International Journal of Medical and Health Research
ISSN: 2454-9142, Impact Factor: RJIF 5.54
www.medicalsciencejournal.com
Volume 2; Issue 9; September 2016; Page No. 89-95

Prevalence of acute exacerbation of chronic obstructive pulmonary disease in family medicine health center Modriča

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Abstract
Chronic Obstructive Pulmonary Disease is a leading, but not enough acqnowledged cause of morbidity and mortality worldwide. Today this disease is the fourth leading cause of death in adults, and the World Health Organization predicts that by 2020, to become the third the most common cause of death worldwide.
The aim of this study was to investigate the frequency of exacerbations in patients with chronic obstructive pulmonary disease in relation to sex, age, smoking status, disease severity, and present comorbidities and quality of life of patients.
The study included 120 patients registered in 4 teams of family medicine at the Public Health Institution Health Center in Modriča, where the disease is diagnosed based on GOLD criteria. Respondents are selected randomly. Data were collected by using a questionnaire created for the purpose of research and CAT questionnaire to assess the quality of life of patients. The study was conducted prospectively, during the six-month period from December 10th 2014 to June 10th 2015.

Keywords: chronic obstructive pulmonary disease, acute exacerbations, frequency, quality of life

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is characterized by airflow limitation through the airways, which is not fully reversible, it is usually progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. It occurs after many years of exposure to harmful agents. The main cause of the disease is smoking, and other risk factors include air pollution, indoors or outdoors, occupational exposure to dust or chemicals, congenital deficiency of alpha-1-antitrypsin deficiency, frequent infections of the lower part of the respiratory tract in childhood and socioeconomic status [1].
Today the disease is the fourth leading cause of death in adults, but the WHO predicts that by 2020 Chronic obstructive pulmonary disease will become the third most common cause of death worldwide [2]. The prevalence of moderate and severe disease in adults over 40 years of age is about 10.1% and is higher in men (11.8%) than women (8.5%) [3].
The clinical course of the disease is characterized by periods of stable condition and exacerbation periods. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines an acute exacerbation of the disease as an event in the natural course of the disease which is characterized by changing of the degree of dyspnea, cough and phlegm production, and/or daily variability in relation to the patient's baseline condition. It has an acute onset and may require changes in the regular medical therapy [1]. Another widely accepted definition of this disease given by Anthonisen and colleagues involves the presence of three clinical criteria: worsening of dyspnea, increase in volume and an increase in phlegm production. Based on these criteria exacerbations can be divided into three types (Table 1) [4].

Table 1: Anthonisen- this classification of AE - COPD

Type I (severe)	Type II (Moderate)	Type III (mild)
All three symptoms present (increased dyspnea and phlegm production)	Presence of any of the two symptoms	One of these symptoms plus one of the following: - Upper respiratory tract infections in the past 5 days - Enhanced wheezing - Enhanced cough - The temperature of the unknown cause - An increase in respiratory rate by 20% - Tachycardia

Acute exacerbations are usually caused by a viral or bacterial infection, air pollution or low temperatures. It is estimated that about 50-60% of exacerbations are caused by respiratory infections, 10% of air pollution, and 30% are of unknown origin. The major bacterial cause are Haemophilus influenzae, Streptococcus pneumoniae, Haemophilus parainfluenzae, and Moraxella catarrhalis as well as the atypical bacteria Mycoplasma pneumoniae and Chlamydia pneumoniae. Pseudomonas aeruginosa is frequently isolated in patients with very severe disease. Bacterial colonization of the lower

respiratory tract includes about 20-30% of the patients with this disease during clinically stable state. Viral respiratory tract infections are a common cause of exacerbations and are frequent during the winter months. The most common viral cause of acute exacerbations are influenzae virus, rhinovirus and respiratory syncytial virus, and rarely parainfluenzae viruses, adenoviruses, picornaviruses, coronaviruses, and human metapneumovirus [5].

Acute exacerbations of COPD are responsible for about 14 million outpatient visits and 500 000 hospitalizations in the US annually. Patients with COPD have in average of 1-3 acute exacerbations annually. Several studies have shown that approximately 50% of these exacerbations are not reported to doctors, which further complicates the treatment. From reported exacerbations 3-16% requires hospitalization and hospital mortality ranges from 3-10% in heavy patients.

