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Evaluation of COPD progression based on spirometry and exercise capacity

Ocena progresji POChP na podstawie badania spirometrycznego i zdolności wysiłkowej

Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is characterized by an airflow limitation that is usually progressive. The progression of COPD expressed as the rate of an annual decline in FEV_1 is very heterogeneous. Exercise capacity in COPD patients is often diminished and becomes worsened over the time.
The purpose of the study was to examine how the change in FEV_1 and exercise capacity would deteriorate over long-term observation.
Material and methods: A total of 22 men with COPD were examined. At the beginning the average age was 59 $\pm$ 8.1 years and the mean post-bronchodilator FEV_1 was 52 $\pm$ 14.9% predicted. Pulmonary function testing was performed at entry and then each year for 10 years, and exercise testing on a cycle ergometer was performed at entry and after 10 years.
Results: FEV_1 and maximum oxygen uptake (VO_{2max}), maximum mechanical work (W_{max}), maximum minute ventilation (V_{Emax}) and maximum tidal volume (V_{Tmax}) declined significantly over the observation time. The mean annual decline in FEV_1 was 42 $\pm$ 37 mL, and the mean decline for VO_{2max} was 30 $\pm$ 15 mL/min/yr and 0.44 $\pm$ 0.25 mL/min/kg/yr. Regression analysis revealed that the changes in FEV_1 do not predict changes in VO_{2max}. We observed a correlation between the annual change in V_{Emax} and annual change in VO_{2max} ($r = 0.51$ $p < 0.05$). The baseline FEV_1 (expressed as a percentage of predicted and in absolute values) is the predictor of FEV_1 annual decline ($r = 0.74$ and 0.82; $p < 0.05$).
Conclusions: We observed over time deterioration in exercise capacity in COPD patients which is independent of decline in airflow limitation. The long term follow-up of exercise capacity is important in monitoring of COPD patients in addition to pulmonary function.

Key words: COPD, exercise capacity, COPD progression, annual FEV_1 decline

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Streszczenie

Wstęp: Przewlekła obturacyjna choroba płuc (POChP) charakteryzuje się trwałym ograniczeniem przepływu powietrza przez dolne drogi oddechowe, które zwykle postępuje. Tempo progresji POChP wyrażane wielkością rocznego ubytku natężonej objętości wydechowej pierwszosekundowej (FEV_1) jest bardzo zróżnicowane. Przewlekła obturacyjna choroba płuc powoduje zmniejszenie zdolności wysiłkowej, które zwykle pogłębia się w miarę upływu choroby.
Celem pracy była ocena progresji POChP na podstawie wielkości rocznego ubytku FEV_1 oraz zdolności wysiłkowej wyrażonej maksymalną konsumpcją tlenu (VO_{2max}) w okresie 10 lat obserwacji.
Materiał i metody: Grupę badaną stanowiło 22 mężczyzn chorych na POChP w wieku 59,4 $\pm$ 8,1 roku, u których wyjściowa wartość FEV_1 po leku rozszerzającym oskrzela wynosiła 52 $\pm$ 14,9%. Badania czynnościowe układu oddechowego były przeprowadzane na początku oraz co roku przez 10 lat. Badania wysiłkowe wykonano na początku i po 10 latach.
Wyniki: Wartość FEV_1 oraz wskaźniki uzyskane podczas badania wysiłkowego — maksymalne zużycie tlenu (VO_{2max}), maksymalna praca mechaniczna (W_{max}), maksymalna wentylacja minutowa (V_{Emax}) oraz maksymalna objętość oddechowa (V_{Tmax}) uległy istotnym zmianom po 10 latach: FEV_1 obniżyło się średnio o 42 $\pm$ 37 ml na rok, a średni ubytek VO_{2max} wynosił 30 $\pm$ 15 ml/min/rok

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i 0,44 ± 0,25 ml/min/kg/rok. Nie stwierdzono korelacji między rocznym ubytkiem FEV_1 i rocznym ubytkiem VO_{2max}. Wykazano dodatnią korelację między rocznym ubytkiem V_{Emax} i rocznym ubytkiem VO_{2max} ($r = 0,51$ $p < 0,05$). Wyjściowe FEV_1 (wyrażone jako % wartości należnej i w wartościach bezwzględnych) koreluje z rocznym ubytkiem FEV_1 ($r = 0,74$ i $0,82$; $p < 0,05$).
Wnioski: Progresja POChP określana wielkością utraty FEV_1 w ciągu roku wykazuje bardzo zróżnicowane tempo. Wraz z czasem trwania choroby dochodzi do obniżenia zdolności wysiłkowej wyrażanej VO_{2max} i jest to niezależne od tempa utraty FEV_1. Ocena progresji POChP może być zatem dokonywana nie tylko na podstawie badania czynnościowego układu oddechowego, ale także badań wysiłkowych.

