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Pulmonary Function Tests: An Update

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ABSTRACT: Indications for pulmonary function tests (PFTs) have widened substantially, ranging from screening smokers for early lung disease to determining the diagnosis and prognosis of pulmonary conditions. Current indications also include screening for drug-induced lung toxicity and preoperative screening for lung resection surgery. In the workup of respiratory symptoms, such as dyspnea, cough, and wheezing, PFTs can identify obstructive or restrictive patterns that may suggest a diagnosis such as asthma or interstitial lung disease. The ratio of FEV_1 to forced vital capacity is very sensitive to the presence of airflow limitation, although bronchoprovocation testing may be needed to diagnose asthma, especially in patients with mild intermittent disease. Measurements of lung volumes and carbon monoxide–diffusing capacity (D_LCO) provide crucial information in selected patients. For example, a reduced D_LCO may be a sign of more advanced disease, such as emphysema or pulmonary hypertension.

Since the first description of the spirometer by John Hutchinson in the late 1800s, pulmonary function tests (PFTs) have expanded to include spirometry; lung volumes; carbon monoxide–diffusing capacity (D_LCO) (transfer factor); respiratory muscle performance; and exercise and functional testing, such as the 6-minute walk test (6MWT) and cardiopulmonary exercise testing (CPET).

Indications for PFTs have widened substantially, ranging from screening smokers for early pulmonary disease or screening patients for drug-induced lung toxicity to determining the diagnosis and prognosis of pulmonary conditions (**Table 1**).

In this article, we will address the use of PFTs in common pulmonary diseases and the indications most relevant to the primary care practitioner.

SCREENING

Screening for obstructive lung disease in smokers. The significance of office spirometric screening for chronic obstructive pulmonary disease (COPD) in high-risk patients (such as persons who have smoked for more than 10 years) is well established. Spirometric signs of airway obstruction have been found in 24.3% of asymptomatic smokers compared with 14.4% of nonsmokers.[1] The Lung Health Study showed that early intervention with smoking cessation in those identified to be at risk for COPD could modify disease progression.[2]

The Third National Health and Nutrition Examination Survey suggested that undiagnosed airflow obstruction was found in 12% of patients surveyed and was more common than physician-diagnosed COPD (3.1%) or asthma (2.7%).[3] After adjusting for smoking, obesity, and comorbid conditions, the risk of impaired health and functional status with undiagnosed airflow obstruction was independently associated with the severity of forced expiratory volume in 1 second (FEV_1) impairment.[3]

A consensus statement from the National Lung Health Education Program recommends that all patients

aged 45 years and older who are current smokers and all patients with respiratory symptoms undergo office spirometry or diagnostic spirometry.[4] There are no recommendations to perform screening PFTs for asymptomatic nonsmokers, because no studies have shown any advantage in doing so.

Preoperative screening for lung disease. PFTs have a clear role in preoperative screening for lung resection surgery, but the role of PFTs in non–lung resection surgery is less clear. This is partly due to the lack of a unified definition of postoperative pulmonary complications in studies examining this role; the complex interaction of respiratory factors (obstructive or restrictive pulmonary disease, respiratory muscle weakness, smoking) and nonrespiratory factors (age, obesity, nutritional status, operative factors, proximity to diaphragm, type of anesthesia) affecting postoperative respiratory status; and the rapid pace of change in surgical techniques.

The 1990 American College of Physicians' guidelines indicated that PFTs should not be done in patients without evidence of lung disease at physical examination who were to undergo nonthoracic surgical procedures.[5] However, PFTs were recommended for patients with a history of tobacco use or dyspnea who were to undergo coronary artery bypass grafting or upper abdominal surgery and for all patients who were to undergo lung resection.[5] The role of PFTs in these settings is "not to determine candidacy, but to guide postoperative care to reduce pulmonary complications."[6] No studies have reported results of routine preanesthesia office spirometry.[7]

DIAGNOSIS

The role of PFTs in evaluating respiratory symptoms such as dyspnea, cough, and wheezing is obvious. PFTs can identify different physiologic patterns of abnormal lung function, including obstructive, restrictive, upper airway, and neuromuscular weakness patterns; however, they cannot pinpoint a specific disease entity (**Table 2** and **Figure**).

