Review Article

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When Pulmonary Function Test is Available, Should we Wait for the COPD Symptoms to Develop?

Internal Medicine Section

VARSHIL MEHTA[1], NIMIT DESAI[2], SMIT PATEL[3]

ABSTRACT

Adolescent smokers are more likely to be addicted to nicotine and develop a chronic habit. Chronic smoking has a direct impact on quality of life and life expectancy. Repeated environmental exposure and smoke inhalation can be deleterious to health. In order to evaluate the core functioning of the lungs, Pulmonary Function Tests (PFTs) are conducted. This panel of tests should be advised for all patients complaining of shortness of breath. Since clinical features resulting from chronic smoking tend to appear late in the course of the disease, PFTs are immensely useful for early identification of abnormalities in asymptomatic adult smokers. Numerous studies have shown that normal PFT parameters begin to deteriorate immediately after smoking is initiated. However, most physicians prefer to wait for characteristic signs and symptoms of Chronic Obstructive Pulmonary Disease (COPD) to develop before proceeding with PFTs in the patients. This leads to inadvertent and often dangerous delay in reaching a definitive diagnosis and initiating treatment. Therefore, we undertook this review to determine whether conducting PFTs in asymptomatic adult smokers can facilitate the early detection and/or prevention of COPD. We reviewed and analyzed articles from PubMed, Google Scholar, Index Medicus, WHO Global Health Library and Scopus, which specifically demonstrated the presence of abnormal PFT changes in asymptomatic adult smokers.

With PFTs, we now have the advantage of diagnosing early changes in the lung volumes. Hence, we conclude that PFTs should be performed early in smokers and cessation of smoking should be encouraged to check the increasing incidence of COPD.

Keywords: Asymptomatic smokers, Early detection, Prevention of chronic obstructive pulmonary disease, Pulmonary function test advantage

INTRODUCTION

The tobacco epidemic is a global health problem and kills nearly six million people annually. Out of which, more than five million people die due to direct tobacco use while more than 0.6 million non-smokers die due to second-hand smoking. In short, it kills nearly up to half of its users [1]. It is noted that approximately one person dies every six seconds due to chronic tobacco usage [2]. It has been estimated that more than 500million people will eventually die from the diseases caused by smoking cigarettes [3].

People who start smoking at their adolescent age are more likely to get addicted to nicotine and become chronic smokers, or die due to any one of the multiple chronic diseases associated with smoking and tobacco use. From many years, the effects of smoking on chronic diseases have been a matter of particular interest for public health prevention, but its adverse effects on acute health conditions have been elucidated recently. The most notorious disease caused by smoking is lung cancer. Compared with non-smokers, the mortality rate from lung cancer is 8-25 times more in smokers [4].

According to the World Health Organisation (WHO) 2014 update, Chronic Obstructive Pulmonary Disease (COPD) will become the third most common preventable cause of death in the world by 2030 [5].

Cigarette smoking is implicated as the cause of 87% of the total number of deaths attributed to lung cancer. It is also responsible for a wide spectrum of cancers and other health problems. Evidence suggests that smoking may have significant adverse effects on many other acute disorders and chronic diseases [6]. This includes an increased risk and/or severity of diseases like pneumonia, sepsis, delirium, cerebrovascular accidents, and myocardial infarction, diverticulosis and perioperative complications after elective surgery [3,4]. Women who smoke cigarettes have a greater chance of complications during and after pregnancy, including Sudden Infant Death Syndrome (SIDS). Second-hand smoking is also of serious concern as non-smokers constantly breathe in the carcinogenic substances released in cigarette smoke, which increases the overall risk of many of the aforementioned diseases in the general population and constitutes a serious threat to public health [7].

In order to evaluate the core functioning of the lungs, Pulmonary Function Test (PFT) is essential. By assessing PFTs which includes lung volumes, lung capacities, rates of flow and gas exchange, we get information which helps us to diagnose multiple lung disorders, especially COPD. This is particularly important for patients complaining of shortness of breath. It can also be very useful to identify early-stage abnormalities in asymptomatic, adult smokers because clinical features of COPD often present later in the course of the disease. However, at present, PFTs are only recommended for patients with positive pulmonary symptoms.

