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**Clinical Science**

# Gastroesophageal Reflux Symptoms in Patients with Chronic Obstructive Pulmonary Disease

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## Abstract

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**Key words:** GER symptoms; COPD; airway obstruction; FEV<sub>1</sub>; dyspnea.

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**BACKGROUND:** It is known that there is some relation between airways obstruction and gastroesophageal reflux symptoms (GER) symptoms in patients with chronic obstructive pulmonary disease (COPD).

**AIM:** The aim was to determine frequency of GER symptoms and correlation with pulmonary function tests in patients with COPD.

**MATERIAL AND METHODS:** The study included 58 patients. First group had 20 patients with mild COPD, second group had 18 patients with moderate COPD and third group had 20 patients with severe COPD. We had also a control group with 12 healthy subjects. All subjects completed their self-reported questionnaire about symptoms like: acid-regurgitation, heartburn, dysphagia, dyspnea and chronic cough.

**RESULTS:** COPD patients with airways obstruction and significant GER symptoms had their respiratory symptoms associated with reflux events. More of COPD patients had significant GER symptoms defined as regurgitation and dysphagia once or more per week. Patients with FEV<sub>1</sub> less than 50% showed more prevalent GER symptoms compared to those with values of FEV<sub>1</sub> greater than 50%.

**CONCLUSION:** GER symptoms are more prevalent in patients with severe airways obstruction when compared to less airways obstructed group and controls. We could suggest an association between the degree of airways obstruction in patients with COPD and the increased rate of GER symptoms.

## Introduction

COPD is a major cause of chronic morbidity and mortality throughout the world: it is the fourth leading cause of death in the world. COPD is a chronic, slowly progressive disorder characterized by airflow limitation with nonreversible airways obstruction (reduced FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ratio) which does not change markedly over several months. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles and gases [1, 2]. An acute exacerbation of COPD is defined by the presence of worsening dyspnea, increased sputum production, or the development of purulent sputum, and may be accompanied by hypoxemia and worsening hypercapnia [1, 3].

Gastroesophageal reflux disease (GERD) is the collective term used to describe abnormal reflux of gastric content into the esophagus as well as the symptoms and mucosal disease associated with it. Clinical manifestations of GERD include heartburn, regurgitation, dysphagia, chest pain, cough and other esophageal symptoms [4, 5].

It is known that there is some relation between airways obstruction and gastroesophageal reflux (GER) disease. The association between respiratory symptoms and GER symptoms is well recognized in asthma [6-8]. In contrast to asthma, the relationship between GER and chronic obstructive pulmonary disease (COPD) is not well established in previous years, but in last decade there are more studies that investigate the relation between GER and COPD.

Two explanations have been proposed: Reflux induces microaspiration of gastric contents that irritate airways or symptoms may be induced without direct exposure of the airways to refluxant material; acid reflux into distal esophagus induces vagally mediated reflex bronchoconstriction [1-3, 5].

Mokhlesi et al. in their article in Chest 2001 suggest a possible correlation between COPD severity and more frequent symptoms of GER [5]. Some authors found an increased prevalence of GER symptoms in patients with COPD [9].

In our study we investigated whether GER symptoms were more frequent in COPD patients than in healthy controls. We also examined the correlation between pulmonary function tests and symptoms of GER.

### Materials and Methods

We have examined 58 patients with a diagnosis of COPD treated at the Clinic of Pulmology and Allergology (38 males and 20 females) and 12 healthy subjects.

Inclusion Criteria (American Thoracic Society) for COPD patients were: age over 50 years; over 30 years smoking period; and abnormal findings on pulmonary function tests demonstrating nonreversible airways obstruction.

The classification of COPD patients by the severity of airflow limitation was according to the actual version of the Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD), i.e. GOLD 1, GOLD 2 and GOLD 3 (mild, moderate and severe airflow limitation).

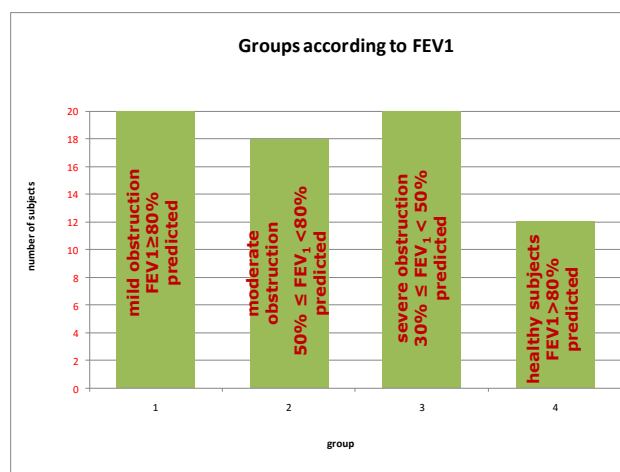
**Table 1: Measurement of forced expiratory volume in one second (FEV<sub>1</sub>).**

