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Use of Spirometry for Case Finding, Diagnosis, and Management of Chronic Obstructive Pulmonary Disease (COPD)

Summary

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is manifested by chronic cough, sputum production, wheezing and, in later stages, dyspnea, poor exercise tolerance, and signs/symptoms of right-sided heart failure. Symptomatic COPD affects more than 5 percent of the adult population, is the fourth leading cause of death, and the twelfth leading cause of morbidity in the United States.[1,2] In more than 80 percent of cases, cigarette smoking is causally linked to the development of COPD. Smoking status should be assessed in all adults, and smokers should be advised to abstain from tobacco.

COPD is diagnosed in symptomatic individuals through spirometric testing that demonstrates irreversible airflow obstruction.[3] Spirometry for case-finding diagnosis and management of all adults with persistent respiratory symptoms or having a history of exposure to pulmonary risk factors has been recommended in primary care settings for all current and former smokers as well as never smokers who have persistent respiratory symptomsor have history of exposure to other COPD risk factors. This report was prepared to provide objective evidence and recommendations to inform the work of the American Thoracic Society (ATS), in collaboration with the American Academy of Family Physicians, the American College of Physicians, and the American Academy of Pediatrics Spirometry Task Force in clarifying usage of spirometry as part of the management of COPD. A systematic literature review was undertaken to address four questions:

1. What is the prevalence of COPD and airflow obstructions in various adult populations as defined by: (1) spirometry and (2) clinical examination?
2. Can use of spirometry lead to increased smoking cessation rates?
3. Does the effectiveness of COPD-specific therapies to improve clinically relevant outcomes vary based on baseline severity or change in spirometry?
4. Is prediction of future COPD status based on spirometry, with or without clinical indicators, more accurate than prediction based on clinical indicators alone?

Methods

Articles published in the English language from 1966 to May 2005 were identified by searching MEDLINE® and the Cochrane Database. Because the individual questions addressed different areas, the search strategies, types of eligible studies, populations, interventions, and outcomes varied. Emphasis was placed on studies that assessed outcomes from adults in primary care or population-based settings who had or were at risk for COPD according to race, gender, age, smoking, symptom, and spirometric status.

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Evidence-Based Practice

Children or individuals with asthma, or alpha-1 antitrypsin disease were excluded. Ten cohort studies [4-13] were included to estimate COPD/airflow obstruction prevalence and diagnostic accuracy. Seven randomized controlled trials (RCT)[14-20] met inclusion criteria for smoking cessation studies, 52 RCT[21-72] and six meta-analyses of RCT[73-78] were included for assessment of COPD-specific therapies, and five cohort studies were included for prognosis.[10, 79-82] The main outcomes according to question were:

1. Prevalence of airflow obstruction as determined by spirometry and clinical examination according to race, gender, age, smoking, and symptom status and previous diagnosis of COPD.
2. Long-term sustained smoking abstinence rates among smokers randomized to receive results of spirometry alone or in combination with other interventions compared to controls.
3. Exacerbations, hospitalizations, mortality, and respiratory health status according to type of treatment; baseline symptom status and FEV1; acute change in FEV1 or slope in FEV1 over time.
4. Independent prognostic value of airflow obstruction as determined by spirometric stage to predict future COPD status (stage and symptoms).

Data were used to estimate the number of adults according to smoking status that would require symptom and spirometric assessment and subsequent treatment to prevent COPD exacerbations, reduce mortality or hospitalizations, and improve smoking cessation or respiratory health status.

Results

More than one-third of the adult U.S. population reported respiratory symptoms compatible with symptomatic COPD. Compared to clinical examination, spirometry plus clinical examination improves diagnostic accuracy of clinically significant disease in adults who report respiratory symptoms (especially dyspnea). Based on the National Health and Nutrition Examination Survey (NHANES) III results, 12.8 percent of adults report a current or past diagnosis of obstructive lung disease (emphysema, chronic bronchitis, or asthma). However, only 17.4 percent of adults reporting a diagnosis of chronic bronchitis or emphysema (COPD) had 1987-ATS defined low lung function suggesting that many of these individuals have normal lung function. Fewer than half of individuals reporting a diagnosis of chronic bronchitis or emphysema stated that they were bothered by shortness of breath. Based on gender, age, and smoking status, between 40 and 80 percent of NHANES III participants with low lung function as determined by spirometry in the absence of bronchodilator testing reported no prior clinical diagnosis of COPD. However, there were no data regarding prevalence or type of respiratory symptoms in this group.