Mortality after 6 months, 1 year and 2 years after hospitalization is 13.4%, 22% and 35.6%. Hospital mortality after admission to the intensive care unit is 15-24%, and in patients older than 65 years to 30%. Half of the patients who were hospitalized require rehospitalization within the next 6 months. In only 75% of patients, peak expiratory flow (PEF) returns to the previous level of 35 days after an exacerbation, and in 7% of patients will not be returned to basal levels of lung function not even 91 days after exacerbation [6]. The frequency of exacerbations increases with age, severity of the disease and chronic hypersecretion of mucus. Associated diseases such as ischemic heart disease, congestive heart failure or diabetes mellitus increase the risk of severe exacerbations which require hospitalization [7]. Frequent exacerbations reduce patient's quality of life, lead to rapid deterioration of lung function and increase mortality of patients, as well as an increase in use of health resources and increase in costs of treatment. Patients with frequent exacerbations have significantly greater drop in forced expiratory volume in 1 sec (FEV1) of 40 mL per year, and the decline in peak expiratory flow (PEF) of 2.9 L / min per year, in comparison to patients with less frequent exacerbations in which the reduction in FEV1 is 32 / mL per year and peak expiratory flow (PEF) 0.7 L / min per year [8, 11]. It is considered that the success of the treatment of this disease, and particularly preservation of lung function in patients largly depends on the speed and quality of care of acute exacerbations [12].

2. Materials and methods

The prospective study included 120 patients with chronic obstructive pulmonary disease, registered in the 4 teams of family medicine at the Health Center Modriča, to whom the disease is diagnosed based on GOLD criteria. All patients were previously examined by pneumophtisiologist and treated according to the GOLD guidelines. Respondents were selected randomly and surveyed in the six-months period from December 10th 2014 to June 10th 2015. Data were collected by using a questionnaire created for research purposes, and the CAT questionnaire to assess the quality of life of patients with this disease. CAT questionnaire was completed by the patients in a stable phase of the disease. This questionnaire is simple, validated questionnaire which consists of eight simple questions that provide the best framework concept description of the disease. Each question qualifies impact of the disease on the quality of life of the patient based on the semantic scale from zero to five. The values on this scale circles the patient for each of the following eight questions. The values of the obtained results range from zero to forty. The lowest score corresponds to the best, the highest to the worst quality of life. Acute exacerbations of the disease were recorded during the patient's visits to the doctor. The subjects were divided into two groups depending on whether or not they had an acute exacerbations during the monitored period. The research results are presented in tables and graphs.

3. Results

The study included 120 patients with a COPD, and 46 (38.33%) patients had an acute exacerbation during the six-month monitoring (Figure 1).

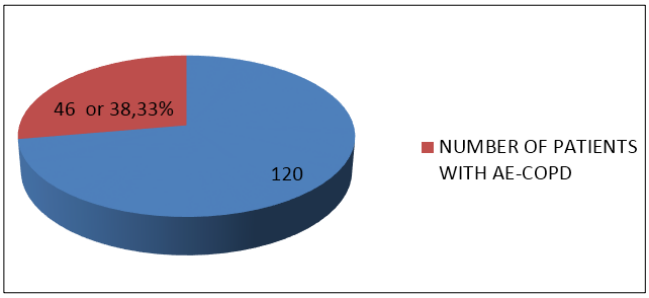


Fig 1: Number of patients with AE-COPD compared to the total number of patients with COPD

In the study of 46 patients with Acute Exacerbations of COPD, 35 (76.09%) of patients had an exacerbation, and 11 (23.91%) of patients had 2 Acute Exacerbations (Figure 2).

