

THE INFLUENCE OF DEPRESSION, ANXIETY AND STRESS ON CHANGES IN LOCOMOTOR PARAMETERS IN PATIENTS WHO ARE PRONE TO DEVELOP COPD

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SUMMARY

Background: Depression and anxiety are the most prevalent diseases that contribute to global disability, especially if they are not early recognised and properly treated. They occur as part of many chronic diseases, often remain unrecognised at an early stage, and significantly contribute to the progression of the underlying disease reducing the quality of life in these patients. Numerous studies have shown that anxiety / depression and dyspnea are the leading symptoms in patients with COPD that are associated with high morbidity and mortality. The aim of this study was to determine the relationship between the degree of depression, anxiety and stress, using DASS- 21 scale, and changes in locomotor parameters in smokers who are prone to develop COPD.

Subjects and methods: The study included 164 patients, smokers and non-smokers, who underwent spirometry, 6-minute walk test and bicycle ergometer. They were all measured for body weight, height, waist circumference, pulse, blood pressure and each patient completed DASS-21, CAT and IPAQ questionnaire.

Results: The results of the IPAQ questionnaire indicated a statistically significant difference in the physical activity of smokers and non-smokers. A statistically significant was found between DASS-21 and patients physical activity ($p=0.0001$), 6-minute walk test ($r=-0.186$, $p=0.017$), VO2 max ($r=-0.220$, $p=0.005$) and weekly calorie consumption ($r=-0.222$, $p=0.004$).

Conclusion: According to the results of the study, an increased degree of anxiety, depression and stress is an important factor influencing changes in locomotor parameters in smokers who are prone to develop COPD.

Key words: depression – anxiety – stress – smoking - COPD

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INTRODUCTION

Smoking and chronic obstructive pulmonary disease (COPD) are in the focus of many studies in the past 20 years, not only as a disease that affects the lungs but also the whole body. COPD is a progressive disease and is considered the third world leading cause of death after heart disease, malignancy and accidents (Rana et al. 2020). It's a disease of unknown etiology but is pathogenetically associated with exposure to harmful particles of gases and fumes, primarily tobacco smoking. Secondhanded smoke, especially in the childhood or teenage age, can increase the risk of developing COPD (Atlanta 2014). The fact is that one of four Americans with COPD has never smoked cigarettes, while 38% of the nearly 16 million adults in the U.S. who have been diagnosed with COPD, stated they are smokers (Wheaton et al. 2017, Wheaton et al. 2013).

In the initial stage of COPD, the disease mostly remains unrecognized because the first symptoms appear when lung function falls below 55% of the reference values. Some of the first symptoms of the disease are cough, productive coughing and increased fatigue, wheezing, shortness of breath in exertion and tightness in the chest. As the disease progress, many

complications that limit the patient's daily activities occur, and ultimately lead to loss of ability to work as well as frequent need for hospital treatment.

The diagnosis of COPD is associated with comorbidities such as lung cancer, cardio and cerebrovascular diseases, diabetes, osteoporosis, dysfunctional myopathy, depression and anxiety but also many others which are strongly expressed in these patients (Berry & Wise 2010, McGarvey et al. 2007, Hill et al. 2008). The pathologies with greatest impact on the life expectancy of patient with COPD are cancers, atrial fibrillation, coronary heart disease and congestive heart failure, pulmonary fibrosis, diabetic neuropathy, but also with anxiety and depression (Divo et al. 2012, Yohanes 2005). A major public health concern is the high association of smoking with mental illness and it is believed that mental illness combined with smoking greatly contributes to reduced life expectancy (Fluharty et al. 2017). There is a lot of studies that report a positive association between smoking and mental illness emphasizing that in those patients the smoking rate has increased three times compared to the population without mental disorders (Farrell et al. 1998, de Leon & Diaz 2005). Some studies have provided evidence that smoking is associated with the development of depression and/or anxiety (Markou et al. 1998, Rose et al. 2001,

Weinberger et al. 2017). Some other studies provided connection between depression and anxiety and later smoking behaviour, suggesting that smoking in these patients alleviate symptoms of anxiety and depression (Weinberger et al. 2017, Boden et al. 2010). It is certainly a two-way direction in the approach to this issue.