Spirometry, when used in primary care settings for case finding of all adults with persistent respiratory symptoms or having a history of exposure to pulmonary risk factors, is likely to label a relatively large proportion of individuals as diseased with airflow obstruction but who do not have respiratory symptoms or whose symptoms are unlikely to affect their health status. Conversely, spirometry is normal in a relatively large percentage of adults who report respiratory symptoms including dyspnea, the respiratory symptom having the greatest impact on quality of life. Prevalence and severity of airflow obstruction and symptomatic COPD vary widely according to definitions utilized and country and populations studied. The percentage of adults having normal spirometry and no respiratory symptoms (normal/asymptomatic) ranged from 56 to 91 percent. Compared with previous definitions of airflow obstruction, use of recent criteria tripled the number of adults being labeled as "at-risk" or having "low lung function" (from 6.8 to 20 percent). Normal spirometry with chronic sputum production ("at-risk") was present in 7.2 percent of subjects. An additional 13.9 percent of adults had prebronchodilator spirometrically detected airflow obstruction (mild, moderate, or severe to very severe airflow obstruction = 7.2 percent, 5.4 percent, and 1.5 percent respectively). Prevalence was higher in current smokers and older individuals. The percentage of individuals reporting respiratory symptoms increased with airflow obstruction severity. However, one-third of individuals with normal spirometry reported respiratory symptoms (21 percent reported shortness of breath). Some of these individuals may have had asthma and thus might have normal spirometry at the time of testing. Approximately, 21 percent of individuals with severe to very-severe airflow obstruction (similar to Global Initiative for Obstructive Lung Disease Stage 3,4) were asymptomatic and 35 percent did not report shortness of breath.

Smoking cessation is the most important factor in reducing the development and/or progression of airflow obstruction and symptomatic COPD. All adults should be asked about smoking and current smokers encourge to quit. However, evidence indicates that baseline symptom and spirometric status are of limited clinical use in reliably predicting a patient's future likelihood of quitting smoking. Spirometric testing as a motivational tool to improve smoking cessation rates is unlikely to provide more than a small benefit. Results from observational studies of spirometry are mixed. RCT of other biomarkers used as motivational tools for smoking cessation are generally negative. The only randomized controlled trial that

assessed the independent contribution of spirometry and counseling on smoking cessation rates reported a nonsignificant 1 percent greater quit rate at 12 months in the group assigned to receive spirometry plus repeat counseling compared to repeat counseling alone (6.5 percent vs. 5.5 percent). Quit rates were lower in the spirometry group than in participants who received repeat counseling plus nicotine replacement therapy (7.5 percent). Two other studies approximated an independent effect and their results were mixed. The self-reported 6-month point prevalent abstinence rates for the intervention group assigned to receive spirometry in combination with advice plus carbon monoxide values were lower than the group that received advice alone (9 percent vs. 14 percent). The one study that showed an improvement in smoking cessation rates compared a 50-minute educational intervention with a group that received the educational intervention plus a questionnaire and discussion of symptom status, spirometric results, and carbon monoxide levels. At 12 months, the biologically verified point prevalent quit rates were 20 percent in the intervention group and 6.7 percent in the control group. Four other trials that evaluated spirometry demonstrated an improvement in smoking cessation but all included concomitant interventions proven to increase abstinence.

