Spirometry quality in patients with COPD exacerbation, related to the “frequent exacerbator” phenotype

Calitatea spirometriei la pacienții cu exacerbare de BPOC, legată de fenotipul “exacerbator frecvent”

Abstract

Aim. The study aims to assess the quality of spirometry sessions in patients with chronic obstructive pulmonary disease (COPD) exacerbation, to compare the spirometry quality in patients with frequent exacerbations (two or more in the previous year) and in patients without exacerbations.

Subjects and method. Consecutive COPD patients with moderate infectious exacerbation were evaluated at presentation. The quality of spirometry (ATS/ERS 2005: at least three acceptable curves with repeatable values for FVC and FEV1) and the time needed to obtain a spirometry session were evaluated and compared to the spirometries obtained 3-6 months before, in a stable period.

Results. Eighty COPD patients were evaluated, mean age was 63 years old, 60 males. Although all patients had valid spirometry sessions in the stable period, 12 subjects (15%) could not obtain a valid session during exacerbation due to cough, shortness of breath and/or fatigue. More efforts were necessary to obtain a spirometry session during exacerbation (4.6±1.2 efforts) compared to the stable period (3.8±0.9 efforts, p=0.001). The time needed to obtain a spirometry session was significantly higher in exacerbation (5.7±1.4 minutes) compared to the stable period (4.8±1.6, p=0.001). Frequent exacerbators (33 patients; 41%) had similar spirometry quality in exacerbation and in the stable period, and similar amount of time needed to perform the spirometries compared to the patients with no exacerbations (p=0.05).

Conclusions. Good spirometry quality could be obtained in 85% of patients, and a longer period needed to obtain a spirometry session was seen in exacerbation compared to a stable COPD period. Similar spirometry quality was seen in patients with frequent exacerbations, as in patients without exacerbations in the previous year.

Keywords: COPD, exacerbation, spirometry

Rezumat

Scop. Studiul își propune să evalueze calitatea sesiunilor de spirometrie la pacienții care prezintă o exacerbare de bronhopneumopatie obstructivă cronică (BPOC), să compare calitatea spirometriei la pacienții cu exacerbări frecvente (două sau mai multe în anul precedent) și la pacienții fără exacerbări.

Subiecții și metode. Pacienții consecutivi cu exacerbări infecțioase moderate de BPOC au fost evaluați la prezentare. Calitatea spirometriei (ATS/ERS 2005: cel puțin trei curbe acceptabile cu valori repetabile pentru FVC și FEV1) și timpul necesar pentru obținerea unei sesiuni de spirometrie au fost evaluat și comparat cu spirometriile obținute cu 3-6 luni înainte într-o perioadă stabilită.

Rezultate. Au fost evaluați 80 de pacienți cu BPOC, vârsta medie 63 de ani, 60 de bărbați. Deși toți pacienții au avut sesiuni de spirometrie valabile în perioada stabilită, 12 subiecți (15%) nu au putut obține o sesiune valabilă în timpul exacerbării din cauza tusei, a dispneii și/sau a oboselii. Mai multe eforturi au fost necesare pentru a obține o sesiune de spirometrie în timpul exacerbării (4,6±1,2 eforturi) comparativ cu perioada stabilă (3,8±0,9 eforturi, p=0,001).

Timpul necesar pentru obținerea unei sesiuni de spirometrie a fost semnificativ mai mare în timpul exacerbării (5,7±1,4 minute) comparativ cu perioada stabilită (4,8±1,6, p=0,001).

Exacerbatorii frecvenți (33 de pacienți; 41%) au avut o calitate similară a spirometriei în exacerbare și în perioada stabilită și o perioadă similară de timp necesară efectuării spirometriei în comparație cu pacienții fără exacerbări (p=0,05).