The depression and anxiety are the most prevalent mental diseases that contribute to the global disability (Kessler et al. 2009, Andrews et al. 2001). The prevalence of depression in primary care is around 15% and 5% in the general population (Hansson et al. 2009). There is a lot of self-rating scales like Hospital Anxiety and Depression Scale (HADS), Primary Care Evaluation of Mental Disorders (PRIME-MD), Depression Anxiety Stress Scale-21 (DASS-21), Patient Health Questionnaire (PQH-9) and many others which proved to be relevant in screening for the dimensions of anxiety and depression (Bjelland et al. 2002, Spitzer et al. 1999, Osman et al. 2012, Lowe et al. 2004, Sinclair et al. 2012).

Since there is no treatment for COPD that could reduce the mortality from this chronically progressive disease, one of the preventive measures except smoking cessation is the early recognition and treatment of comorbidities that come with the disease and significantly affect the life expectancy of these patients. It is already known that depressed patients are more inclined to avoid physical activities and that COPD is a disease that affects also the musculoskeletal system, not just the lungs, and it is very likely that changes in these patients occur even before the diagnosis of COPD.

The aim of this study was to determine the relationship between the degree of depression, anxiety and stress, using the DASS-21 scale (Sinclair et al. 2012), and changes in locomotor parameters in smokers who are prone to develop COPD.

SUBJECTS AND METHODS

This study was conducted on patients who underwent medical rehabilitation or medically programmed vacation in the Special Hospital for Medical Rehabilitation Daruvarske toplice, Croatia, in the period of two years, as a part of another large study involving changes in locomotor parameters in smokers as an early predictor of COPD. The sample included 164 patients, 81 smokers and 83 non-smokers, aged 40-65 years. The patients approached the study after reading and signing informed consent. All patients underwent spirometry and those with a FEV1 / FVC ratio less than 0.70 (forced expiratory volume in 1st second / forced vital capacity), or with a diagnosis of COPD were excluded from study.

The excluding criteria for this study were also inflammatory rheumatic diseases, malignant diseases, acute or severe heart and lung diseases, unregulated arterial hypertension, major surgery in the last year or implanted hip, knee or ankle partial or total prosthesis. All patients

were measured for body weight and height, waist circumference, pulse, oxygen saturation (SpO₂) and blood pressure. The patient's cardiorespiratory and muscular ability was tested using 6-minute walk test (Przybyłowski et al. 2015) and a 'Lifecycle 97C' bicycle ergometer ride for 5 minutes. We recorded values in meters during 6-minute walk test and the value of maximum oxygen uptake (VO₂ max ml/kg/min) after a bicycle ride. Patients were, on 2 occasions, tested for muscle strength on an isokinetic device, but this is not the topic of this paper. Each patient completed a CAT questionnaire (COPD Assessment Test) (Jones et al. 2009), a DASS-21 questionnaire (Depression Anxiety Stress Scale Test) and an IPAQ questionnaire (International Physical Activity Questionnaire) (Craig et al. 2003) on the basis of which the weekly consumption of kilocalories and intensity of physical activity were calculated. Physical activity is divided into 3 groups according to intensity: low, moderate and high (Ainsworth et al. 2006).

Statistical analysis

Statistical analysis as performed using SAS System software package (SAS Institute Inc., North Carolina, USA). Descriptive statistics were made. Numerical data are shown by arithmetic mean and standard deviation if they follow a normal distribution or median and interquartile range (IQR) in the case of a distribution that is not normal. The normality of the distribution of numerical variables was tested by the Shapiro-Wilk test. The relationships between the two numerical variables were tested using Spearman's correlation coefficient. The differences of the normally distributed numerical variables between the two independent groups were tested by the Student's t-test and in case of deviation from the normal distribution the Wilcoxon Rank Sum test was applied. Variables for inclusion in the multivariate regression model were identified. All those that had a statistically significant effect on the dependent variable in the univariate analysis were included as independent variables, while insignificant variables were omitted from the regression model. Multicollinearity among the variables was examined by reviewing the correlation matrix and the suitability of the model was analyzed using the coefficient of determination (R²). P-values less than or equal to 0.05 were considered statistically significant.

Ethical Statement

We declare that this research was executed in accordance with the ethical principles, the Declaration of Helsinki and the Health Care Act of the Republic of Croatia (NN 169/04). The research was approved by the Ethics Committee of the University of J. J. Strossmayer in Osijek of the Faculty of Medicine Osijek and the Ethics Committee of the Special Hospital for Medical Rehabilitation Daruvarske toplice.

