDS correlated with the change in FSS (Spearman Correlation Coefficient 0.525, $p < 0.0146$). The COPD cohort had a pre-PR GDS score of 5.5 ± 4.0 and a post-PR GDS score of 4.0 ± 3.2 while the ILD/IPF cohort had a pre-PR GDS score of 4.6 ± 2.5 and a post-PR GDS score of 4.6 ± 2.4.

Despite improvement in both fatigue and depression scores, improvement in 6MWT was not observed in these patients.

Table 1. Patients — demographics

	Diagnosis No (%)			
Sex	**COPD**	**ILD/IPF**	**Other**	**Total**
Male	5 (23.8)	3 (14.29)	1 (4.7)	9 (42.8)
Female	10 (47.6)	2 (9.52)	0 (0.0)	12 (57.4)
Total	15 (71.43)	5 (23.81)	1 (4.76)	21 (100.0)

Table 2. Pulmonary function testing results (means ± SD) of COPD patients (n = 15)

Spirometry	Reference	Actual measure	Predicted percent of reference
FVC (L)	3.11 ± 0.62	1.82 ± 0.60	58.2 ± 13.79
FEV_1 (L)	2.40 ± 0.46	1.09 ± 0.56	45.13 ± 20.2
FEV_1/FVC%	–	0.57 ± 0.15	–
FEF25–75% (L/sec)	2.30 ± 0.53	0.63 ± 0.46	28.93 ± 22.38
Lung volumes			
TLC (L)	5.32 ± 0.87	5.30 ± 1.67	96.86 ± 20.97
RV (L)	2.09 ± 0.27	3.09 ± 1.03	149.20 ± 52.93
Diffusing capacity			
DLCO [mL/mm Hg/mm]	22.45 ± 4.65	10.48 ± 5.07	46.33 ± 17.25

Table 3. Pulmonary function testing results (means ± SD) of ILD/IPF patients (n = 5)

Spirometry	Reference	Actual measure	Predicted percent of reference
FVC (L)	3.60 ± 1.35	2.98 ± 0.57	63.6 ± 14.77
FEV_1 (L)	2.87 ± 0.98	2.43 ± 0.32	66 ± 13.11
FEV_1/FVC (%)	–	0.82 ± 0.06	–
Lung volumes			
TLC (L)	5.65 ± 1.79	5.01 ± 0.47	64.8 ± 13.85
RV (L)	1.91 ± 0.53	1.79 ± 0.22	64.5 ± 20.14
Diffusing capacity			
DLCO [mL/mm Hg/mm]	27.0 ± 3.80	14.32 ± 7.22	41.25 ± 3.69

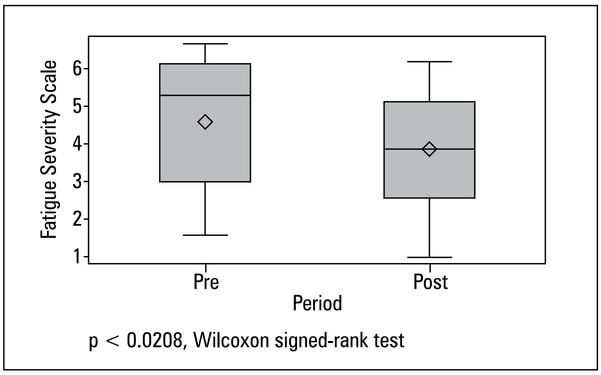

Figure 1. Effects of pulmonary rehabilitation on Fatigue Severity Scale

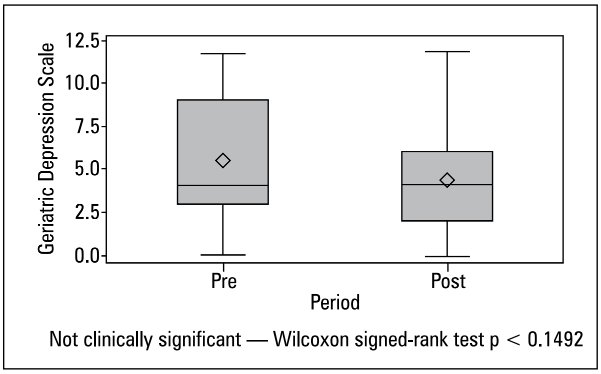

Figure 2. Effects of pulmonary rehabilitation on Geriatric Depression Scale

Discussion

Fatigue is defined as extreme, persistent tiredness and mental, physical weakness or exhaustion [1, 4, 5]. Although it has been studied in COPD [21, 22], there exists a paucity of data in other advanced diseases lung in general. Our retrospective study shows that in patients with severe lung disease there exists above normal levels of fatigue as measured by the FSS. In our study, in addition to fatigue a high GDS score was also common amongst these patients signifying presence of underlying depression. After participation in a structured PR program, not only did fatigue symptoms improve but there was a slight improvement in depression as well. The change in fatigue symptoms as per FSS after participation in PR was statistically significant ($p < 0.0208$, Wilcoxon signed-rank test). However, the change in depression symptoms as per GDS was not significant ($p < 0.1492$, Wilcoxon signed-rank test). This shows that the change in FSS symptoms after PR is independent of change in depression symptomatology. This observation was similar across both COPD and ILD/IPF groups.