Concluzii. La 85% dintre pacienții ar putea fi obținută o calitate bună a spirometriei, iar în exacerbarea BPOC comparativ cu o perioadă stabilită a fost observat un timp mai îndelungat necesar pentru obținerea unei sesiuni de spirometrie. Calitatea spirometriei a fost similară la pacienții cu exacerbări frecvente și la pacienții fără exacerbări în anul precedent.

Cuvinte-cheie: BPOC, exacerbare, spirometrie

Introduction

Chronic obstructive pulmonary disease (COPD) is a widespread disease generally related to smoking, characterized by chronic progressive and irreversible obstruction of the airways.

The prevalence of COPD is estimated at 7.6%. Figures may vary according to the diagnostic procedures used: patient reported diagnosis – 3.9%, physician diagnosis – 4.1%, diagnosis by spirometry – 10.1% (3).

Acute exacerbations of COPD are considered important and deleterious events in the course of the disease, accounting for decreased quality of life, accelerated drop in the lung function and increased mortality (2). COPD patients experience 0.5-3.5 exacerbations per year, according to different surveys. In 2008, a number of 822,500 hospital admissions were recorded for COPD exacerbations in US (3).

According to Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations, functional respiratory testing is essential for the correct diagnosis and staging in COPD patients (4). In current clinical practice, only about a third of the patients diagnosed with COPD
have an accurate spirometry related to their diagnosis, as demonstrated by a Swedish study.\(^5\)

Patients are sometimes diagnosed for the first time with COPD during a hospital visit for an acute exacerbation. Even though it is recognized that spirometry is essential for proving the obstruction and staging, usually clinicians are reluctant to perform a spirometry during an exacerbation. A low quality of the tests is expected due to worsened clinical status and reluctance of patients to perform the efforts needed for spirometry when they feel worse.

The exploration of the respiratory function can give valuable information about the presence of obstructive syndrome and its severity, allowing the design of a correct management plan and avoiding misdiagnosis. Respiratory function is directly linked to the risk of mortality and hospital admission. In a study by Anthonisen, the overall mortality over 3 years was a mean of 23% in patients admitted for acute exacerbations of COPD, patients with FEV1<40% having a significantly higher mortality rate than patients with FEV1 > 40% predicted, who had a mortality similar to that of healthy smokers.\(^6\)

However, this is not the only parameter that can evaluate the severity of COPD. The 2014 GOLD update\(^7\) proposed a combined assessment of COPD severity according to functional impairment, severity of symptoms and exacerbation history. Some COPD patients have typically few exacerbations (less than two per year), while others, called “frequent exacerbators”, have two or more exacerbations per year, this being correlated with a worse prognosis and higher mortality\(^7\).

The aim of this study was to evaluate whether good quality spirometries can be performed in COPD patients during an acute exacerbation, and if the quality of the tests could be correlated to the status of “frequent exacerbator” of the patients. We aimed to assess the quality of the spirometry sessions in patients presenting with COPD exacerbations. In addition, we compared the quality of spirometry in COPD patients with previous frequent exacerbations (two or more in the previous year) with those performed in COPD patients without exacerbations.

**Materials and method**

This was a prospective, observational study, on consecutive COPD patients with an exacerbation, performed in ARENSIA research unit within the “Marius Nasta” Institute of Pneumophtisiology, Bucharest, over a one-year period. The patients were included in the study on the occasion of the preselection for a randomized clinical trial aiming to determine treatment for COPD exacerbation. For this observational study, only information from the preselection visit and medical history was used, without interfering with the conduct and the data of the randomized clinical trial.

**Subjects:** 80 patients with COPD who had an episode of moderate exacerbation and presented in the pulmonology department were included in this study. All patients had a previous diagnosis of COPD for at least 6 months and, at the moment of the exacerbation, were receiving maximal bronchodilator treatment as recommended by a pulmonologist. The exacerbation was defined according to Anthonisen criteria, as an increase in cough, sputum volume and purulence, and worsening of dyspnea.\(^8\)

The inclusion criteria were: age between 40-80 years old, history of smoking (at least 10 PA), previous diagnosis of COPD stage II-IV GOLD confirmed by spirometry (obstructive syndrome: FEV1/FVC ratio <0.7).