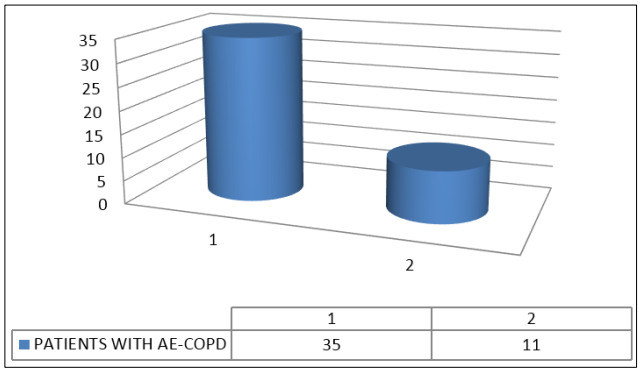
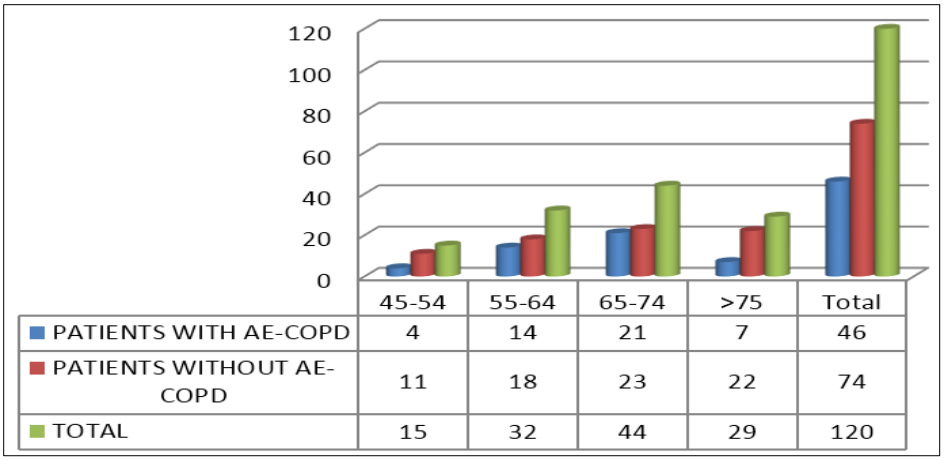


Fig 2: Distribution of patients with AE-COPD according to the number of exacerbations

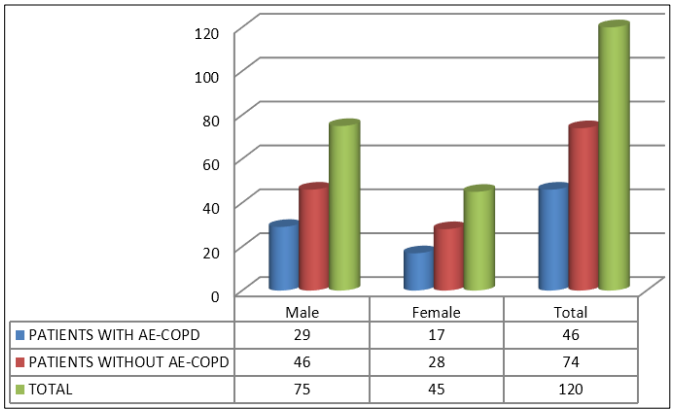
Acute exacerbations of COPD were the most represented in the age group of 55-64 and 65-74 year old, where 43.75%, that is 47.73% of patients had exacerbations. At the age of 45-54 year old exacerbations had 26.67% of patients, and older than 75 24.14% (Figure 3).



	45-54	55-64	65-74	>75	Total
PATIENTS WITH AE-COPD	4	14	21	7	46
PATIENTS WITHOUT AE-COPD	11	18	23	22	74
TOTAL	15	32	44	29	120

Fig 3: Age structure of patients with and without COPD Acute Exacerbations

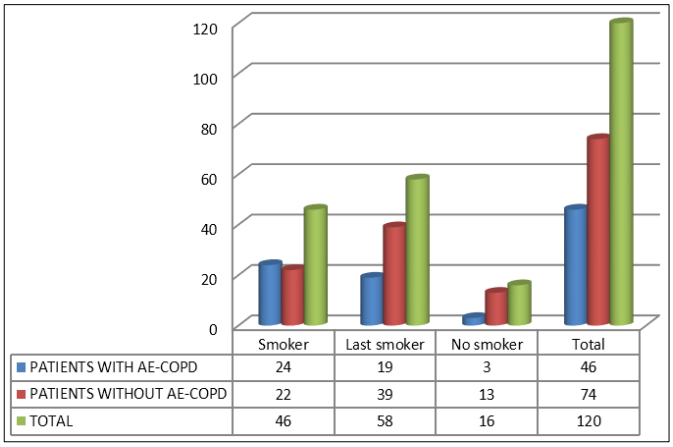
The study comprised 75 (62.5%) male patients and 45 (37.5%) of female patients. Acute exacerbations of COPD were slightly more prevalent in men 38.67%, than in women 37.78% (Figure 4).



