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Comparison of New COPD Diagnostic Methods to Traditional Spirometry Method

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ABSTRACT

Chronic obstructive pulmonary disease (COPD) is one of major non-communicable diseases affecting millions of people around the world. It is slowly developing and progressing disease characterized by mostly irreversible pathophysiological changes resulting in gradual loss of pulmonary function. It presents with different phenotypes associated with specific pathophysiological changes in individual patients. Diagnostic evaluation of COPD traditionally includes pulmonary function tests (PFT) using spirometry. Spirometry is considered to be the internationally accepted gold standard diagnostic method during evaluation for COPD. Although spirometry is commonly used to diagnose COPD, it may sometime lack adequate sensitivity to detect fine pathophysiological changes associated with particular phenotypes of COPD. Development and use of new alternate diagnostic methods could improve not only diagnosis of COPD, but also optimize the management and treatments.

Keywords

COPD, Diagnosis, Methods, Spirometry, FRI, IOS.

Introduction

Individuals with respiratory abnormalities such as chronic obstructive pulmonary disease (COPD) should be carefully evaluated since their functional vulnerability, especially considering effects of the recent COVID-19 global pandemic [1]. The WHO estimates that COPD is the third leading cause of death worldwide (3.8 million deaths) with cases constantly on the rise which has had a negative impact on the quality of life and a significant economic burden on the society [2]. COPD is slowly developing and progressing disease characterized by mostly irreversible pathophysiological changes resulting in gradual loss of pulmonary function [3]. It presents with different phenotypes associated with specific pathophysiological changes in individual patients [4]. The question is whether the current COPD diagnostic techniques are capable of detecting early stages of COPD in patients who are not necessarily symptomatic but are still at significant risk of contracting COVID-19. Determination of pulmonary function tests (PFT) using spirometry is currently the gold standard of diagnosing COPD [5,6]. Spirometry is readily available in many health care facilities around the world. However, it is not sensitive enough to detect COPD in some individuals with respiratory symptoms and smoking history. This may leave these individuals at increased risk of further progression to fully developed COPD. Also, incorrect or inaccurate spirometry readings occur either due to low level mastery of the skill by the clinician on how to properly carry out the procedure, or poor compliance by patients due to poor compliance with instructions [7]. Some techniques, such as functional respiratory imaging (FRI) and impulse oscillometry systems (IOS), have shown potential in the diagnosis of early stages of COPD. The aim of this paper is to see if these methods can serve as viable diagnostic alternatives, or additional diagnostic tools together with spirometry.

Spirometry

The GOLD executive report suggests that COPD should be considered in patients with symptoms of dyspnea, chronic cough or sputum production, a history of lower respiratory tract infections, a history of harmful respiratory exposures for the disease, and the use of spirometry to make a diagnosis of COPD with a post-

bronchodilator FEV₁/FVC < 0.70 [7]. Severity of the disease is classified as mild (GOLD 1), moderate (GOLD 2), severe (GOLD 3), and very severe (GOLD 4), based on post-bronchodilator FEV₁ value using spirometry [7,8]. Since the correlation between FEV₁, symptoms, and impairment of patient's health status is weak, formal symptomatic assessment is required [9,10]. Although this serves as good diagnostic criteria for COPD and reduces the risk of over diagnosing in individuals who do not necessarily have the disease, it does not address the issue of under diagnosing and in some instances incorrectly ruling out individuals with early stages COPD who have not developed abnormal spirometry metrics.

The COPDGene cohort study was conducted with the goal of redefining the definition of COPD [11]. All 8,784 participants included in the study were current or former smokers with at least 10 pack-years smoking history. The primary goal of the study was to compare the current GOLD diagnostic criteria of COPD to new diagnostic criteria consisting of 4 main parts which included minimum exposure of 10 pack-year smoking history, self-reported dyspnea and/or chronic bronchitis (chronic cough and phlegm), CT abnormality defined as \geq 5% emphysema, and abnormal spirometry values (FEV₁ < 80% predicted and/or FEV₁/FVC < 0.70). The subjects were followed and after 5 years were evaluated again to monitor progression of the disease. The results of the study showed that the current GOLD guidelines would diagnose 4,062 of the study participants as having COPD, but the proposed study would diagnose additional 3144. The results of this study further highlighted the insufficiencies of using spirometry as the main diagnostic criteria in COPD because a significant number of patients have an early stage of COPD and if diagnosed early, would be able to receive treatment to stop further disease progression to when they eventually have abnormal spirometry metrics.