Spirometry is useful for determining at what threshold of airflow obstruction initiation of therapy is likely to improve clinical outcomes in adults with bothersome respiratory symptoms. However, monitoring with spirometry to guide additional therapy or to initiate interventions in individuals who do not report bothersome respiratory symptoms does not appear to be beneficial. COPD trials typically were of short duration, they involved subjects with an established clinical diagnosis of COPD who had moderate to severe respiratory symptoms, frequent COPD exacerbations, and severe to very severe baseline airflow obstruction, and they used varying outcome definitions for exacerbations. On average, interventions reduced the relative risk of exacerbations by 20 to 25 percent and the absolute risk by 5 to 6 percent. Treatments improved measures of dyspnea and respiratory functional status, although the average improvement from inhaled bronchodilators and corticosteroids on validated health status measures failed to achieve a predetermined level of clinical significance. However, some individuals will notice greater and clinically significant improvement in respiratory symptoms. Few studies reported information on hospitalizations, but in those that did reduction was 4 to 7 percent. Mortality was similar between treatment and control groups, though there were relatively few events and the available information cannot rule out an improvement with long term inhaled treatment. Information related to the effectiveness of short-acting inhaled medications used for acute symptomatic rescue therapy was not available.

Benefits from interventions are mostly limited to reduction in exacerbations in patients having activity limiting respiratory symptoms and severe to very severe airflow obstruction (FEV1 <50 percent predicted). Five large studies of greater than 1-year duration (one assessing a short-acting anticholinergic and four evaluating inhaled corticosteroids) found little to no improvement in respiratory outcomes among subjects with mild to moderate airflow obstruction or those with normal airflow but having chronic sputum production ("at risk" individuals). Analysis of one of these studies that enrolled a subgroup of individuals that had mild to moderate airflow obstruction but denied respiratory symptoms demonstrated that ipratropium did not prevent development of symptoms at 3 years of followup. Subgroup analysis of other studies indicated that treatment benefit was almost exclusively confined to adults with bothersome respiratory symptoms and severe to very-severe airflow obstruction. Five additional comparative studies of long-acting inhaled b-agonists and corticosteroids indicated that combination therapy was similar to monotherapy regarding exacerbations (ARR 1-2 percent) and mortality (ARR 0-1 percent). Combination therapy with short- or long-acting beta-agonists plus anticholinergics was not superior to anticholinergics alone but did reduce exacerbations versus short-acting beta-agonists (ARR = 6 percent). Adverse effects of inhaled interventions during the study followup periods were generally mild but included bone loss, thrush, dry mouth, and serious cardiovascular events. About 50 percent of subjects remained compliant with therapy. Withdrawals from therapy were greater in subjects assigned to placebo than to active treatments.

Studies have not examined the value of spirometry to monitor need for additional therapy or to identify candidates for treatment among patients who do not report symptoms. It is unlikely to be beneficial because data indicated that: (1) clinical improvement was not associated with an individual's spirometric response to therapy; (2) treatments other than smoking cessation did not alter the rate of spirometric decline over time; (3) there was wide intra-individual variation in spirometric decline; (4) higher doses of inhaled interventions or combination therapy were not superior to lower doses or to monotherapy; and, (5) interventions were not effective in asymptomatic individuals or those with mild to moderate airflow obstruction.

Based on NHANES III results if all "at risk" adults (i.e., smokers and ex-smokers regardless of symptom status as well as never smokers with persistent respiratory symptom) undergo an office-based spirometric test then nearly two-thirds of the adult

population, approximately 110 million adults, would receive spirometric testing.

- If a primary care clinic was comprised of 10,000 adults with similar demographic, smoking, symptom, and spirometric status as NHANES III respondents then 6,588 would undergo spirometric testing, 129 (1.3 percent) would be potential candidates for COPD therapy and 7 (0.08 percent) would have reductions in exacerbations (i.e., an estimated 1,010 current smokers, 960 former smokers, and 2,043 never smokers would undergo spirometric and respiratory assessment to identify candidates for treatment consisting of an inhaled bronchodilator or corticosteroid to prevent an individual from having one or more exacerbations).
- If subjects with moderate airflow obstruction (FEV1 50-80 percent predicted; approximately Global Initiative for Obstructive Lung Disease Stage 2) benefit to a similar magnitude as severe to very severe airflow obstruction, then 529 adults (5.3 percent) would be candidates for treatment and 32 adults (0.3 percent) would benefit from having at least one exacerbation prevented compared with placebo. Approximately 76 (0.8%) would report a clinically noticeable improvement in respiratory health status. Reserving testing and treatment for individuals with respiratory symptoms (especially dyspnea, exercise intolerance, or exacerbations) would maintain benefits.
- If spirometry was targeted to individuals with dyspnea, regardless of smoking status, the number needed to screen and treat for severe to very severe airflow obstruction would be 475.