The exclusion criteria were: severe exacerbation requiring ventilatory support, severe respiratory acidosis (pH<7.26), abnormalities on chest X-ray (e.g., pneumonia, pneumothorax, lung tumors, tuberculosis), history of malignancies in the past 5 years, long-term oxygen therapy.

The patients consented in writing to participate to the study.

**The evaluated parameters** were spirometry quality and the time required to obtain a spirometry session.

Spirometry was performed using a Vitalograph spirometer. The spirometries were performed in the first day of presentation to the clinic, before the initiation of any treatment for the exacerbation. The tests were post-bronchodilator, after the administration of 400 mcg of inhaled salbutamol. At least three tests were performed, observing the acceptability criteria for performance and repeatability. The test was stopped if criteria were not fulfilled in 8 consecutive efforts. The quality of spirometry was assessed using the ATS/ERS 2005 criteria\(^9,10,11\), at least three acceptable values with repeatable curves for forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1).

A spirometry test was considered acceptable if it included at least three efforts without artifacts, an expiration duration of at least 6 seconds or plateau before 6 seconds. The tests were considered reproducible if the difference between the two highest FEV1 and FVC values were both less than 150 ml.

The time needed to obtain all acceptable spirometries was recorded for each patient.

Functional respiratory parameter values measured in this session were compared to those obtained 3-6 months earlier, when the patients were in a stable COPD period.

**Statistical analysis.** For statistical analysis, the SPSS version 17.0 was used. The results were expressed as mean values ± standard deviation. For variable normality analysis, the Shapiro-Wilk test was used. The parameters comparison was made with the Student’s t-test. A p value < 0.05 was considered significant.

**Results**

Eighty patients with mild/moderate COPD exacerbation were included in the study. The mean age was 63 years old. Most patients were men (60 patients).

All patients had at least one valid spirometry performed 3-6 months prior to the moment of exacerbation, recorded in the database of the Research center.
In 12 patients (15%) presenting with exacerbation, a good quality spirometry could not be obtained. The causes were: cough, dyspnea, increased fatigue. These patients had a good quality spirometry recorded previously, during stable the state of the disease.

The other 68 patients (85%) were able to perform the test at the presentation for exacerbation. The number of efforts needed to achieve a good quality spirometry session in these patients was higher during exacerbation (4.6±1.2 efforts) than during the previous stable period (3.8±0.9 efforts), p=0.001 as shown in Figure 1.

Regarding the time required to obtain a spirometry session (Figure 2), it was higher during the exacerbation (5.7±1.4 minutes) than during the stable period (4.8 ± 1.6 minutes) (p=0.001).

According to the history of exacerbations in the past year, patients were divided in a group of frequent exacerbators (two or more per year): 33 patients (41%), and a group of infrequent exacerbators (less than two per year): 47 patients (59%). Actually, these patients had no exacerbation in the past year.

The spirometries obtained during a stable state of disease had similar qualities in the two groups: infrequent exacerbators needed a mean of 3.83 efforts to achieve acceptable spirometries, while the frequent exacerbators needed a mean of 3.82 efforts (Figure 3). The difference is not statistically significant (p=0.870).

Similarly, during the exacerbation, the patients with infrequent exacerbator phenotype needed 4.70 efforts to perform a spirometry, compared with frequent exacerbators that needed 4.33 efforts (Figure 4). The difference is not statistically significant (p=0.065).

When we analyzed the time required to carry out a spirometry during the stable period of disease, it took
5.13 minutes for infrequent exacerbators to perform the tests, versus 5.09 minutes for frequent exacerbators (Figure 5), with no significant difference (p = 0.603).

Similar time periods, with no statistically significant differences, were needed to get the acceptable spirometry during exacerbations: 5.5 minutes for infrequent exacerbators versus 5.52 minutes for frequent exacerbators, p = 0.231 (Figure 6).