	Male	Female	Total
PATIENTS WITH AE-COPD	29	17	46
PATIENTS WITHOUT AE-COPD	46	28	74
TOTAL	75	45	120

Fig 4: Full structure of patients with and without A cute exacerbations of COPD

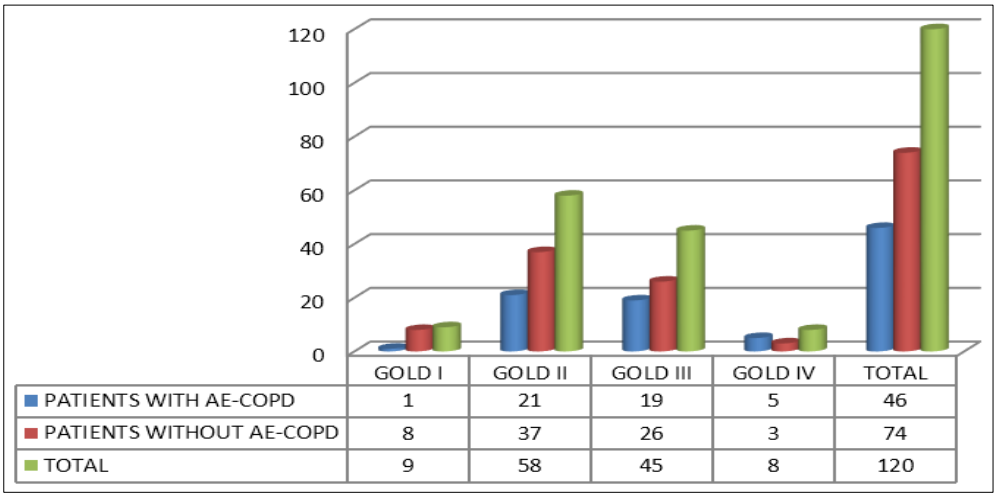
From a total of 120 patients included in the study 46 (38.33%) patients were smokers, 58 (48.33%) former smokers and 16 (13.33%) non-smokers. Exacerbations were the most common in smokers (52.17%), followed by former smokers (32.76%), and least represented in non-smokers (18.75%) (Figure 5).



	Smoker	Last smoker	No smoker	Total
PATIENTS WITH AE-COPD	24	19	3	46
PATIENTS WITHOUT AE-COPD	22	39	13	74
TOTAL	46	58	16	120

Fig 5: Smoking status of patients with and without AE-COPD

The frequency of acute exacerbation of COPD was the greatest in patients with the most severe obstruction by the GOLD classification even 62.5%, followed by the patients in the third degree of obstructive ventilation disorder 42.22%. Large frequency was determined in patients in the second degree of obstruction in 36.21% and the lowest in patients with the first degree obstruction in 11.11% (Figure 6).



	GOLD I	GOLD II	GOLD III	GOLD IV	TOTAL
PATIENTS WITH AE-COPD	1	21	19	5	46
PATIENTS WITHOUT AE-COPD	8	37	26	3	74
TOTAL	9	58	45	8	120

Fig 6: Distribution of patients with and without AE-COPD according to the GOLD classification

The minimum frequency of exacerbations was recorded in patients who did not have comorbidities 21.43%. A higher frequency was found in patients with one or two comorbidities 38.46%, that is 40.74%. The highest frequency of exacerbations had the patients with 3 or 4 comorbidities 41,67% that is 43,75% (Figure 7).

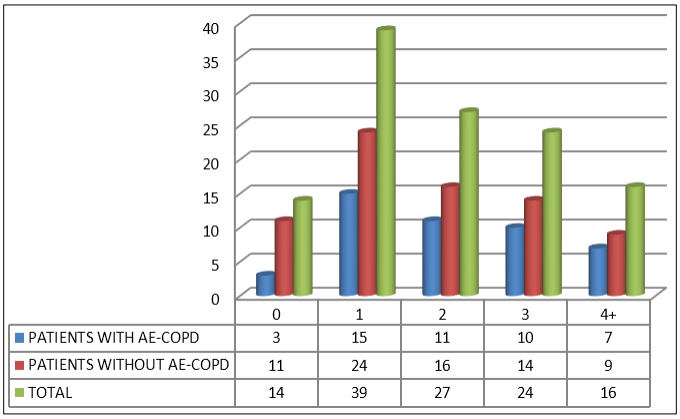


Fig 7: Number of comorbidities in patients with and without AE-COPD

From comorbidity in patients with COPD the most frequent was arterial hypertension in 55.83%, followed by GERD or ulcer disease in 31.67%, rheumatic fever in 28.33% and anxiety/depression in 26,67%. Substantially diabetes mellitus in 15%, ischemic heart disease in 14,17%, cardiac arrhythmias in 14,17% and heart failure in 12.5% were represented (Figure 8).