Group	Subjects	Obstruction	FEV <sub>1</sub>
GOLD1	20	mild	FEV <sub>1</sub> ≥ 80% predicted
GOLD2	18	moderate	50% ≤ FEV <sub>1</sub> < 80% predicted
GOLD3	20	severe	30% ≤ FEV <sub>1</sub> < 50% predicted
4	12	healthy	> 80% predicted

We made measurement of forced expiratory volume in one second (FEV<sub>1</sub>) in all subjects and we subdivided them by the value of lung function in three groups. GOLD1 have mild obstruction with FEV<sub>1</sub> ≥ 80 predicted, GOLD2 have moderate obstruction with 50 ≤ FEV<sub>1</sub> < 80 predicted and GOLD3 have severe obstruction with 30 ≤ FEV<sub>1</sub> < 50 predicted by using the fixed ratio postbronchodilator FEV<sub>1</sub>/FVC ≤ 0.70 to define airflow limitation (GOLD 2013 [1]) (Table 1). In the same time all patients have documentation about diagnosed GERD before admission in the study.

The groups completed their self-reported questionnaires about following symptoms: heartburn, acid-regurgitation, dysphagia, chronic cough, wheezing, and shortness of breath. The questions defined occurrence of symptoms, once or more per

week, during a period of three months.



**Figure 1: Measurement of forced expiratory volume in one second (FEV<sub>1</sub>).**

Statistical analysis was performed with one-way ANOVA test for proportion. The associations between binary variables were tested using  $\chi^2$ -test.

### Results

The results show that: there is significantly higher prevalence of GER symptoms in COPD patients vs control subjects. ( $p < 0.05$ ; COPD patients vs control subjects), and patients with FEV<sub>1</sub> < 50% have higher prevalence of significant GER symptoms, compared with less severe COPD patients with FEV<sub>1</sub> > 50% ( $p < 0.05$ ; FEV<sub>1</sub> < 50% vs FEV<sub>1</sub> > 50%) (Table 2).

**Table 2: Relation between GER symptoms and FEV<sub>1</sub> in patients with COPD compared with healthy subjects.**

Symptoms	FEV <sub>1</sub> ≥ 80% predicted N=20	50% ≤ FEV <sub>1</sub> < 80% predicted N=18	30% ≤ FEV <sub>1</sub> < 50% predicted N=20	Controls N=12
Heartburn	3	5	10	2
Acid regurgitation	5	6	11	2
Disphagia	2	6	9	2

### Discussion

In our study it was found that significant GER symptoms once or more per week, are more prevalent in COPD patients when compared with control group. We also found relation between severity of airways obstruction and GER symptoms.

The study of Mokhlesi et al., also shows that there is increased prevalence of GER symptoms in patients with COPD [5]. There is significant finding that patients with the diagnosis of COPD and weekly

GER symptoms have more acute exacerbations of COPD than patients with COPD without GER symptoms [3]. The study of Casanova et al., has shown that COPD is associated with an abnormally high prevalence of oesophageal acid reflux when compared to volunteers of similar age. In the same study some patients manifest oxygen desaturation that coincides with periods of acid reflux [10]. In a study, the authors investigate the proportion of GER symptoms in patients with COPD and its association with the severity and worsening of the symptoms of COPD [11]. In this study the authors concluded that a higher proportion of frequent gastro-esophageal symptoms were noted by COPD patients than control subjects and higher proportion of gastro-esophageal symptoms was noted in severe COPD patients [11]. We also found that GER symptoms are more prevalent in COPD patients with severe airways obstruction.

Local irritation in the esophagus can cause symptoms that vary from indigestion, like chest discomfort and abdominal pain, to coughing and wheezing [12]. Patients with a diagnosis of COPD are at a significantly risk of a diagnosis of GERD compared with subjects without COPD diagnosis [13]. The severity of hyperinflation and dyspnea may be important associated risk factors for the incidence of GERD symptoms in patients with clinically stable COPD [14]. Terada et al., also concluded that GERD symptoms were identified as an important factor associated with COPD exacerbation [15-17].

It is important that GER symptoms are not as common in COPD as they are in asthma. There is a limited number of studies that investigate if there is a link between GERD and COPD. In some clinical information in respiratory reviews, there is still the question "Does GER exacerbate COPD?" But, whether having COPD predisposes patients to GER or vice versa remains to be proven in further investigations.

We concluded that the prevalence of GER symptoms is high in patients with COPD. GER symptoms are more prevalent in COPD patients with severe airways obstruction when compared to less airways obstructed group and controls. We suggest an association between the degree of airways obstruction in COPD patients and increased rate of GER symptoms.

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