In recent years, PFTs are easily available and the cost of each PFT ranges from approximately 7.5 to 22.5 U.S. Dollars [8]. Due to these reasons, it has become the investigation of choice for screening and detection of pulmonary diseases in smokers. Also, PFTs detect changes in lung volumes even in asymptomatic smokers, which can help us to evaluate the damage done to the lungs before any signs and symptoms develop [9]. Moreover, the increased awareness of the findings of studies such as this may help the patients to quit smoking which in turn can reduce morbidity and mortality rates [10,11]. Hence, it has become very important for physicians to give preference to PFTs even in asymptomatic smokers so that the major chronic diseases can be prevented. The present review seeks to advocate the benefits of PFTs and promote awareness, with the recommendation that physicians advise the test as early as possible, without waiting for COPD symptoms to appear.

CONSUMING TOBACCO IN VARIOUS FORMS: AN ANCIENT HABIT

Tobacco has been consumed since 5000 BC in the American Continent as part of shamanistic rituals. It later became a part of European culture [12,13]. Since then, tobacco has been consumed in many forms across cultures. Currently, the most common route of tobacco intake is via smoking cigarettes. The second most common substance which is smoked is cannabis [14]. Generally, the tobacco in India is smoked in different forms, including beedis, cigars, cigarettes, electronic cigarettes, hookah, pipe smoking, hand-rolled cigarettes etc., [15]. Tobacco is also consumed in India in other forms such as paan, maawa, and gutka.

MECHANISM OF ACTION/PHYSIOLOGY AND ADVERSE EFFECTS OF SMOKING

The active substances in tobacco take effect when the leaves are burned and the vaporized gas that emerges is inhaled by the smoker. It is then quickly absorbed into the alveolar walls and enters the blood stream. The substances contained in cigarette smoke give rise to the disease process as follows:

Inflammatory reaction with reference to COPD: Accumulation of inflammatory cells such as CD8+ T-lymphocytes, B cells, neutrophils and macrophages, in response to irritants found in smoke inhalation, is responsible for an inflammatory reaction phase [15]. Activation of these cells causes release of various inflammatory mediators like Tumor Necrosis Factor – Alpha (TNF-α), Interleukins (IL-1, IL-6, IL-8), Interferon Gamma (IFN-γ), Matrix-Metalloproteinases (MMP-6, MMP-9), C-Reactive Protein (CRP), and fibrinogen [16]. These mediators then lead to local tissue damage which causes chronic inflammation. Chronic inflammation leads to many structural and functional changes in the lungs, which accelerate the development of COPD (emphysema and chronic bronchitis).

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

COPD is defined as a preventable and treatable disease which is characterized by continuous airflow limitation that is generally progressive. It is also associated with an increase in chronic inflammatory response in the lungs to noxious particles or gases [17].

Tobacco smoking is the most common cause of COPD, along with a number of other factors such as air pollution and genetics playing a smaller role in the pathogenesis [18]. In the developing world, one of the prevalent sources of air pollution is from poorly vented cooking and heating fires. Long-term exposure to these irritants causes an inflammatory response in the lungs resulting in narrowing of the small airways and the breakdown of lung tissue, giving rise to Emphysema [17]. The diagnosis of COPD is based on poor airflow measurements which can be observed in PFT [19].

PULMONARY FUNCTION TESTS

PFTs are non-invasive diagnostic tests that provide an understanding of the quality of lung function. PFTs should be considered in symptomatic lung diseases or for those with the presence of risk factors to develop lung diseases [20]. This can be done by assessing lung volumes, capacities, rates of flow and gas exchange. When a patient is referred for PFTs, a series of tests are carried-out which includes: spirometry, diffusing capacity for carbon monoxide, static lung volume measurement, respiratory muscle strength, airways resistance and arterial blood gases. Spirometry is the most important component in PFT [21].