Be careful not to interpret PFT results as "normal" or "abnormal" without incorporating them in the clinical context. For example, patients with primary pulmonary hypertension (PH) may have completely normal PFT findings, especially in the early stages of disease,[8] whereas an obese patient may have a small-airway obstruction pattern with a decrease in expiratory reserve volume in the absence of significant pathology, an abnormality that usually disappears with weight reduction.[9]

Obstructive airway diseases. PFTs play an essential role in the diagnosis and grading of severity of obstructive airway diseases. Measures of airflow limitation include the following: peak expiratory flow (PEF), FEV_1, forced vital capacity (FVC), FEV_1:FVC, and flow-volume loops. Measurements of FEV_1, FVC, and FEV_1:FVC are very reproducible, with coefficients of variation usually at 5% or less if done in certified laboratories that follow the American Thoracic Society (ATS) standardization guidelines.[10]

FEV_1:FVC has been shown to be very sensitive to the presence of airflow limitation.[11] However, normal spirometric measurements may not be sufficient to exclude mild intermittent asthma when patients are asymptomatic.[12] In this case, bronchoprovocation testing may be the only way to establish the diagnosis of asthma.[13]

Other PFTs, such as measurements of lung volumes and DLCO, play a lesser role in the diagnosis of airway obstruction but can shed more light on the pathophysiology of the disease. For example, increased functional residual capacity, residual volume (RV), and RV/total lung capacity (TLC) signify air trapping, which may indicate a more severe airflow limitation, and the reduction of DLCO in these settings may be the result of advanced disease (increased dead space, as in emphysema and/or PH).

Interstitial lung disease. PFTs play an essential role in the diagnosis of interstitial lung disease (ILD). In addition to the commonly encountered restrictive pattern (decreased TLC, decreased vital capacity [VC], and increased FEV_1:FVC) seen with ILD, other abnormalities on PFTs may suggest an alternative diagnosis. Spirometric evidence of airway obstruction is frequently found in patients with sarcoidosis, rheumatoid arthritis, eosinophilic granuloma, lymphangioleiomyomatosis, and obliterative bronchiolitis. **Table 3** categorizes abnormalities seen with some common types of ILD.[14]

Changes in DLCO appear to be one of the earliest abnormalities noted in patients who have ILD. Epler and associates[15] reported that DLCO was the most common PFT abnor-

Table 1 – Indications for pulmonary function tests

- Screening for COPD in smokers
- Detecting and diagnosing respiratory diseases
- Following the progression of respiratory diseases
- Monitoring the response to therapy
- Monitoring pulmonary drug and radiation toxicity
- Grading the severity of illness and aiding in management decisions
- Predicting prognosis for patients with pulmonary diseases
- Predicting postoperative pulmonary complications
- Assessing disability and impairment as a result of respiratory disease or complaint

COPD, chronic obstructive pulmonary disease.

Table 2 – Examples of PFT abnormalities in respiratory diseases

	Lung function parameter							
Disease pattern	**FEV_1**	**FVC**	**FEV_1:FVC**	**TLC**	**TLC/RV**	**DLCO**	**Pimax**	**Flow-volume loop**
Obstructive	↓	→↓	↓	→↑	→↓	↑→↓	→	Scooped expiratory limb
Restrictive	→↓	↓	→↑	↓	→↓	→↓	→	Small (generally)
Upper/central airway obstruction	→↓	→↓	→↓	→	→	→	→	Abnormal inspiratory/ expiratory limbs
Pulmonary vascular disease	→	→	→	→↓	→	↓	→	Normal
Neuromuscular weakness	→↓	→↓	→↓	→↓	→	→	↓	Abnormal inspiratory/ expiratory limbs

PFT, pulmonary function test; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; TLC, total lung capacity; RV, residual volume; DLCO, carbon monoxide–diffusing capacity; Pimax, maximum inspiratory pressure.

mality in 44 patients with proven ILD by lung biopsy and normal chest adiography.

PFTs (including DLCO), however, are unable to identify the type of ILD or the presence or absence of inflammation in a given patient. Other radiographic or histologic correlates (such as high-resolution CT and lung biopsy) are needed to establish the diagnosis and the degree of inflammation/fibrosis.