Słowa kluczowe: POChP, zdolność wysiłkowa, progresja POChP

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by a permanent airflow limitation, which is usually progressive [1]. The progression of COPD expressed as the rate of annual decline in FEV_1 is very heterogeneous [2–4]. Factors that increase annual decline in FEV_1 are: cigarette smoking, advanced emphysematous changes, bronchial hyperresponsiveness and frequent exacerbations [2, 4–8]. The progression of COPD causes deterioration of efficiency of pulmonary ventilation and reduces exercise tolerance [9–11]. Thus far only a few publications have evaluated changes in exercise capacity over time, based on the 6-minute walk test (6MWT) [10, 11] or exercise testing with measurement of maximum oxygen consumption VO_{2max} [9].

Numerous research projects have reported relationship between spirometric indices at rest (FEV_1, VC, IC), the area under the curve MEFV (Aex) and exercise capacity in COPD patients [12–23]. We still know little about the influence respiratory impairment on exercise capacity in this group of patients during long-term observation.

The purpose of the study was to evaluate COPD progression based on the annual decline in FEV_1 and its influence on actual exercise capacity expressed as maximum oxygen consumption (VO_{2max}) during 10 years of observation.

Material and methods

The examined group consisted of 22 men with COPD, in accordance with criteria defined by the GOLD guidelines [24].

Criteria for including patients in the group were the following: cigarette smoking history of minimum 10 pack-years, spirometric criteria — FEV_1 %FVC < 0.7, and FEV_1 after salbutamol < 80% of lower limit of normal. The patients were examined in a stable period of the disease, without exacerbations over the preceding 6 weeks. At the moment of inclusion into the group and during observation the patients were diagnosed with any coexistent diseases, especially neoplastic or cardiovascular system diseases.

The research was conducted within standard diagnostics of COPD patients treated in the Pulmonary Outpatient Clinic SP CSK.

Pulmonary function tests were conducted at least 12h after discontinuation of inhalatory drug application, bronchodilator, and according to current guidelines for the performance of spirometry [25, 26]. Spirometry was performed before and 15 minutes after inhalation of 400 ug of salbutamol using MasterLab (Jaeger). Predicted values were defined with the help of a computer program based on the standards described by Quanjer [27].

Exercise tests were performed on a cycle ergometer the following day, according to the Wasserman protocol [28]. In accordance with the guidelines, at the beginning of the test there was a 3-minute resting registration preceding a 3-minute warm-up (pedalling without load), and then exercise (pedalling at a speed of 60 rotations per minute), with gradually increased load up to the appearance of symptoms preventing continuation of exercise or up to the moment of the appearance of objective signs ordering cessation of the exercise [29, 30].

Pulmonary function tests were conducted once a year for 10 years, and exercise tests were performed at the beginning of observation and then they were repeated after 10 years. During observation neither cardiovascular system nor neoplastic diseases appeared in the examined patients.

Statistical analysis was conducted with the aid of Statistica 10 software. Data analysis included calculations of mean values, standard deviation (SD) and range. Assuming a significant correlation coefficient $p < 0.05$, the Wilcoxon signed-rank test, Mann-Whitney U-test and Spearman rank correlation test were applied.

Table 1. Baseline characteristics of the 22 men with COPD

Characteristics	Mean	Range
Age	59.4 ± 8.1	46–72
FEV_1 [L]	1.55 ± 0.53	0.9–2.6
FEV_1 (%w.n.)	52 ± 14.9	28–79
VO_{2max} [mL/min/kg]	15.25 ± 5	8–27
VO_{2max} [L/min]	1.18 ± 0.4	0.5–2
W_{max} (W)	86.13 ± 31	30–150
V_{Emax} [L]	43.18 ± 17.24	24–91
V_{Tmax} [L]	1.46 ± 0.41	0.7–2.4
BMI	24.8 ± 3.5	21–33
MRC	1.54 ± 0.8	0–3

Table 2. Final characteristics of the 22 men with COPD

Characteristics	Mean	Range	P value
FEV_1 [L]	1.13 ± 0.33	0.9–2.6	< 0.05
FEV_1 (%w.n.)	41.5 ± 8.5	23–53	< 0.05
VO_{2max} [mL/min/kg]	10.8 ± 4.44	5–25	< 0.0001
VO_{2max} [mL/min]	0.89 ± 0.35	0.28–1.7	< 0.0001
W_{max}	62 ± 25	20–130	< 0.0001
V_{Emax}	43 ± 17.2	24–91	< 0.0001
V_{Tmax}	1.18 ± 0.36	0.63–2.2	0.0001
BMI	24.8 ± 4	20–34	NS
MRC	2 ± 0.7	1–3	< 0.0001