Spirometry is the measurement of the volume of air inhaled and exhaled, with respect to the function of time [22]. Spirometry measures the following volumes: Forced Vital Capacity (FVC) — the total volume of air that is forcibly exhaled from the beginning of complete inspiration; Forced Expiratory Volume (FEV1) in one second—the air exhaled in the first second of FVC and (FEV1/FVC ratio)— the ratio of FEV1/FVC expressed in percentage. Furthermore, it can also measure Slow Vital Capacity (SVC), Tidal Volume (TV), Expiratory Time (TE), Inspiratory Time (TI) and FEV1/SVC (the ratio of FEV1 to the SVC).

Spirometry is the most effective way of determining the severity of COPD. A major advantage of spirometry is that it enables us to detect volume changes even before symptoms of a disease become apparent. Thus, it can confirm the presence of COPD even in mild or moderate stages [23].

AIRFLOW MEASUREMENTS IN COPD PATIENTS [24]

In a healthy and normal adult male, FEV1 are above 80% of the predicted value and the ratio of FEV1/FVC is normal between 0.7 and 0.8. Values below 0.7 are suggestive of an airway obstruction (COPD), except in older adults where values 0.65–0.7 may be normally seen. The severity of COPD is decided on the basis of the GOLD criteria depicted in [Table/Fig-1].

I: Mild COPD	FEV1/FVC < 0.7 FEV1 ≥ 80% predicted	At this stage, the patient may or may not be aware that their lung function is abnormal.
II: Moderate COPD	FEV1/FVC < 0.7 50% ≤ FEV1 < 80% predicted	Symptoms usually progress at this stage, with shortness of breath typically developing on exertion.
III: Severe COPD	FEV1/FVC < 0.7 30% ≤ FEV1 < 50% predicted	Shortness of breath typically worsens at this stage and often limits patients' daily activities. Exacerbations are especially seen beginning at this stage.
IV: Very Severe COPD	FEV1/FVC < 0.7 FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure	At this stage, quality of life is very appreciably impaired and exacerbations may be life-threatening.

[Table/Fig-1]: Gold spirometric criteria to assess COPD severity [25-27].

ASSOCIATION OF ABNORMAL PFT CHANGES WITH SMOKING

Cigarette smoking is the most important risk factor for COPD. Cigarette smokers generally have a higher probability of respiratory symptoms which are often accompanied by pulmonary function abnormalities with a greater annual rate of decline in FEV1 as compared to non-smokers. Cigarette smokers tends to have higher mortality rate followed by pipe and cigar smokers when compared with non-smokers [17,28].

There is a rapid decline in PFTs due to smoking. This decline is more evident in tests indicating the diameter of airways such as FEV1. Obstruction in small airways is indicated by decrease in maximal expiratory flow volume in flow rates. This decline in volume can be even seen in teenagers who have smoked only for a few years. If smoking causes noticeable changes in small airway calibre at such an early age, smoking will also cause acute changes in these small airways. It is suggested that 15% to 20% of heavy smokers develop airway obstruction due to abnormalities in airways with less than 2mm internal diameter. Airway obstruction is associated with a chronic inflammatory process in the membranous and respiratory bronchioles, as shown by previous studies. The airway constriction in COPD and decline in PFTs are thought to be irreversible [29].

As a person smokes over a period of time, his/her lung volumes decrease. Thus, it is evident there is a need for early detection, to prevent long term morbidity and mortality due to smoking related illnesses. Lower pulmonary function test results and the obvious deleterious impact of smoking on quality of life can be emphasized, which may serve as evidence to help convince the patient to contemplate quitting the habit. Due to the prevalence of smoking, early screening may lead to an overall improvement in community health.

DISCUSSION

The U.S. Preventive Services Task Force (USPSTF) has previously recommended that clinicians should not screen asymptomatic patients for COPD [30]. Again, the same recommendation has been published recently in the Journal of American Medical Association [31]. The USPSTF found no evidence in the literature that screening in asymptomatic individuals improves health-related quality of life, morbidity and mortality. Furthermore, the task force described that early detection of COPD in such patients has no bearing on patient outcomes.

