Spirometry screening for airway obstruction in asymptomatic smokers

Juan Wisnivesky
Gwen Skloot
Andrew Rundle
Tracey A Revenson
Alfred Neugut

Background

Screening spirometry might help identify patients with chronic obstructive pulmonary disease (COPD) at an earlier stage. In this study, we evaluated the prevalence of airway obstruction in a cohort of asymptomatic smokers who underwent spirometry as part of a routine health maintenance examination.

Methods

The study cohort consisted of a consecutive sample of 386 asymptomatic smokers (≥5 pack-years) without a history of COPD or asthma, who completed spirometry testing as part of a routine health maintenance examination.

Results

Overall, 9 study subjects (2.3%, 95% confidence interval: 1.1–4.4%) had evidence of airway obstruction on spirometry. Univariate and multiple regression analyses showed that the risk of airway obstruction was not significantly associated with age, sex, race, smoking history or past history of respiratory symptoms.

Discussion

Spirometry screening of asymptomatic smokers may help detect a small number of patients with airway obstruction who are at high risk for COPD.

Keywords

mass screening; spirometry; pulmonary disease, chronic obstructive

Chronic obstructive pulmonary disease (COPD) is a respiratory disorder characterised by longstanding airflow obstruction caused by emphysema or chronic bronchitis.[1] The disease typically presents with symptoms of chronic cough, exertional dyspnoea, expectoration of sputum and wheeze in conjunction with airway hyperresponsiveness. Affecting approximately 10% of the general population, COPD is responsible for significant morbidity, early mortality, high death rates and substantial costs to the healthcare system. COPD is projected to be the third most frequent cause of death worldwide by 2020 and the fifth leading cause of years lost through early disability.[2] Numerous epidemiological studies show that smoking is overwhelmingly the most important risk factor for COPD.

COPD is frequently underdiagnosed in clinical practice; several studies show that 25–50% or more of patients found to have COPD on screening spirometry have no prior or current diagnosis of COPD.[3–7]Another barrier to appropriate treatment is that COPD is frequently diagnosed late in its natural course, when lung function is poor and therapeutic options are mostly palliative.[6] During early stages of the disease, patients may adapt to their condition or neglect milder symptoms, delaying diagnosis. Moreover, mild and even moderate COPD can occur without complaints or symptoms, also impeding early diagnosis.[8]

Screening by means of spirometry might increase detection of COPD in early stages. Early diagnosis may motivate smoking cessation, which is known to slow down the loss of lung function associated with COPD. Few studies have evaluated the use of spirometry for COPD screening.[6, 9–11] Most of these studies included symptomatic subjects, non-smokers or patients with a known prior history of obstructive lung disease. Thus, the potential value of spirometry screening for early diagnosis of COPD in asymptomatic smokers remains undetermined. In this study we used data from a consecutive cohort of asymptomatic smokers undergoing a health maintenance examination, to investigate the prevalence of airway obstruction suggestive of COPD and to identify risk factors of abnormal spirometry.

Methods

The data for this study were obtained from a consecutive cohort of asymptomatic smokers who underwent a health maintenance examination at the New York City offices of EHE International, Inc (EHE) between January 2008 and December 2010. EHE provides annual routine screening physical examinations as part of a corporate preventive medicine plan.[12] The examinations are provided free of charge to employees and their spouses. Potential participants were identified from EHE's electronic database. Participants were eligible if they were ≥30 years old, had a smoking history of ≥5 pack-years, and had completed spirometry testing as part of the examination. We excluded people with a physician diagnosis of asthma, COPD or another chronic respiratory condition, as well as those reporting active pulmonary symptoms (an indication for diagnostic spirometry). Additionally, the study was limited to white and African American participants, as predictive equations for normal lung function values have not been well validated for other

racial or ethnic groups.[13] The Institutional Review Board of Mount Sinai School of Medicine approved the study protocol (approval number 11-0270).

Sociodemographic data (age, sex, race, ethnicity, and marital status) were obtained from a standardised health questionnaire routinely administered before health maintenance examinations. The survey includes validated items to collect information about smoking history, including age of initiation, number of years of smoking, average number of cigarettes smoked per day, whether the subject was an active or former smoker and, for former smokers, approximate date of discontinuation. Using this information we classified individuals as current or former smokers and calculated the number of pack years smoked by each study subject. Data were also collected about self-reported history of physician diagnosis of asthma or COPD, as well as about respiratory symptoms (past, current, or never) of cough, blood-streaked mucus, wheezing and snoring.