Functional Respiratory Imaging (FRI)

A recently developed technology called functional respiratory imaging (FRI) is based on multi-slice high resolution computed tomography CT (HRCT) scans, and computational fluid dynamics to quantify anatomic and functional characteristics of pulmonary system [12]. This technology has shown clinical significance in diagnosis and management of COPD [13,14]. Unlike spirometry which measures pulmonary functions, FRI measures hyperinflation, airway diameter, and air resistance of lung segments. This is achieved with a high degree of accuracy since it does not require active patient involvement [15].

A prospective cohort study was conducted using FRI to observe changes taking place in the lungs during an acute exacerbation as compared to changes in spirometry values [13]. The main goal of the study was to determine the correlation between changes in lung function and parameters measured by FRI during an exacerbation. From the results, comparisons were made between two patients who had similar profiles (i.e., both female, similar age, smoking history, GOLD 3), who both had similar FEV1 values at baseline (39.0% and 40.5% predicated). Although spirometry measurements were the same for both patients, FRI parameters showed clear differences. At baseline, the first patient was hyperinflated with a total lung

volume of 140.6% in contrast to 95.4% of the second patient. This shows that although both patients could not be differentiated based on severity of their disease using standard spirometry values and GOLD classification, FRI was able to detect a greater degree of disease severity in the first patient compared to the second patient. These findings are promising and could be helpful in diagnosing individuals who are early-stage COPD patients and do not meet the clear spirometry diagnostic criteria but still have significant lung abnormalities. However, a key weakness noted was the need to carry it out in stable patients and not during an acute exacerbation to help in diagnosing early-stage COPD.

In a recent randomized, double-blind crossover study, FRI was used to assess the effects of the long-acting muscarinic antagonist (LAMA) glycopyrrolate metered dose inhaler (GP MDI), and the long-acting β_2 agonist formoterol fumarate (FF MDI), on airway volume and resistance in patients with moderate to severe COPD [16]. Primary endpoints of the study included specific image-based airway volume and specific image-based airway resistance, determined with FRI. Secondary endpoints included additional parameter determined by FRI, spirometry, and body plethysmography. Post-dose efficacy assessments were done within 60 to 150 minutes of dosing on day 15. FRI endpoints indicated increased sensitivity compared to spirometry and body plethysmography in detecting differences between treatments in a small number of patients.

Impulse Oscillometry Systems (IOS)

In the pathogenesis of COPD, early changes developing in the lungs are not always detected by spirometry. Some of these early changes include air way narrowing, mucus gland hypertrophy and collagen deposition, which are more evident in small airways [17]. A new noninvasive technique called impulse oscillometry systems (IOS) was recently developed to measure respiratory resistance and reactance at different oscillation frequencies. This technique was developed as an alternative method to the traditional spirometry. Pressure-flow oscillations are applied at the mouth, superimposed on the patient's tidal breaths to assess respiratory system resistance and reactance [18-20]. This method is effort independent.

A cross-sectional study was conducted to compare IOS to spirometry in diagnosing COPD using endobronchial optical coherence tomography [21]. The results of the study showed some correlation between IOS and spirometry recorded values in COPD patients. Further, IOS detected small airway abnormalities found in individuals with early-stage COPD, who had no significant airway obstruction and were not detected by spirometry. Results also showed that the parameters of IOS measurements were highly sensitive in detection of abnormalities in the airways of both, early-stage COPD and heavy smokers. However, some limitations to the study, such as the low sample size and lack of variation in patient characteristics reduces the accuracy of the study. Also, IOS is still relatively new method, and has no standard normal reference values for their findings to be compared against, leaving room for more research in this area.

Conclusion

Although spirometry is presently required for the diagnosis and monitoring of disease progression of COPD in patients, there is a need to look to newer techniques to help improve the diagnosis and management of early-stage COPD in patients who do not necessarily have abnormal spirometry values, but have significant lung imaging abnormalities and respiratory symptoms. Techniques such as FRI or IOS need to be researched further, and their diagnostic potentials explored. Exposing the body to unnecessary levels of radiation needs to be considered, and a benefit to risk comparison needs to be made based on individual patients.

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