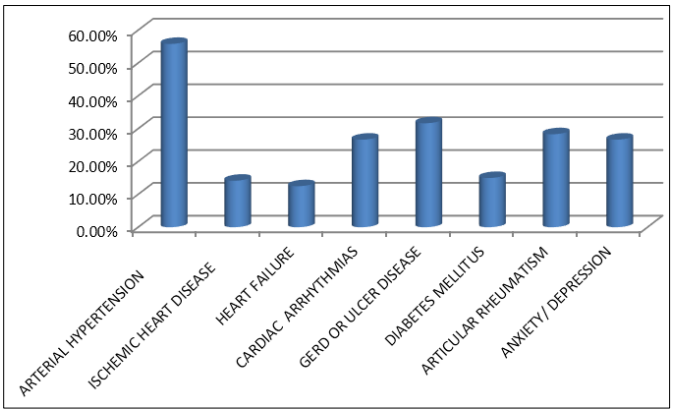


Fig 8: Display of he most common comorbidities in patients with COPD

The majority of patients 61.67% had the CAT score <10 (the small impact of the disease on the quality of life), 30.83% of patients had a CAT score between 10-20 (moderate impact on the quality of life), and the smallest number of patients 7,5 % had the CAT score over 20 (the major impact on the quality of life) (Figure 9).

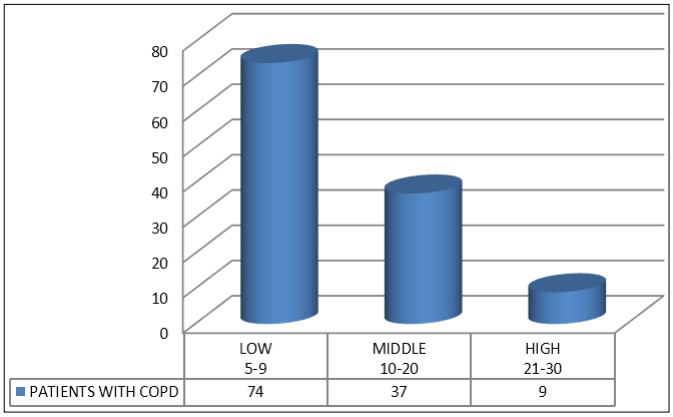


Fig 9: Cat score in patients with COPD

4. Discussion

The majority of previous studies have examined the frequency and natural course of acute exacerbations of COPD in patients treated at the secondary and tertiary health care. Limited data exist about the frequency of these exacerbations in patients in primary health care. In our study, the frequency of acute exacerbations of COPD in patients with chronic obstructive pulmonary disease was 38.33%, which is similar to the results of the study conducted in the Netherlands [13].

During the six-month monitoring there were 57 episodes in total, during which 35 (76.09%) patients had one, and 11 (23.91%) 2 acute exacerbations. According to the frequency of acute exacerbations of the disease patients can be divided into those who have rare (0-1 per year) and those who have frequent exacerbations (2 or more per year). Considering that there are significant differences in the frequency of exacerbations in patients with a similar degree of severity of the disease, it is considered that there are two different phenotypes which classify patients in two categories previously mentioned. More frequent exacerbations lead to more rapid loss of lung function and reduce the patient's quality of life [14, 15].

The study included 75(62.5%) men and 45(37.5%) women with chronic obstructive pulmonary disease, and acute exacerbations of COPD were almost equally represented in both sexes at 38.67% of men and 37,78% of women. In contrast to our study, a retrospective study conducted in England showed a higher frequency of acute exacerbations in women. [16]. The results of several studies suggest that women with COPD are at greater risk of loss of lung function caused by smoking, exhibit severe dyspnea and have poorer quality of life than men. Also, the non-smokers with COPD are more often women [17].

The frequency of acute exacerbations COPD was in correlation with age. So the highest percentage of AE- COPD is registered in patients aged 65-74 years of age 47.73%, followed by the age group 55-64 years of age in 43,75%. In the age group 45-54 years, exacerbations had 26.67% of patients. Smaller percentage of exacerbations (24.14%) was recorded in the oldest group of respondents, over 75 years of age, it is probably due to the increased number of visits to doctors because of comorbidities, especially cardiovascular disease, rather than reduced number of exacerbations of COPD in this age. Studies have confirmed that aging is a risk factor for COPD and frequent exacerbations of the disease [18].