Table 1. Characteristics of smokers and non-smokers

	Smokers (n=81) Median (IQR) or n (%)	Non-smokers (n=83) Median (IQR) or n (%)	P*
Age (years)	53.0 (7.0)	54.0 (8.0)	0.17
Gender (female / male)	17 (21) / 64 (79)	6 (7) / 77 (93)	0.01
Height (cm)	178.0 (10.0)	180.0 (10.0)	0.04
Weight (kg)	92.0 (25.2)	89.3 (17.1)	0.67
BMI (kg/m ²)	29.0 (5.9)	27.6 (3.3)	0.09
Waist circumference (cm)	96.0 (18.0)	97.0 (12.0)	0.94

Note: Numeric data are presented as median (interquartile range), and categorical as N and ratio (%); IQR = Interquartile range; BMI = Body mass indeks; * Mann-Whitney U test for continuous, and chi-square test for categorical variables

Table 2. Comparison of cardiovascular and respiratory parameters between smokers and non-smokers

	Smokers (n=81) Median (IQR)	Non-smokers (n=83) Median (IQR)	P*
Heart rate (bpm)	76.0 (16.0)	78.0 (14.0)	0.39
Oxygen saturation (%)	97.0 (2.0)	97.0 (2.0)	0.81
Systolic pressure (mmHg)	130.0 (20.0)	130.0 (20.0)	0.67
Diastolic pressure (mmHg)	80.0 (15.0)	80.0 (10.0)	0.89
VO2 max (ml/kg/min)	34.0 (7.5)	38.1 (6.4)	<0.001
6-minute walk test (m)	665.0 (82.0)	676.0 (104.0)	0.22
FEV1/FVC	0.998 (0.157)	1.010 (0.165)	0.45

IQR = Interquartile range; bpm = beats per minute; VO2 max = maximum oxygen uptake after a bicycle ride; FEV1/FVC = ratio of forced expiratory volume in 1st second and forced vital capacity; * independent samples t-test for parametric and Mann-Whitney U test for non-parametric data distribution

RESULTS

The sample included 164 patients, 81 (49.4%) smokers and 83 (50.6 %) non-smokers. The two groups differed in distribution according to gender, and patients within the non-smoking group were slightly higher, but the groups did not differ according to BMI. Demographic characteristics of patients with regards to smoking, are shown in Table 1.

There were no differences in cardiovascular functions regarding to smoking, while VO2 max was significantly higher in non-smokers compared to smokers, as shown in Table 2.

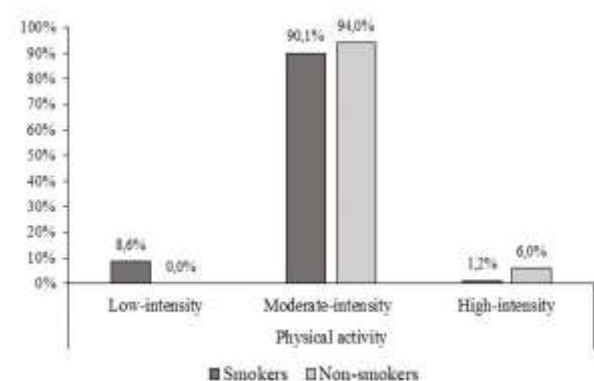


Figure 1. Comparison of the intensity of physical activity (measured with IPAQ) between smokers and non-smokers

Analysis of kilocalories expended on physical activity in the past 7 days indicated a generally higher physical activity of non-smokers compared to smokers. The median kcal consumed was 2335.0 for non-smokers (IQR=937.0) and for smokers 1894.0 (IQR=1376.0) (p=0.001).

The results of the IPAQ questionnaire indicated a statistically significant difference in the physical activity of smokers and non-smokers as shown in Figure 1.

CAT values were generally higher in the group of smokers compared to non-smokers with the median values of 8.0 (IQR=6.0) and 4.0 (IQR=4), p<0.001, respectively.