Pulmonary hypertension. PFTs are not helpful in diagnosing PH, but they are used in determining the cause of secondary PH, such as airway disease, ILD, and neuromuscular/chest wall diseases. PFTs are also used in patients with PH who are being considered for lung transplantation surgery.

In primary PH, PFT findings may be normal or show a restrictive defect and/or decreased DLCO. Of all PFTs, DLCO was the most consistent parameter that was reduced, with a mean of 69% of predicted[16]; however, DLCO may be normal in precapillary PH. In the evaluation of dyspnea, an isolated reduction in DLCO in the absence of other abnormalities on spirometry and lung volume measurement should raise the suspicion for PH in the appropriate clinical settings.

ASSESSING SEVERITY OF ILLNESS AND PROGNOSIS

PFTs are excellent tools for evaluating respiratory disease severity, hence providing valuable information to assess prognosis and the management plan.

Obstructive lung diseases. Once FEV_1:FVC indicates airway obstruction, FEV_1 or PEF (besides other clinical parameters) can be used in evaluating the severity of asthma (**Table 4**).[17] PFTs also help determine the prognosis in patients with asthma by identifying the degree of lung function decline. In a 15-year follow-up study, the decline in FEV_1 normalized for height was greater among persons with asthma than among those without the disease.[18] Other studies have shown that the decline in FEV_1 is more pronounced if measured repeatedly early after the diagnosis and in asthmatic patients who smoke.

FEV_1 decline in patients with asthma is significantly influenced by baseline FEV_1, disease duration, and FEV_1 variability. Moreover, the rate of FEV_1 decline appears to increase in younger persons who have a poor baseline FEV_1 compared with those who have a higher baseline FEV_1.[19] It is, therefore, surprising that most physicians appear to rely solely on subjective assessments of the patient's asthma and rarely measure FEV_1 or FEV_1:FVC.

The ability of routine PFTs to identify patients at risk for a fatal or near-fatal asthma attack is somewhat debated. Prospective case-control studies have failed to document that routine PFTs predict near-fatal asthma.[20,21] However, in one retrospective review, Lee and colleagues[22] were able to distinguish patients who required intubation and mechanical ventilation (as a measure of near-fatal asthma) from those who did not. They used an index that combined the degree of airway narrowing (measured as the provocative dose of inhaled histamine or methacholine required to produce a 20% fall in FEV_1 [PD_{20}]) and excessive bronchoconstriction (reflected by the maximal percentage fall in FVC at PD_{20} [Δ FVC%]) in a bronchoprovocation test: Δ FVC%/log (PD_{20}).[22] ▶

Despite the controversy surrounding the conclusion by Traver et al[23] that FEV_1 is the most powerful predictor of mortality in COPD patients **(Table 5)**, PFTs, especially FEV_1, continue to be very important tools in determining prognosis in COPD. Hodgkin[24] noted that FEV_1 of less than 0.75 L is associated with a mortality rate of about 30% at 1 year and 95% at 15 years.

A recent study showed that the categorization of patients with COPD based on the level of dyspnea was more discriminating than staging of disease severity using the ATS guideline (that uses FEV_1) with respect to 5-year survival.[25] Decreased DLCO in patients with airway obstruction reasonably predicts clinically relevant emphysema and/or PH and