Spirometry was performed by trained respiratory technicians using a spirometer (Spirovit SP-1, Schiller America, Doral, FL) and following standard procedures.[14,15] Prior to spirometry, participants underwent weight and height measurements. The best forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were recorded and the FEV_1/FVC ratio was calculated. Spirometric results were compared to age-, sex-, race- and ethnicity-dependent reference values and interpreted following established guidelines.[13] Obstruction was defined as FEV_1/FVC below the lower limit of normal (LLN; ie. the 5th percentile of a healthy, non-smoking population).

Statistical analyses

The proportion of participants with evidence of airway obstruction on spirometry was calculated with 95% exact confidence intervals based on the binomial distribution. Differences in the baseline characteristics of subjects with and without airway obstruction were evaluated using the Wilcoxon test or Fisher's exact test, as appropriate. Exact logistic regression analysis was used to evaluate the independent predictors of airway obstruction on spirometry testing. All analyses were conducted with SAS software (SAS Institute, Cary, NC).

Results

Between January 2008 and December 2010, 487 asymptomatic smokers eligible for the study were identified from EHE's computerised database. Of these, we excluded 32 individuals (7%) due to poor spirometry technique, 4 (1%) due to missing spirometry results, 54 (11%) who were classified as Asian, 'other race' or of Hispanic ethnicity, and 11 (2%) who were <30 years of age, leaving a cohort of 386 study participants each contributing a single spirometry assessment. The baseline characteristics of the study cohort are described in *Table 1*. Mean age of the study population was 50±9 years and 66% were male. Overall, 95% of subjects were classified as white and 5% as African American. The median number of pack-years smoked for the study cohort was 16, interquartile range 12.

Overall, 9 study subjects (2.3%, 95% confidence interval [CI]: 1.1–4.4%) had evidence of airway obstruction on spirometry (FEV_1/FVC ratio below LLN). Univariate analysis showed that rates of airway obstruction were not significantly different according to age, sex, race or marital status (P>0.05 for all comparisons). Similarly, we did not find significant differences in the prevalence of airway disease according to number of pack-years of smoking or between participants who reported being current,and those who were former smokers (P>0.05 for both comparisons). A prior history of respiratory symptoms (wheezing, chronic cough, blood-streaked sputum or snoring) was also not significantly different across the two study groups (P>0.05 for all comparisons). Multiple regression analysis showed that age (odds ratio [OR]: 1.24, 95% CI: 0.16–15.22 for 40–49 years and 0.48, 95% CI: 0.05–7.16 for ≥50 years versus 30–39 years), male sex (OR: 1.42, 95% CI: 0.27–9.56), body mass index (OR: 0.32, 95% CI: 0.28–2.20 for 25–30 kg/m^2 and 0.63, 95% CI: 0.06–4.25 for ≥30 kg/m^2 versus <25 kg/m^2), number of pack-years (OR: 0.88, 95% CI: 0.12–6.42 for 10–15 pack-year and 1.25, 95% CI: 0.15–10.41 for >15 pack years versus 5–10 pack-years) or current smoking (OR: 1.03, 95% CI: 0.10–6.25) were not independently associated with the presence of airway obstruction (*Table 2*).

Discussion

COPD is a highly prevalent condition that is associated with considerable morbidity, premature disability, mortality and high healthcare expenditure. The disease is frequently unrecognised or only diagnosed at a late stage, when there are very limited interventions to arrest the progressive nature of COPD. In this study, we evaluated the results of spirometry screening on a large cohort of asymptomatic smokers undergoing a health maintenance examination. We found that the prevalence of undiagnosed airway obstruction in this population was 2.3%. While these findings suggest it may be feasible to identify asymptomatic smokers with airway obstruction, additional data about the actual benefit of early interventions and the cost-effectiveness of screening are needed before spirometry can be routinely adopted in clinical practice.

There have been prior attempts to detect undiagnosed COPD patients using screening spirometry or case finding. An epidemiological study in Poland found airway obstruction in 23% of the participants screened for COPD.[11] A prospective survey and spirometry testing of participants aged 35–70 years (30% smokers) visiting their primary care physician found evidence of obstructive airway disease in 18% of participants with respiratory complaints, compared with only 4% among those without symptoms.[9] Bednarek and colleagues performed a case-finding study in 1960 primary care patients over 40 years of age using a questionnaire, physical examination, and spirometry.[6] This study revealed that approximately 9% of these patients had airway obstruction only 18% of whom had been previously diagnosed with COPD. Similarly, a study in two general practices in the Netherlands found that 18% of patients had evidence of airway obstruction on spirometry.[10] However, these studies included patients with respiratory symptoms, a factor that may explain the higher rates of airway obstruction among the participants. Symptomatic smokers should undergo diagnostic spirometry and thus, would not be considered candidates for screening. Additionally, several studies included participants with known COPD as well as non-smokers, further limiting the generalisability of their results. Conversely, our study focused on asymptomatic smokers without history of obstructive lung disease, which is the most logical choice of candidates for spirometry screening for early detection of COPD.