These estimates assume individuals with airflow obstruction and respiratory symptoms have COPD as the cause of their symptoms and that effective detection by clinical examination and treatment would not have occurred without spirometry. Based on 2004 Red Book prices the annual long-acting inhaled drug costs would be over $4.5 billion to treat the estimated 4 percent of adults with dyspnea and severe to very-severe airflow obstruction (n = 4,630,000). If combination therapy was routinely used instead of monotherapy, effectiveness would be similar but drug costs would be considerably higher. Compared to diagnosis and treatment based on clinical examination alone, spirometry may reduce the number of symptomatic individuals who are diagnosed with, and treated for, COPD but do not have airflow obstruction of severity that is likely to benefit from treatment.

Spirometry provides independent prognostic value regarding respiratory symptoms, morbidity, and mortality, though level of dyspnea is a better predictor of symptom progression and mortality. Baseline spirometry predicts rate of spirometric decline over time in male smokers. Spirometric levels may be useful as a guide for initiation of inhaled medications and pulmonary rehabilitation among individuals having disabling respiratory symptoms, especially frequent exacerbations. Subjects with chronic sputum production and normal spirometry (Stage GOLD 0 condition) are not at increased risk for developing airflow obstruction compared to individuals without chronic sputum production, and more than half of these subjects do not have chronic sputum production after 10 years of followup.

Discussion

Spirometry in addition to clinical examination improves COPD diagnostic accuracy compared to clinical examination alone and it is a useful diagnostic tool in individuals with symptoms suggestive of possible COPD. The primary benefit of spirometry is to identify individuals who might benefit from pharmacologic treatment in order to improve exacerbations. These include adults with symptomatic, severe to very severe airflow obstruction. In individuals where a diagnosis of asthma is suspected bronchodilator responsiveness, testing may be indicated. The evidence does not support widespread use of spirometry in primary care settings for all adults with persistent respiratory symptoms or having a history of exposure to pulmonary risk factors for case-finding, improving smoking cessation rates, monitoring the clinical course of COPD, or adjusting COPD interventions.

Routine spirometric testing in primary care settings is likely to result in considerable testing and treatment costs, resource utilization, and health care personnel time. It might reduce the number of individuals being labeled as having COPD or receiving disease-specific treatment in the absence of severe to very-severe airflow obstruction. However, it is likely to label a large number of individuals (many not reporting bothersome respiratory symptoms or having nondisabling symptoms) as diseased who would not benefit from testing or treatment. Treatment effectiveness (beyond short acting medications used for “acute rescue therapy”) is largely limited to reducing exacerbations among subjects who have bothersome dyspnea, frequent exacerbations, and severe to very-severe airflow obstruction. Nearly all the benefit from treatment could be obtained by reserving spirometry for those having activity limiting respiratory symptoms and targeting therapy to those who have reached a spirometric threshold of airflow obstruction of approximately a FEV1 less than 50 percent predicted. Spirometric response to therapy or change over time has not been shown to be associated with clinical outcomes, nor does it appear to be beneficial in modifying therapy. Future studies should be conducted to determine if spirometry improves

smoking cessation rates; if treatment effectiveness in established COPD varies according to an individual's baseline or followup spirometric value; if treatment benefits individuals with airflow obstruction and moderate to no reported respiratory symptoms; or if therapy improves the rate of decline of FEV1. Spirometry provides independent prognostic value for predicting respiratory and overall morbidity and mortality.

Availability of the Full Report

The full evidence report from which this summary was taken was prepared for the Agency for Healthcare Research and quality (AHRQ) by the Minnesota Evidence-based Practice Center, under Contract No. 290-02-0009. It is expected to be available in September 2005. At that time, printed copies may be obtained free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requesters should ask for Evidence Report/Technology Assessment No. 121, *Use of Spirometry for Case Finding, Diagnosis, and Management of Chronic Obstructive Pulmonary Disease (COPD)*. In addition, Internet users will be able to access the report and this summary online through AHRQ's Web site at www.ahrq.gov.

Suggested Citation

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