In 2011, the American College of Physicians (ACP), American College of Chest Physicians (ACCP), American Thoracic Society (ATS) and European Respiratory Society (ERS) had recommended that spirometry should be used in order to diagnose airflow obstruction in patients with respiratory symptoms and not asymptomatic patients [32].

In 2010, the United Kingdom National Institute for Health and Care Excellence (NICE) suggested that at least a patient (smoker) should have one respiratory symptom to be considered for PFT [33]. The Global Initiative for Chronic Obstructive Lung Disease issued guidelines which also did not recommend screening asymptomatic populations for COPD [34].

But with that said, there are many clinical studies which have been conducted since last few decades, shows the advantage of using PFT in asymptomatic patients.

In 1977, Fletcher and Peto conducted an epidemiological study of the early stages of COPD in London. They concluded that FEV1 falls gradually over time. Smoking causes irreversible obstructive changes which do not revert back to normal even if smoking is stopped, but the average further rates of loss of FEV1 will decline [35]. Therefore, COPD can be prevented by conducting PFTs in the early middle age in smokers, which can help the doctors to encourage patients to stop smoking.

In 1993, Yang SC conducted a study on 311 healthy normal Chinese men to evaluate the association between smoking habits and lung function changes with conventional spirometry. A total of 180 non-smokers and 131 smokers between 28 to 78 years of age were included in the study. When current and ex smoker's PFT, were compared with that of non-smokers, the FEV1/FVC ratio was significantly lower in the former than that of later. They also concluded that in some cases, a person may have a history of up to 5 years of smoking before PFT changes are demonstrated. Thus, this study concluded that cigarette smoking is undoubtedly associated with a decrease in pulmonary function, although these changes may take some time to develop and may not be immediately apparent after taking up the smoking habit [36]. This study further justifies the early use of PFTs in asymptomatic smoking adults.

Jan Zielinski and Michal Bednarck in the year 2001, conducted a clinical study on 11,027 subjects in order to evaluate the efficacy of spirometry in detecting early airflow abnormalities. Signs of airway obstruction were found in 24.3% of the subjects who were screened. The spirometry screening test was conducted in the smokers with a smoking history of more than 10 packs/year and age being more than that of 39 years. Airway obstruction was found in 30.6% of smokers aged ≥40 years with smoking history >10 pack/year. In younger smokers aged <40 years, who had a smoking history of <10 pack/year, airway obstruction was found to be 8.3%. Airway obstruction was found to be 14.4% in 2200 subjects who had never smoked. Therefore, the maximum changes seen in PFTs were clustered among smokers who were less than 40 years of age [37]. Thus, it becomes of utmost importance to conduct PFTs at the earliest in order to reduce COPD incidence, even in asymptomatic patients.

Nicholus R. Anthonisen and John E. Connett in the year 2002 conducted a study on 5887 subjects to examine the effect of smoking on FEV1 through spirometry. They observed subjects with a history of smoking for 11 years continuously, 38% of smokers had an FEV1 less than 60% of the predicted normal value compared with 10% of sustained quitters [38]. Therefore, the findings of this study also showed that giving up smoking at the earliest would help revert the PFT values to normal.

Viju T Mhase et al., in 2002 conducted a study to evaluate the effect of smoking on workers exposed to dust and fumes using PFTs. They conducted PFTs in 115 workers occupationally exposed to dust and fumes, irrespective of their present complaint(s). Parameters such as FVC, FEV1, and FEV1/FVC ratio were noted. It was noted that respiratory disorders were significantly higher in smokers and were correlated to their smoking behaviour. The deviation in parameters was found to be as follows—FVC ($p<0.001$), FEV1 ($p<0.001$) and FEV1/FVC ($p<0.001$)—suggesting the combined effect of smoke and dust or fumes on the disease process [39].