Fatigue may be multifactorial in nature and is reported in many conditions such as deconditioning, depression, muscle weakness, obstructive sleep apnea, osteoporosis, cardiac manifestation and medications as well. These factors should be individually assessed and treated for as they might all contribute to a feeling of fatigue (Fig. 3).

Quantitative measurement of fatigue in other diseases has relied heavily on patient self reported fatigue questionnaires which used a 1–5 Likert scale system [23]. The Fatigue Severity Scale was originally described by Krupp et al. [4] and was studied in patients with multiple sclerosis and systemic lupus erythematosus (SLE). The FSS has been further validated [24] and has also been utilized in other diseases such as hepatitis C [25] and Parkinson's disease [26] where fatigue is one of the most commonly reported symptoms. Fatigue is routinely measured in COPD using the St. George's and Chronic Respiratory questionnaires [27], however the FSS scale has not been widely utilized. Fatigue in COPD has also been associated with reduced quality of life in moderate to severe disease using the Multidimensional Fatigue

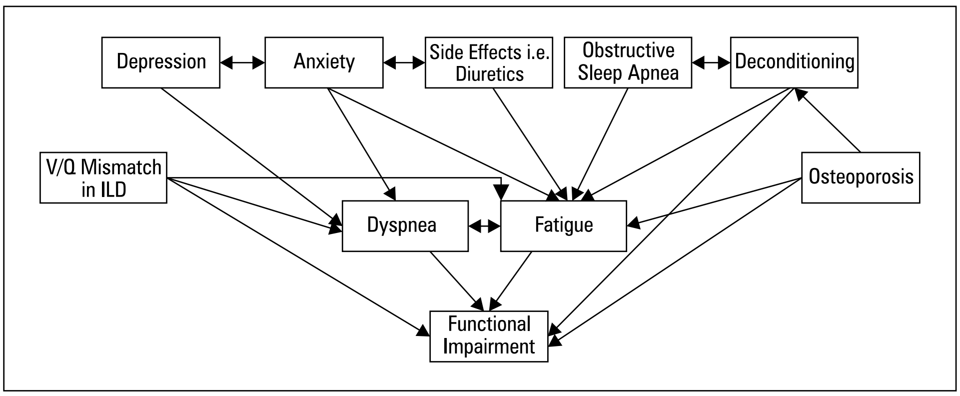

Figure 3. Multifactorial nature of fatigue

Inventory [28]. This is important to recognize as there exists a strong relationship between respiratory symptoms and fatigue [29]. Fatigue has been reported to have a strong, direct and negative effect on functional performance [30] and per se will affect physiologic tests such as a six-minute walk testing. To the best of our knowledge this is the first study to utilize the Fatigue Severity Scale to study fatigue across a multifaceted advanced lung disease population.

In addition, despite fatigue being one of the most commonly reported symptoms in ILD [31] there exists a paucity of data on self-reported fatigue. Patients with a diagnosis of ILD are often treated with pulmonary rehabilitation according to ATS guidelines [9]. Our study was able to demonstrate that PR improves fatigue in the ILD/IPF cohort as well.

Our study showed that patients that participate in a pulmonary rehabilitation program will experience improvement in their fatigue symptoms as well as depressive symptoms. We also believe that fatigue represents as an independent therapeutic endpoint measurement in the advanced lung disease patient population. This study lays the framework for understanding the relationship between fatigue and QoL. We do know that QoL is improved after patients participate in pulmonary rehabilitation [32]. If this effect is in part contributed by improvement in fatigue needs yet to be explained by further prospective studies.

Conclusions

Patients with advanced lung disease reported a measurable component of fatigue and participating in a pulmonary rehabilitation program resulted in significant improvement in the patients' self reported fatigue severity. Our results suggest that fatigue and depression are two different domains of psychosomatic impairment that can be objectively measured. Further prospective studies with a larger patient population are necessary to evaluate and design interventional programs to address fatigue as a possible therapeutic endpoint in the setting of advanced lung disease.

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Conflict of interest

The authors declare no conflict of interest.

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