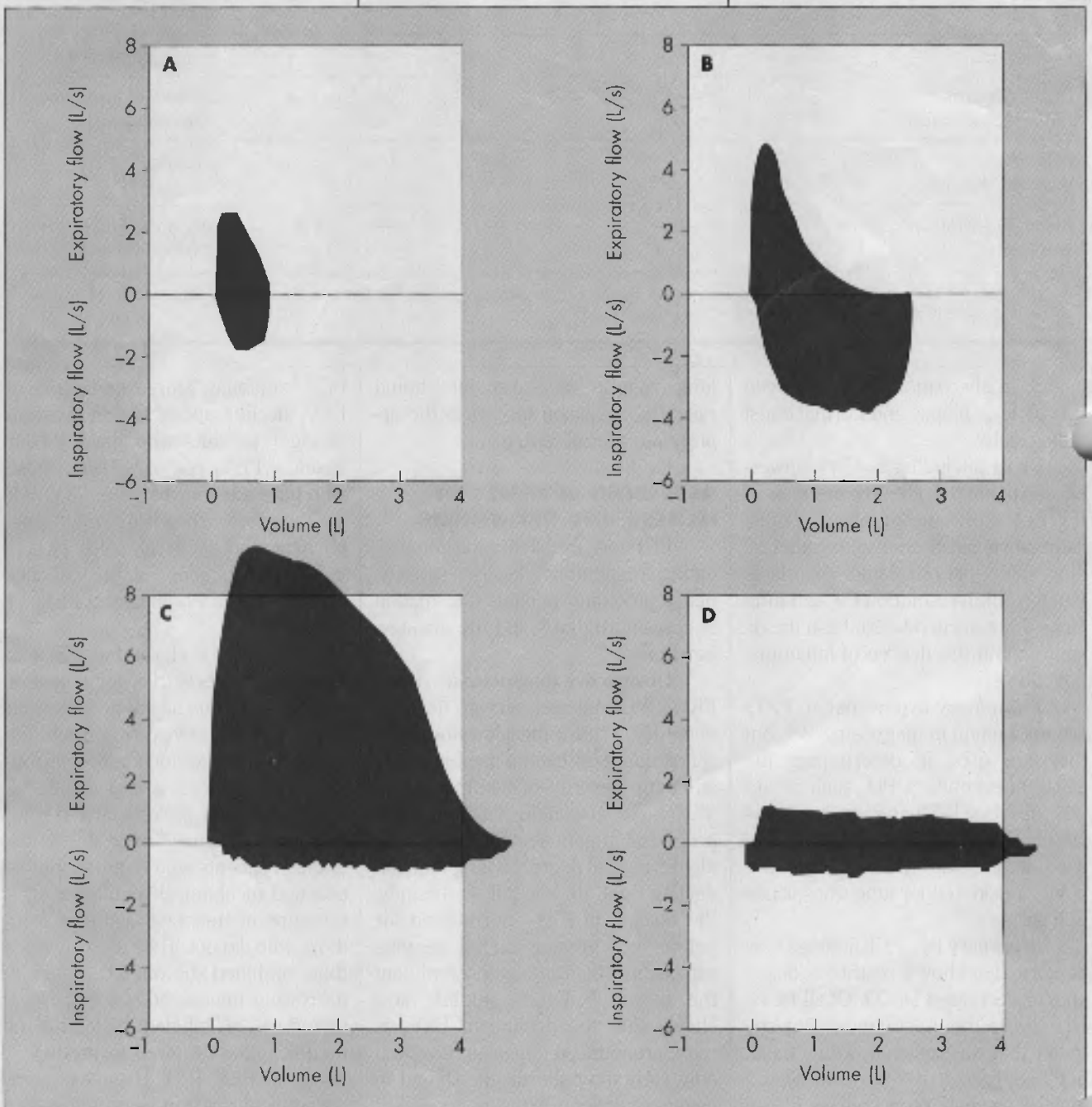

Figure – These flow-volume loops show a variety of abnormalities, including a restrictive pattern (A), an obstructive pattern (B), variable extrathoracic upper airway obstruction (C), and fixed upper airway obstruction (D). While pulmonary function tests can identify different physiologic patterns of abnormal lung function, they cannot pinpoint a specific disease entity.

indicates worse prognosis in those with COPD.[26]

Studies have suggested a good correlation between the degree of DLCO reduction and the severity of airway obstruction and, to a lesser degree, exercise hypoxemia.[27,28] The 1995 ATS guidelines for COPD management suggest that DLCO be measured in the initial evaluation and later if disease severity is considered to be significant.[29]

Other functional tests to predict prognosis in COPD include CPET, the 6MWT, and the shuttle walk test. The

Table 3 – Usual patterns of PFT abnormalities associated with interstitial lung diseases

Disease	FVC	FEV_1:FVC	DLCO	TLC	Exercise $P(A\text{-}a)O_2$
Idiopathic pulmonary fibrosis	↓ ↔	↑ ↔	↓	↓ ↔	↑ ↑
Connective tissue disease	↓ ↔ ↑	↑ ↔ ↓	↓	↓ ↔	↑ ↔
Sarcoidosis	↓ ↔	↑ ↔ ↓	↓ ↔	↓ ↔	↑ ↔
Hypersensitivity pneumonia	↓ ↔	↑ ↔ ↓	↓ ↔	↓ ↔ ↑	↑ ↔
Pulmonary alveolar proteinosis	↓ ↔	↑ ↔	↓ ↔	↓ ↔	↑ ↔
Langerhans cell histiocytosis	↓ ↔	↑ ↔ ↓	↓	↔ ↑	↑
Lymphangioleiomyomatosis	↓ ↔	↓ ↔	↓	↑ ↔	↑
Cryptogenic organizing pneumonia	↓	↑ ↔ ↓	↓	↓	↑
Obliterative bronchiolitis	↓	↓ ↓	↓	↑	↑