Our study showed that the AE-COPD were the most represented among smokers (52.17%), followed by former smokers (32.76%), but they are also identified in the group of non-smokers (18.75%). It is well known that smoking is a major risk factor for COPD and for more frequent exacerbations. However, it is considered that the prevalence, clinical features, including the severity of the disease, as well as risk factors for the development of COPD at non-smokers are not yet sufficiently studied. In a study conducted in northern Sweden, prevalence of COPD in non-smokers was close to 7% and is associated with age. One of seven men, and one in four women with COPD never smoked [19].

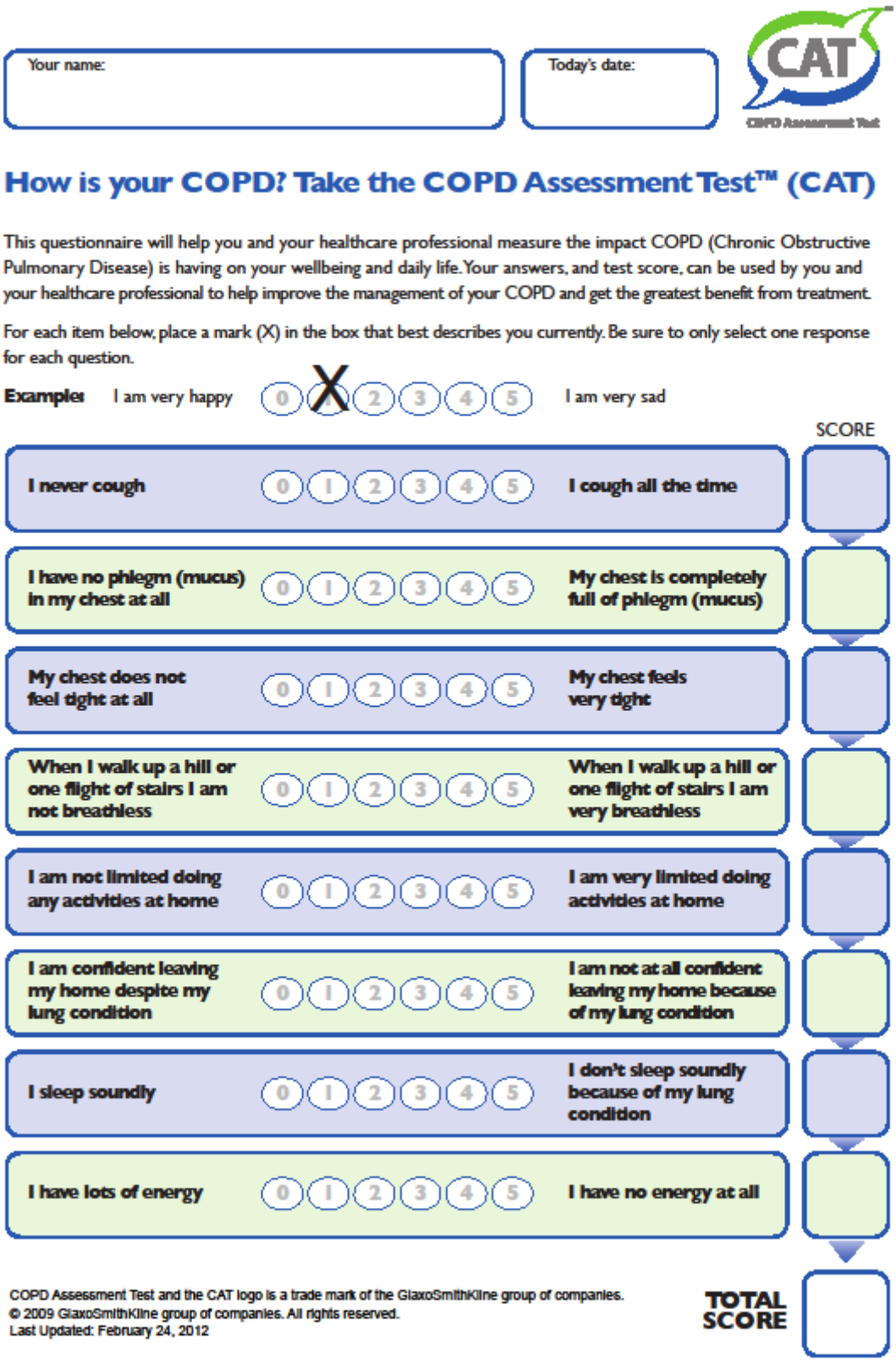
The majority of studies deals with the frequency of AE- COPD with moderate and severe chronic obstructive pulmonary disease, so little is known about the frequency of exacerbations in mild COPD. In our study the frequency of acute exacerbations of COPD was in correlation with the severity of obstructive disorders. The highest percentage of exacerbations was recorded in patients with the most severe obstruction by the GOLD classification even 62.5%, then in the third GOLD stage 42.22%. A high percentage of AE-COPD was determined in patients with second degree of obstructive disorders in 36,21% and exacerbations were recorded also in patients with mild obstruction of 11.11%. These results are similar to results of other studies, which have examined the frequency of exacerbations in medium-severe and severe COPD. English study confirmed that exacerbations occur in the mild obstructive disorder, and that the increased number of previous exacerbations is the best indicator of the risk of future exacerbations in each patient [14].