Classical screening criteria suggest, among other things, that there should be an accepted treatment for the condition being diagnosed early and that the cost of case finding and treatment should be economically balanced with other medical expenditures.[16] The potential benefits of spirometry screening of high-risk individuals are primarily related to the possibility of initiating smoking cessation interventions. Cigarette smoking is the most important risk factor for the development and progression of COPD and smoking cessation is the most effective intervention to slow down loss of lung function.[17,18] Prior studies have demonstrated that smoking cessation at an early stage of COPD is associated with an improvement in FEV_1 followed by a decline in lung function that is comparable to that of non-smokers.[17] Smokers may be more motivated to stop smoking if they became aware that they already have evidence of airway disease and, consequently, are at high risk of developing symptomatic COPD or other tobacco-related conditions. Thus, early diagnosis of airway obstruction might create a period of high motivation, potentially increasing the effectiveness of physician counselling and/or smoking cessation treatment. Moreover, smoking cessation counselling combined with spirometry testing has been shown to increase the success of smoking cessation interventions in COPD patients in some studies.[19,20] However, the evidence supporting spirometry as an independent motivational tool for smoking cessation remains inconclusive.[21] Additionally, active smokers with normal spirometry may feel reassured and be less motivated to engage in smoking cessation activities, a potential unwanted consequence of screening.

COPD is characterised by airway and systemic inflammation; inhaled corticosteroids may be useful in reducing this inflammation.[22] Treatment of asymptomatic smokers with airway obstruction with anti-inflammatory drugs might be another intervention that, in addition to smoking cessation, could slow down the

Table 1. Baseline characteristics of study participants according to the presence of obstructive airway disease

Characteristic	Total (n = 386)	No obstruction (n = 377)	Obstruction (n = 9)	*P* value
Age in years, median (IQR)	51 (43–80)	51 (43–80)	45 (40–54)	0.11
Sex, n (%)				0.62
Male	253 (66)	247 (66)	6 (67)	
Female	133 (34)	130 (34)	3 (33)	
Race, n (%)				0.99
White	367 (95)	358 (95)	9 (100)	
African American	19 (5)	19 (5)	0 (0)	
Marital status, n (%)				0.17
Married/domestic partner	291 (75)	286 (76)	5 (56)	
Separated/divorced/widowed	45 (12)	43 (11)	2 (22)	
Single	50 (13)	48 (13)	2 (22)	
Body mass index, kg/m^2, median (IQR)	26 (24–30)	27 (24–30)	25 (24–27)	0.56
Smoking status, n (%)				0.66
Current	67 (17)	65 (17)	2 (22)	
Former	318 (83)	311 (83)	7 (78)	
Pack-years, median (IQR)	11 (8–20)	11 (8–20)	11 (8–16)	0.55
History of respiratory symptoms				
Wheezing, n (%)				0.99
Never	341 (89)	333 (89)	8 (89)	
Past	44 (11)	43 (11)	1 (11)	
Chronic cough, n (%)				0.99
Never	349 (91)	340 (90)	9 (100)	
Past	36 (9)	36 (10)	0 (0)	
Blood-streaked mucus, n (%)				0.99
Never	370 (96)	361 (96)	9 (100)	
Past	15 (4)	15 (4)	0 (0)	

IQR: interquartile range

progression of disease.[23] The impact of inhaled corticosteroids treatment on disease progression, as measured by the annual rate of FEV_1 decline, has been evaluated in several randomised trials and meta-analyses.[24–31] The largest randomised study, the TORCH trial, showed that inhaled corticosteroids slowed the decline in lung function in 6112 patients with moderate-to-severe COPD.[32] Similarly, one of the meta-analyses also found that inhaled corticosteroid therapy positively affected disease progression.[29] However, other studies and a different meta-analysis found no beneficial effect of inhaled corticosteroids on lung function.[28] Additionally, trials evaluating the role of inhaled corticosteroids have not been performed in asymptomatic patients with mild COPD or airflow limitation. Consequently, clear evidence that early detection and subsequent treatment with inhaled corticosteroids leads to clinical benefits in patients diagnosed with COPD is still lacking. Moreover, the cost-effectiveness of a COPD screening program has not been evaluated.