Results

At the start of the observation 22 men at the age of 59.4 ± 8.1 years participated in the research. There were 11 current and 11 former cigarette smokers at the age of 56.9 ± 7.7 years (46–69) and 61.9 ± 8.2 years (49–72), respectively. For the whole group the mean baseline post-bronchodilator FEV_1 was 52 ± 14.9% of predicted value.

Baseline FEV_1 in the group of former smokers was 49.45 ± 12.0 % of predicted value (28–65), and in the group of current smokers it was 54.54 ± 17.5% of predicted value (35–79). There was no significant difference in age (p = 0.1) or FEV_1 (p = 0.7) between the groups.

Baseline results for the whole groups are presented Table 1.

Volume of FEV_1, dyspnoea intensification according to MRC and the rates obtained during exercise test — maximum oxygen consumption (VO_{2max}), maximum mechanical work (W_{max}), maximum minute ventilation (V_{Emax}) and maximum tidal volume (V_{Tmax}) changed significantly after 10 years. Only BMI did not significantly change (Tab. 2). In the whole group, decline in FEV_1 was 42 ± 37 mL/yr (36–123 mL/yr). In 19 patients (86%) decline in FEV_1 of 51 ± 31 mL/yr (range 7–123 mL), on average, was noted, and in 3 patients (14%) an increase of 13 ± 6 mL/yr (range 8–21 mL/yr). In the group of former smokers decline in FEV_1 was 33 ± 23 mL/yr, and in the group of current smokers it was 51.4 ± 39 mL/yr. Dependence between baseline FEV_1 expressed both as an absolute value and as a percentage of predicted value, and an annual decline in FEV_1 was noted (correlation coefficient was 0.82 and 0.74 p < 0.05 respectively) (Fig. 1, 2).

A mean decline in VO_{2max} was 30 ± 15 mL/min/yr and 0.44 mL ± 0.25 mL/min/kg/yr.

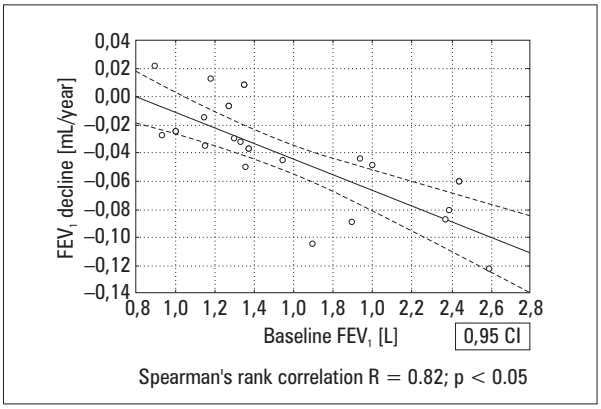


Figure 1. Annual decline of FEV_1 vs. baseline FEV_1 [L]

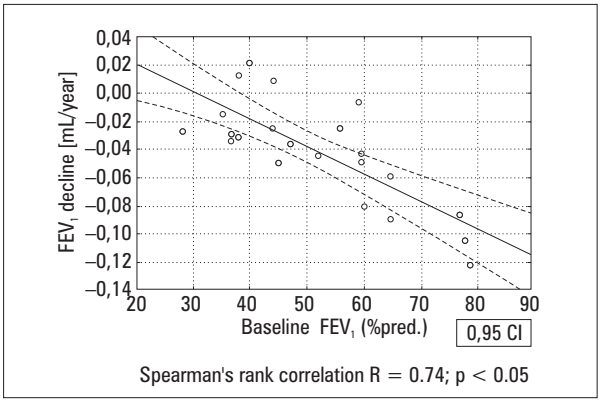


Figure 2. Annual decline of FEV_1 vs. baseline FEV_1 (%pred.)