Mohammad H.B. et al., in 2003 conducted a study with PFTs in smokers, which concluded that smoking leads to the constriction of large and medium airways. The constriction was correlated with the duration of smoking instead of the quantity of smoking [40]. These findings reinforce our viewpoint on the benefits of conducting PFTs early, even in asymptomatic smokers.

Urrutia Isabel and Sunyer Jordi in 2005 conducted a study on 1500 male and female subjects, aged between 20-45 years. This study evaluated the independent correlation of smoking with respiratory symptoms and lung function in young adults. After conducting spirometry, they concluded smoking was associated with an increased risk of chronic bronchitis and other respiratory symptoms. They further stated that the risk of pulmonary diseases was directly related to the number of cigarettes smoked per day. Furthermore, the decrease in FEV1 and FEV1/FVC ratio was directly associated with the number of cigarettes smoked per day. The PFT changes were also noted in young adults that can have devastating consequences if not acted upon early [41].

Aslam Khan et al., in 2010 concluded that the prevalence of undetected airflow obstruction in smokers is high. Therefore, targeted screening and regular follow-up in smokers should be considered in order to view the decline in pulmonary function [42].

S. Clennell et al., in 2008 conducted a cohort study on 3286 subjects, between 43 and 53 years of age, to study the lung function in smokers, non-smokers and former smokers. The study concluded that the rate of lung function decline of the current smokers was faster than non- smokers by a rate of 8.4ml/year (95% CI –12.0 to –5.0). However, the study found no significant difference in rate of decline in lung function in former smokers when compared to those who had never smoked. When smoking status at age 25 years was examined for rates of change in lung function, similar results were obtained [43].

Rubeena Bano et al., (2009) conducted a study which noted that in India, smoking is a common habit prevalent in both urban and rural areas. The study examined the PFT findings amongst smoking and non-smoking adults in a rural area. Spirometry screening test were performed on 100 male subjects that comprised of 50 smoking and 50 non-smoking adults. There was significant reduction in almost all the pulmonary function parameters in smokers, most common of which was obstructive pulmonary impairment. It was also observed that pulmonary function was 17.3 times more impaired in smokers as compared to that of non-smokers. Majority of the people who subsequently developed COPD were found to be light smoker in the age group of 41-50 years, who continued to smoke [44].

Similarly, Burrows et al., stated that there is a quantitatively significant association between the decrease in ventilator function and duration and frequency of smoking. Early diagnosis of COPD with the help of PFTs can expedite the development of a treatment plan and expedite management [45].

Ritesh M. Karia et al., in 2012 studied the effects of smoking on various spirometric parameters like FVC, FEV1 and FEV1/FVC ratio in apparently healthy tobacco smokers and non-smokers, and compared the result of both the studies to assess the effects of smoking. The results indicated that the actual values of spirometric parameters are significantly lower in all smokers (even mild smokers) than in non-smokers. The significant change in the PFT values in mild smokers shows the importance of conducting PFTs from the beginning [46].

A review of data collected by Jeneth Berlin Raj T. et al., leads us to believe that in 62% of asymptomatic smokers there was a decrease in expiratory volume. This highlights the importance of monitoring the pulmonary function in all smokers, even without the presence of symptoms suggestive of smoking-related illnesses. Therefore, a decline in lung function can be picked up even by spirometry. Early intervention and cessation of smoking can lead to the reduction of morbidity and an increase in quality of life parameters [47].

A recent study conducted by Anand Mistry et al., aiming to find out a difference in PFT values in smokers and non-smokers. It showed a decrease in FEV1/FVC ratio with an increase in the number of years of smoking. The mean FEV1/FVC ratio in the patients who had smoked for 11-20years was 74.48, 21-30years was 72.16, 31-40years was 70.70. They also compared the FEV1/FVC ratio between smokers and smokers by dividing them into age groups. At every age group, smokers group had reduced PFT values, making them prone to get COPD in future. Hence, it is beneficial to conduct PFT at the earliest and help the patients to quit smoking [48].