There are some limitations of our study. Although airway obstruction is an essential characteristic of COPD, it is not diagnostic of the disease. In order to diagnose COPD, it is also necessary to measure lung volumes and diffusing capacity of carbon monoxide, to assess reversibility after bronchodilators and to exclude other obstructive lung diseases. However, the finding of airway obstruction among high-risk smokers without history of asthma is highly suggestive of COPD. Additionally, simple spirometry without the use of bronchodilators to find subjects at high risk of COPD is the most reasonable first step to screen an asymptomatic population.

Our study population consisted of a consecutive cohort of individuals undergoing a voluntary health maintenance examination. Thus, selection of healthy individuals may limit the generalisability of our findings. However, study participants are probably representative of the population that would undergo screening if spirometry were adopted during routine primary care visits. Study participants were recruited from a single practice, which may hamper the external validity of our findings.

The typical age of onset of COPD is in the fourth or fifth decade of life and the prevalence of the disease increases with age. We included smokers aged ≥30 years in our study, a factor that may have resulted in lower rates of airway obstruction. However, asymptomatic airway obstruction in susceptible smokers is expected to develop several years before clinically apparent COPD; thus, screening spirometry may include younger subjects. Moreover, rates of airway obstruction were similar in secondary analyses limited to study subjects aged ≥40 years (1.9%) or ≥50 years (1.6%). Given the limitations in the validity of prediction equations for normal spirometry values, we restricted our analyses to non-Hispanic, white and black participants. Thus, we were not able to assess the potential findings of spirometry screening in individuals from other racial or ethnic groups. Finally, given the low prevalence of airway disease in the study population, our study had very limited power to assess if the sociodemographic variables or smoking history were associated with the presence of airway disease.

Table 2. Adjusted association between sociodemographic characteristics and smoking history with airway obstruction

Characteristic	Odds ratio (95% confidence interval)
Age, years	
30–39	Reference
40–49	1.24 (0.16–15.2)
≥50	0.48 (0.05–7.16)
Sex	
Female	Reference
Male	1.42 (0.27–9.56)
Body mass index, kg/m^2	
Normal (<25)	Reference
Overweight (25–30)	0.32 (0.28–2.20)
Obese (≥30)	0.63 (0.06–4.25)
Pack-years of smoking	
5–10	Reference
10–15	0.88 (0.12–6.42)
>15	1.25 (0.15–10.41)
Smoking status	
Former	Reference
Current	1.03 (0.10–6.25)

Implications for general practice

- Spirometry screening of asymptomatic smokers may help detect a small number of individuals with airway obstruction who are at high risk of developing COPD.
- Additional data is necessary regarding the clinical benefit and cost-effectiveness of screening before spirometry can be recommended in general practice.

Authors

Juan Wisnivesky MD, DrPH, Professor of Medicine, Division of General Internal Medicine and Division of Pulmonary, Critical Care and Sleep Medicine, Mount Sinai Hospital, New York, USA. juan.wisnivesky@mountsinai.org

Gwen Skloot MD, Associate Professor Medicine, Division of General Internal Medicine and Division of Pulmonary, Critical Care and Sleep Medicine, Mount Sinai Hospital, New York, USA

Andrew Rundle, Associate Professor of Epidemiology, Co-Director, Obesity Prevention Initiative, Mailman School of Public Health – Epidemiology, Columbia University, New York, USA

Tracey A Revenson PhD, MA, BA, Professor of Psychology, Deputy Executive Officer of the Doctoral Program in Psychology, Hunter College and The Gradute Center, City University of New York, New York, USA

Alfred Neugut DrPH, MPH, BS, Professor, New York Presbyterian Hospital and Columbia University Medical Center of Epidemiology, New York, USA

Competing interests: JW, AR, TAR and AN receive financial compensation as advisory board members for EHE, the company providing the patient information that is being analysed in this study. EHE did not have a role in the design of the study, analyses or interpretation of the data, in the decision to submit the manuscript for publication or in the writing of the manuscript. JPW has received consulting honoraria from UBS, IMS Health, and Merck, and was awarded a research grant from GlaxoSmithKline. GS has no conflict of interest to declare.

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correspondence **afp@racgp.org.au**