In the group of current smokers VO_{2max} decreased by 30 ± 18 mL/yr and 0.47 ± 0.28 mL/min/kg/yr, whereas in the group of former smokers the decline in VO_{2max} was 28 mL ± 13 mL/min/yr and 0.41 ± 0.24 mL/min/kg/yr. There was no significant difference in the results between former and current smokers. Annual decline in V_{Emax} was 0.87 ± 1.16 L (1.8–3.2). The number of cigarettes smoked did

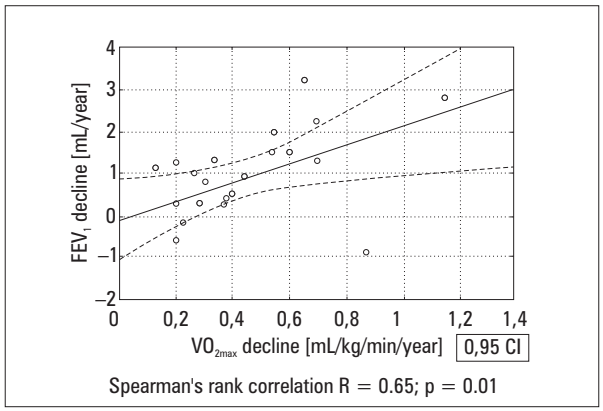


Figure 3. Annual decline of VE_{max} [L] vs. annual decline of VO_{2max} [mL/kg/min]

not influence the annual decline in FEV_1, VO_{2max} or V_{Emax}. Analysis of Spearman's rank correlation showed dependence between the annual decline in VO_{2max} and the annual decline in V_{Emax} ($r = 0.51$ $p < 0.05$) (Fig. 3). Correlations between the annual decline in FEV_1 and the annual decline in VO_{2max} or between the baseline FEV_1 and the annual decline in VO_{2max} were not noted.

Discussion

Numerous research projects that evaluated the annual decline in FEV_1 in COPD have proven that it fluctuates between 25 and 69 mL/yr [2, 4–6, 9, 31–34]. The annual decline concerning the examined patients was within these rates.

According to recent reports, COPD progression expressed as an annual decline in FEV_1 is very heterogeneous [2, 3, 4]. The research project ECLIPSE showed that after 3 years of observation of 2,000 patients with COPD, an annual decline in FEV_1 exceeded 40 mL/yr in 38% of patients. In 31% of the rest of the patients a decline in FEV_1 of between 21 and 40 mL was noted, and in 23% the change in FEV_1 was between a decline of 20 mL/yr and an increase of 20 mL/yr. The increase in FEV_1 of 20 mL/yr was discovered in 8% of patients [2].

Nishimura et al., after 5 years of observation of 279 patients with COPD, noted a group with more rapid annual decline in FEV_1 (rapid decliners, 63 mL/yr), with a slow rate (slow decliners, 31 mL/yr), and patients who maintained pulmonary function on a constant level (sustainers, 2 mL/yr) [4]. During our observation, despite the small group of patients, we also noted a heterogeneous rate of annual decline in FEV_1. During the 10-year observation a decline in FEV_1 of 51 ± 31 mL/yr (range 7–123 mL), on average, was noted in 19 patients (86%), and an increase of 13 ± 6 mL/yr (range 8–21 mL/yr) in 3 patients (14%). Although the definition of COPD assumes the worsening of lung function, which may be expressed as a decline in FEV_1, the present study and other reports [2, 3, 4] have proven that a significant decline in FEV_1 does not always occur in the course of COPD. According to Nishimura et al., a faster rate of an annual decline in FEV_1 occurs in patients with a greater intensification of emphysema [4]. Researchers suggest that it may also be explained by the occurrence of various phenotypes of COPD [2, 4, 35]. Cessation of cigarette smoking may also result in the improvement of ventilation parameters, which has been proven in research conducted on large groups of patients [2, 4–7]. Due to the small number of patients in the examined group, it is difficult to draw conclusions about the cause for such variability of FEV_1 and the cause for the increase in FEV_1. Nevertheless, the patients with an observed improvement of lung function, despite constant airway obstruction, had stopped smoking at the beginning of observation, which may be the cause for the observed increase in FEV_1.

Cigarette smoking is not only the main risk factor of COPD, but also it influences the progression rate expressed as a decline in FEV_1 [2, 6, 7, 31–33].

Our group consisted of men, including former and current cigarette smokers. The difference in an annual decline in FEV_1 between former and current cigarette smokers was not statistically significant, probably due to the small study groups.

In the mentioned ECLIPSE research the annual decline in FEV_1 was, on average, 21 mL/yr greater among cigarette smokers than among non-smokers, which is similar to the results of our study [2]. Furthermore, patients with positive bronchodilatatory test and patients with emphysema of the chest, seen in CT, had an annual decline in FEV_1 greater by 17 mL/yr and 13 mL/yr, respectively [2]. The Lung Health Study (LHS), after 5 years of observation, noted an annual decline in FEV_1 of 31 mL/yr in former cigarette smokers, and 62 mL/yr in current smokers [7].