Sunita Nighute in 2011 concluded that there was a significant reduction in the PFT mean values in smokers as compared to non-smokers ($p<0.001$). This study was conducted on 100 subjects, out of which 75 subjects had normal while 25 had impaired lung functions. Among the 25 subjects with impaired function, 24 were smokers and only one was a non-smoker. The risk of having impaired pulmonary functions was 18 times more in smokers as compared to non-smokers [49].

Juan Wisnivesky et al., in 2014 conducted a study which showed that screening of asymptomatic smokers using spirometry can help detect a small number of patients with airway obstruction who are at high risk for COPD. Airway obstruction on spirometry was observed in nine study subjects out of total 386 asymptomatic smokers (2.3%, 95% confidence interval: 1.1–4.4%) [50].

In a recent study conducted by Barthwal MS in 2014, the overall burden of COPD is likely to reduce by early detection of COPD using spirometry especially in smokers more than 40 years of age and with smoking index of more than 200. In this study, a total of 460 individuals were evaluated by spirometry. Obstruction was seen in 58 (12.60%) subjects, of which 40 (68.9%) showed mild obstruction and 18 (31%) moderate obstruction. In subjects, whose age was less than 40 years, airway obstruction was noticed in 24 (8.82%) while 34 subjects (18%) showed obstruction ($p<0.005$) with above 40 years of age. In subjects, with smoking index more than 200, obstruction was noticed in 42 (24.70%) out of 170 individuals and 16 (5.51%) out of 290 individuals with smoking index of less than 200 ($p< 0.005$). In smokers having smoking index of more than 200 (n=184) and 40 years of age, obstruction was seen in 48 (26%) while that in smokers having smoking index less than 200 (n=276) and less than 40 years of age, obstruction was seen in 15 individuals (5.43%) ($p<0.005$) [51].

In a recent study conducted by Raul H Sonsores et al., in 2015 it was observed that out of 637 asymptomatic smokers, the prevalence rate of COPD was 7%. They further stated that FEV1 was the only predictive factor for COPD in asymptomatic smokers. Hence, it suggested that early use of PFT should be encouraged in asymptomatic smokers as well [52].

In summary, there is contrasting evidence that early assessment using various PFTs can help to detect lower lung function in asymptomatic smokers. But, early detection and proper counselling for smoking cessation can prevent future morbidity and reduce the prevalence of illnesses associated with the smoking habit. Hence, we would suggest the physicians to conduct PFTs at the earliest to rule out COPD by assessing lower lung function values in asymptomatic patients.

CONCLUSION

These studies show that the prevalence of smoking at younger age is increasing daily, which has also been reported in the CDC Guideline Surgeon General's Report 2012 on tobacco use among youth and teens ages from age 18 to 25years.

Due to the advent of PFTs, physicians do not have to wait for the clinical features of pulmonary disease to develop in smokers. It may take some time to demonstrate the abnormal changes in the PFTs, but it is worthwhile to conduct these tests at the earliest. Long-term benefits to the individual and overall community health will be substantial.

Today, PFTs are easily conducted and universally accessible. Moreover, PFTs have been available at around 500 to 1,500 Indian rupees which are approximately 7.5 to 22.5 U.S. Dollars. In view of these conclusions, it should be established as the investigation of choice for screening and detection of early pulmonary disease in smokers.

Thus, we conclude that PFTs should be performed early in smokers (excluding the ones in which PFT are contra-indicated) to rule out reduction in lung volumes and cessation of smoking should be encouraged, especially in countries like India where tobacco is smoked on a large scale.

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PARTICULARS OF CONTRIBUTORS:
1. Student, MGM Medical College, Navi Mumbai, Maharashtra, India.
2. Student, MGM Medical College, Navi Mumbai, Maharashtra, India.
3. Student, B. J. Medical College, Ahmedabad, Gujarat, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Varshil Mehta,
103, Sky High Tower, Orlem, Tank Road, Malad West, Mumbai-400064, Maharashtra, India.
E-mail: varshil91@gmail.com

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