Discussions

Spirometry is an essential tool in the diagnosis of COPD, needed to confirm the clinical suspicion. In clinical practice, only few patients (about 30%) have the COPD diagnosis confirmed by spirometry (5). Moreover, it is generally considered that COPD is a severely under-diagnosed condition, with an estimation of 25% or up to 50% of patients not being diagnosed (1). It is expected that some of these patients will be diagnosed for the first time in a respiratory department on the occasion of an exacerbation. The general assumption is that patients will not be able to perform a reliable spirometry at the moment of an exacerbation and, if they still do it, the values obtained would not be reliable for evaluating the severity of the disease. GOLD guidelines state that “spirometry should be performed when the patient is stable and free from infections” (4). In real life, this restriction may not be operational. Some of these patients are probably never free of respiratory infections, while some will perform their first spirometry on the occasion of their first exacerbation.

The guideline recommendation is based on the assumption that during infection or exacerbation, the spirometric parameters may be lower than the personal best values of the patient that can be recorded in stable state of the disease. Thus, spirometries performed during an exacerbation might induce the inclusion of the patient in a more severe GOLD stage than in stable state. Several previous studies tried to define if there really existed a significant change in FEV1 and FVC after the resolution of the exacerbation. A study conducted on a group of 41 COPD patients compared the spirometry performed at discharge after hospitalization for exacerbation of COPD with the spirometry performed 4 weeks later. No significant differences have been recorded one month after discharge, registering variations of a GOLD level classification with one step up or down (10). Another study demonstrated that changes in lung function associated with exacerbations were small, compared to previous records: a fall of FEV1 by 24 ml, and FVC by 76 ml (13).

In a study that assessed the respiratory function in the first days of admittance for asthma or COPD exacerbation, only 73 percent of the functional lung tests were acceptable, their quality being related to the time elapsed from the onset of the exacerbation (15). This study suggested that performing a spirometry shortly after the onset of an exacerbation could be associated with the inability to produce adequate spirometric traces.

Our study intended to check whether a spirometry performed at the onset of a COPD exacerbation can produce valid data, according to the ERS/ATS criteria. However, in these patients a previous functional test was available. All the patients included in the study were able to perform reproducible tests in stable state, but during exacerbation some patients (15%) could not perform good efforts, due to cough or dyspnea, while most of them (68 patients; 85%) were able to produce valid results, but in significantly more time and with a higher number of efforts.

Our patients performed the spirometry on the first day of presentation to the physician, before the initiation of exacerbation treatment (increased bronchodilation, antibiotics, systemic corticosteroids). In the previous studies published, the spirometry was performed at discharge (12) or after five days of hospitalization (16).
Spirometries during exacerbation can be useful for research, bringing new insights into the effect of exacerbation on lung volumes. This could hypothetically launch the idea of a functional classification of COPD exacerbation (mild, moderate or severe) according to lung volume lost on this occasion. Another use could be the evaluation of novel treatments for exacerbation on lung function.

Our attempt to check if another criterion for COPD severity, the “frequent exacerbator” phenotype, could influence the quality of the function tests showed that this phenotype is not correlated separately with the quality of spirometry. Most likely, the higher difficulty to obtain good tests had other causes, related to the exacerbation itself: the degree of thoracic hyperinflation, cough, impairment of respiratory muscle strength, coexistence of infection, or other.

One limitation of our study was the inclusion in the study group only of patients with mild/moderate exacerbation and the exclusion of patients with severe exacerbation.

Conclusions

In exacerbation, compared to a period of stable COPD, it was more difficult to obtain good quality spirometry, needing more time and more efforts. The percentage of patients who could anyway perform reproducible tests was higher than in previous studies, possibly due to the setting of the study, in a research center. A similar quality of spirometry has been observed in patients with frequent exacerbations, as in patients without exacerbations in the previous year, the phenotype of frequent exacerbator did not have any influence on the spirometry quality.

References