The median DASS-21 value in the set of all patients was 12.0 (IQR=9.0). The distribution of DASS-21 values did not differ statistically significantly between smokers and non-smokers, 11.0 (IQR=7.0) and 13.0 (IQR=10.0), p=0.278, respectively. Statistically significantly higher values of DASS-21 were recorded in women compared to men, 17.0 (IQR=12.0) and 11.0 (IQR=7.0), (p=0.006), respectively. There was a significant association between DASS-21 values and patient physical activity measured by the IPAQ questionnaire (p=0.001). Significant differences were observed in DASS-21 with respect to the level of physical activity. The median DASS-21 of 15.0 (IQR=6.0), 12.0 (IQR=9.0) and 4.0 (IQR=2.0) was measured in patients with low, moderate and high levels of physical activity, respectively (p=0.001).

DASS-21 values were positively correlated with CAT values ($r=0.503$; $p<0.001$), as well as with the patient's age, ($r=0.271$; $p=0.001$). A statistically significant negative correlation was observed between DASS-21 and 6-minute walk test ($r=-0.186$, $p=0.017$), VO₂ max ($r=-0.220$, $p=0.005$) and weekly kilocalories consumption ($r=-0.222$, $p=0.004$).

The multivariate linear regression model examined the combined effect of variables that proved to be statistically significantly related to the DASS index according to the results of univariate analysis. Those variables were age, 6-minute walk test, breathing index, VO₂ max, CAT, and weekly calories burned. Not all variables were kept in the regression analysis, since some did not have a significant effect in the multivariate model. The results of the regression model indicate the expected increase in DASS-21 by 0.827 for a unit increase in CAT, taking into account the constant values of other variables in the model. For a single increase in patient age, the expected increase in DASS-21 is 0.227. Compared to women, the expected value of DASS-21 is lower by 3,917 in male patients. DASS-21 values are shown as summed, not finally multiplied by two as their final result is generally shown.

DISCUSSION

Numerous studies have shown that anxiety/depression and dyspnea are the leading symptoms in patients with COPD that are associated with high morbidity and mortality (Yohannes et al. 2017). Early recognition, not only of the initial symptoms of the disease in smokers prone to develop COPD, but also of the symptoms of comorbidity associated with COPD, is of extreme importance. It was confirmed that smokers, despite normal lung function measured by spirometry, had reduced the conditional capacity and the VO₂ max. The reduced physical activity and consequently reduced weekly consumption of kilocalories according to the IPAQ questionnaire which was observed in smokers, also support the previous statement. These findings could support the later development of skeletal muscle weakness in COPD patients which, according to these results, could be assumed to begin earlier than measurement of pulmonary function tests can prove an impaired lung function. The impaired lung function has been so far considered the most important factor that limits the patient's physical activity and leads to muscle weakness. Although no statistically significant difference was found in DASS-21 values between smokers and non-smokers, patients with lower levels of physical activity according to IPAQ, which turned out to be smokers, had a higher degree of depression, anxiety and stress according to DASS-21. It can be concluded that a higher degree of anxiety and depression leads to a decrease in physical activity, which ultimately leads to a skeletal

muscle weakness. A positive correlation between DASS-21 and CAT favours an increased degree of depression, anxiety and stress in patients with symptoms that are among the initial symptoms of COPD. Lower fitness status (VO₂ max) and poorer results of the 6-minute walk test were observed in patients with higher DASS-21 values which also leads us to the conclusion of more pronounced muscle weakness in patients with higher levels of depression, anxiety and stress. According to previous research, a slightly higher degree of mental disorders has been reported in women and the elderly.

Results of this study have shown that a higher degree of depression, anxiety and stress is one of the causes of reduced physical activity which ultimately leads, not only to decreased muscle mass, but also to changes in locomotor parameters in smokers prone to develop COPD. The lack of this study is that Questionary DASS-21 was not analyzed separately for depression, anxiety and stress, but the results were presented as a total score.

CONCLUSION

According to the results of the study, an increased degree of anxiety, depression and stress is an important factor influencing changes in locomotor parameters in smokers who are prone to develop COPD. Given that anxiety and depression are associated with higher mortality in patients with COPD, it is extremely important to detect the initial symptoms of these mental states and illnesses, treat them and improve work ability and quality of life not only in patients with COPD but also in smokers who are prone to develop this disease.

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Contribution of individual authors:

Goranka Radmilović – main author, research conductor, study design, literature search and analysis, data interpretation, manuscript writing.

Sanja Popović-Grle – study design, literature search and analysis, manuscript writing.

Valentina Matijević – literature search and analysis, data interpretation.

Nenad Nešković – statistical analysis, manuscript writing.

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