In our study, a small percentage of respondents did not have any comorbidities 11.67%, while the one or more comorbidities had 88.33% of the respondents. The number and type of comorbidities influenced the occurrence of AE-COPD. So the highest percentage of AE-COPD was recorded in the group of patients with 4 or more comorbidities 43.75%, then by three 41.67%, by two 40.74%, by one 38.46%, and the lowest percentage of exacerbations had patients without comorbidities 21.43%.

The most common comorbidities in patients with COPD were cardiovascular diseases (hypertension 55.83% of patients, ischemic heart disease in 14.17%, heart failure 12.5%), followed by GERD or ulcer disease (31.67% of patients) articular rheumatism (28.33%), anxiety / depression, 26.67%, and diabetes mellitus (15% of patients). Comorbidities are common in patients with COPD and they have a great impact on the quality of life, choice, and the effect of therapy, the frequency of acute exacerbations and mortality. It is considered that certain diseases occur more frequently in patients with COPD infection than in the general population, and that they have a significant impact on the outcome of the disease. Several comorbidities is associated with an increased frequency of acute exacerbations of COPD, including GERD, anxiety, depression, pulmonary embolism, pulmonary hypertension and cardiovascular disease. Number of comorbidities was also correlated with an increased risk of exacerbations and hospitalizations in patients with COPD. In patients with very severe COPD, respiratory insufficiency is the most common cause of death, while in patients with less severe COPD the most common cause of death are cardiovascular disease and lung cancer [20, 21].

The quality of life is a key factor in assessing the severity of chronic obstructive pulmonary disease and patient response to applied therapy. Several studies have confirmed that the quality of life in patients with COPD deteriorates with the progression of the disease and during exacerbations. Patients who have more frequent exacerbations have worse quality of life in comparison to patients with rare exacerbations. CAT test is a simple and quick test that helps in the diagnosis of COPD, in assessing of the quality of life of patients with COPD, in evaluation of effects of the therapy and in monitoring of recovery after exacerbations. CAT scores are higher in patients with acute exacerbations than in patients in a stable phase of the disease [22]. The results of our study have shown that a significant percentage of patients has a poor quality of life, that is, unsatisfactory control of the disease. The doctors involved in the treatment of patients with COPD have to take into consideration the quality of life of patients when assessing the state of health, because only FEV1 parameter is not sufficient for assessing the clinical severity of a COPD.

5. Appendix



Your name:

Today's date:

CAT
COPD Assessment Test

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 X 2 3 4 5 I am very sad

			SCORE
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	
		TOTAL SCORE	

6. Conclusion

1. The frequency of acute exacerbations of COPD in patients suffering from chronic obstructive pulmonary disease in primary care family medicine Modriča was great.
2. Acute exacerbations of COPD were slightly more frequent in men than in women.
3. Older age, smoking and severe degree of obstructive disorders were correlated with higher frequency of acute exacerbations of COPD.
4. Comorbidities were present in majority of patients with COPD, and their number and type significantly influenced on the frequency of acute exacerbations.

Chronic obstructive pulmonary disease may have a significant impact on the quality of life of patients, that is why when assessing the health status of these patients the wider application of simple CAT questionnaire is important in family medic

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