Should We Consider Screening Spirometry in Individuals Who Are "Asymptomatic"?

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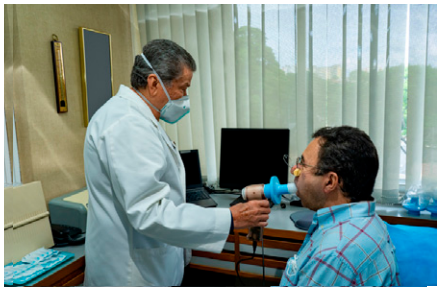

Chronic obstructive pulmonary disease (COPD) diagnosis requires an airflow obstruction (AFO) in spirometry according to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines (1). Spirometric testing is typically reserved for individuals with respiratory symptoms. The USPSTF (U.S. Preventive Services Task Force) recommends against screening individuals who are asymptomatic with the rationale that early diagnosis does not modify the disease course and does not improve patient outcomes (2). Nevertheless, the USPSTF did not find any significant harm from screening besides wasting resources and acknowledged that further studies are needed to assess screening spirometry in high-risk individuals, including those with smoking exposure. This is on par with the GOLD guidelines, which recommend spirometry in those with respiratory symptoms and other risk factors such as more than 20 pack-years of smoking exposure (1).

In the current issue of *AnnalsATS*, Bhatt and colleagues (pp. 1294–1304) demonstrated the importance of detecting AFO in individuals who are asymptomatic (3). Using harmonized data from nine U.S. cohort studies, they analyzed data of 14,024 adults without respiratory symptoms or prior respiratory disease that had spirometric data. In a racially and ethnically diverse sample with 54% females, the prevalence of AFO in individuals who are asymptomatic (SAO) was 13.2%. There were 1,325 COPD-related hospitalizations and 131 COPD-related deaths over a median follow-up time of 16 years. Individuals with SAO had 3 to 5 times higher rates of COPD-related hospitalizations or deaths independent of their smoking history. The authors went one step further and created a probability scoring system to predict SAO using simple variables: age, sex, race, accumulated smoking exposure, current smoking status (current or former smoking), and body mass index. Their scoring system showed a very good discriminative ability to predict SAO with an area under the curve in the receiver operating characteristic curve of 0.81 (95% confidence interval, 0.8–0.82). The 15% probability threshold was found to have the best discriminative ability. Using that threshold, one individual with SAO can be diagnosed for every 3.2 individuals who undergo spirometry.

The study was well conducted and seems free of selection bias as it used data from nine large prospective U.S. cohorts. There may be a misclassification in SAO as spirometries were categorized as AFO or normal. Preserved ratio impaired spirometry was classified as normal while it is well established that it is associated with worse outcomes relative to normal spirometry (4). In addition, a fixed forced expiratory volume in 1 second (FEV_1)/forced vital capacity (FVC) threshold was used (below 0.7), which may overdiagnose AFO in elderly and underdiagnose AFO in young individuals. Nevertheless, a prior study using data from the same cohorts showed that the discriminative ability of FEV_1/FVC less than 0.7 for COPD-related hospitalization and mortality was superior to that of the lower limit of normal (5). Prebronchodilator values were used to diagnose SAO instead of postbronchodilator spirometry, which is recommended by the GOLD guidelines (1). Although postbronchodilator FEV_1/FVC less than 0.7 is a better predictor for respiratory symptoms, chest computed tomography features, and mortality than prebronchodilator FEV_1/FVC less than 0.7, their discriminative ability are marginally different (6).

Apart from the minor potential aforementioned limitations, the study has many strengths. The probability scoring system was validated in an external cohort and showed similar accuracy in the training dataset. Several sensitivity analyses were conducted, demonstrating the robustness of their findings. Most important, the variables used in the probability scoring system were clinically relevant and can be easily extracted using electronic health records. Moreover, the study findings are generalizable because the data were derived from several general population cohorts.

Expanding spirometry testing for COPD has been the research focus of several prior investigations (7). COPD underdiagnosis has been reported to be as high as 81.4% (7). In a sample of individuals from the general population that were at least 40 years old with at least 10 pack-years of smoking exposure and after excluding those with a history of asthma, Colak and

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colleagues showed that 11% of these individuals had AFO (8). Of those participants with AFO, 78% did not carry a COPD diagnosis. Thirty percent of those with no AFO and prior diagnosis of COPD were asymptomatic. Despite the absence of respiratory symptoms, those individuals had a higher risk for exacerbations, pneumonia, and all-cause mortality than those with no COPD. A study using electronic health record data of patients with COPD in the United Kingdom showed that 38% of the patients had only mild dyspnea, defined by the MRC (Medical Research Council) dyspnea scale as one, which corresponds to shortness of breath when hurrying or walking up a slight hill, while 44% of those had moderate dyspnea (MRC dyspnea scale of two), which corresponds to walking slower than peers (9). Even among patients with FEV_1% predicted less than 35%, more than 20% had MRC of one or two. In patients with FEV_1% predicted between 35% and 50%, more than 40% had MRC of one or two. Similarly, the PLATINO (Latin American Project for Research in Pulmonary Obstruction) study data showed that half of the patients with COPD and FEV_1% predicted between 50% and 80%, and one-third of those with FEV_1% predicted less than 50% reported good to excellent health status (10).

Screening spirometry in individuals who are asymptomatic with risk factors like age above 40 years and a history of smoking exposure makes sense. An easy target population is the participants in the lung cancer screening program because they have a significant smoking history (accumulating smoking exposure of 20 or more pack-years) and must be above 50 years of age to qualify for screening. In a lung cancer screening cohort, 34% of the participants had AFO, with 87% of those not having a previous diagnosis of obstructive lung disease (11). Participants in lung cancer screening programs are not only at high risk, but they are also willing to undergo preventive diagnostics tests. The probability scoring system created by Bhatt and colleagues gives the opportunity to increase spirometric testing beyond the lung cancer screening program. The commonly available variables used for the scoring system allow its application in electronic health records via an automated fashion with minimal cost. Such an application can alert the user that the patient is at risk for COPD, thus encouraging screening spirometry.

Whether early identification of COPD in individuals who are asymptomatic improves outcomes is unknown. Nevertheless, early diagnosis may lead to early treatment and improved outcomes. Early treatment improves respiratory symptoms and reduces exacerbations and, therefore, may reduce rapid lung function decline and mortality (12).

Conclusions

The burden of SAO in the U.S. population is high. The probability scoring system provided by Bhatt and colleagues in the current issue of *AnnalsATS* can serve as a tool to identify high-risk individuals who are asymptomatic for COPD that may benefit from screening spirometry. Future research should investigate whether screening spirometry in those individuals improves their outcomes. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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