The same research, after 11 years of observation of patients who ceased smoking at the beginning of the research, noted an annual decline in FEV_1 of 30.2 mL/yr in men and 21.5 mL in women. Current smokers had a significantly greater decline in FEV_1: 66 mL/yr in men and 54 mL/yr in women [6]. It should be emphasized that in the LHS the average age of patients was 48 years and that their COPD was at a mild stage of progression (mean FEV_1 78% of predicted value).

In the UPLIFT research project, which involved a group with moderate and advanced stages of the

disease, the average decline in FEV_1 during 4 years was 59ml/yr in smokers, and 33 mL/yr in non-smokers [32].

We showed that the number of cigarettes smoked did not influence the annual decline in FEV_1. Such dependence has not been discovered by Vestbo et al., either [2].

However, baseline airway obstruction influenced the decline in FEV_1. We discovered a dependence between annual decline in FEV_1 and baseline FEV_1, expressed both as an absolute value and as the percentage of the predicted value. The more advanced the stage of COPD, and consequently the smaller the FEV_1, the smaller was the annual decline in FEV_1. Similar dependence has been found in other research [2, 3, 10, 32, 34].

The ECLIPSE study noted the most serious decline in FEV_1 at GOLD 2 stage (35 mL/yr), and it was significantly more marked than at GOLD 3 stage (25 mL/yr) [2]. Casanova et al. also discovered a significantly greater decline in FEV_1 during the mild stage (112 mL/yr) than during the advanced stage (61 mL/yr) [3]. Another study conducted by the same author also noted a greater decline in FEV_1 at a mild stage of COPD than at an advanced stage (40 mL/yr and 10 mL/yr, respectively) [10].

Deterioration of exercise tolerance is one of the key symptoms of COPD.

The progression of the disease leads to a further impairment in exercise capacity, which was proved using the 6-minute walk test (6-MWT) [10, 11] or ergospirometric exercise test with assesment of maximum oxygen consumption (VO_{2max}) [9]. Our study proved a significant deterioration of exercise capacity expressed as a decrease in maximum oxygen consumption. A similar decline in VO_{2max} was noted by Oga et al. (32ml/min/yr and 0.5 mL/min/kg/yr) during a shorter, 5-year period of observation [9]. It seems that one limitation is the lack of a control group. According to universally applied norms for exercise tests, defined by Jones et al. [36] and according to the ATS/ACCP recommendations [30], the mean annual decline in VO_{2max} is 21 mL/min/yr, whereas in our group it was 30 mL/min/yr on average.

Since cigarette smoking influences the progression rate expressed as an annual decline in FEV_1, it seems probable that the rate of exercise capacity deterioration will also depend on smoking. Our observation showed that cigarette smoking and the number of the cigarettes smoked do not influence the annual decline in VO_{2max}. Due to the small number of subjects in the studied group and the lack of relevant reports, verification of these conclusions in a research project conducted on a larger number of patients is recommended.

We did not find any dependence between the annual decline in FEV_1 and that of VO_{2max}. The study carried out by Oga et al. showed a small correlation between decline in FEV_1 and VO_{2max} ($r = 0.05$ $p = 0.013$) [9]. Pino-Plata et al. did not note any dependence between exercise capacity assessed in 6MWT and annual decline in FEV_1, either [11]. Therefore, deterioration of exercise capacity assessed in a simple 6-minute walk test or exercise testing with determination of VO_{2max} is practically independent of the annual decline in FEV_1.

Moreover, we did not show that the degree of baseline obstruction influences the rate of deterioration of exercise capacity. Such dependence was also not noted by Oga et al., who, additionally, extended the analysis by other indexes — TLC, RV, FRC and DLco [9]. Thus, deterioration of exercise capacity cannot be predicted based on statistical parameters of lung function.

A positive correlation between annual decline in V_{Emax} and annual decline in VO_{2max}, which has been shown in the present study, suggests that the decrease in maximum exercise ventilation caused by disorders of breathing mechanics or by respiratory muscles dysfunction, significantly influences deterioration of exercise capacity during long-term observation.

Conclusions

COPD progression defined by decline in FEV_1 during one year has shown to be very heterogeneous. In the course of the disease, a decrease in exercise capacity expressed as VO_{2max} independent of decline in FEV_1 appears. Therefore, evaluation of the COPD progression may be performed based not only on pulmonary function testing (especially FEV_1), but also on exercise testing with determination of maximum oxygen consumption (VO_{2max}).

Conflict of interest

The authors declare no conflict of interest.

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