PFT, pulmonary function test; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 second; DLCO, carbon monoxide–diffusing capacity; TLC, total lung capacity; $P(A\text{-}a)O_2$, alveolar-arterial oxygen tension gradient.

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Table 4 – Asthma severity classification based on clinical criteria and PFT findings

Asthma severity	Clinical manifestations	Nighttime symptoms	PFT findings
Severe persistent	Continual symptoms, limited physical activity, frequent exacerbations	Frequent	FEV_1 or PEF, ≤ 60% of predicted; PEF variability, > 30%
Moderate persistent	Daily symptoms, daily use of inhaled short-acting β_2-agonist, exacerbations affect activity, exacerbations ≥ 2 times per week	> 1 time per week	FEV_1 or PEF, > 60% to < 80% of predicted; PEF variability, > 30%
Mild persistent	Symptoms > 2 times per week but < 1 time per day, exacerbations may affect activity	> 2 times per month	FEV_1 or PEF, ≥ 80% of predicted; PEF variability, 20% to 30%
Mild intermittent	Symptoms ≤ 2 times per week; asymptomatic and normal PEF between exacerbations; brief exacerbations (from a few hours to a few days), intensity may vary	≤ 2 times per month	FEV_1 or PEF, ≥ 80% of predicted; PEF variability, < 20%

PFT, pulmonary function test; FEV_1, forced expiratory volume in 1 second; PEF; peak expiratory flow.

6MWT is a relatively easy test to administer in the PFT laboratory and, if standardized, can be very helpful in grading the functional disability, and therefore prognosis, of COPD patients. Kessler and colleagues[30] found that the risk of hospitalization is significantly increased in patients with COPD if their 6MWT distance is 367 m or less. In a recent ATS position statement, the 6MWT is indicated as a predictor of morbidity and mortality in COPD.[31]

Interstitial lung disease. Considering the wide range of what is classified as ILD (ILD includes more than 150 diagnoses), the complexity of conducting studies to determine a given ILD prognosis, and the continuing changes in ILD classification, the role of PFTs in determining prognosis in ILD is complex. As mentioned above, physiologic abnormalities in ILD include low TLC, VC, and DLCO; high FEV_1:FVC; and an increased alveolar-arterial oxygen tension gradient, especially with exercise. Although common, these changes are not specific to any particular ILD and may not be present during the early stages of the disease. Doherty and associates[32] found a normal VC and TLC in 21 of 48 patients (most of whom were smokers) with biopsy-proven cryptogenic fibrosing alveolitis/idiopathic pulmonary fibrosis (IPF).

Many studies have been done to establish cutoff values to lead clinicians to better estimates of prognosis in ILD. Some of these studies have looked at absolute values at the time of diagnosis, and others have looked at a percent of decrease over time. The variables evaluated include FVC, DLCO, TLC, and FEV_1:FVC. For example, Hanson and coworkers[33] showed that a decrease in VC of more than 10% and a decrease in DLCO of more than 20% in 1 year was associated with high mortality.

In a recent retrospective report, Timmer and associates[34] compared patients with IPF who died awaiting lung transplantation with those who did not. They found that PaO_2 and FEV_1:FVC were the only 2 variables that were significantly different between the 2 groups. In the recent ATS statement, determining prognosis in ILD was not listed as an indication to conduct the 6MWT[31]; however, there is some evidence that it can be a useful guide in determining the prognosis in patients awaiting lung transplantation, some of whom have ILD.[35]

Pulmonary hypertension. PFTs are not very helpful in predicting prognosis in primary PH. In the national registry for primary PH, DLCO appears to be the only PFT to predict worse outcome.[36] Other predictors of prognosis include the New York Heart Association class of symptoms, mean pulmonary artery pressure, mean right atrial pressure, and measures of exercise limitations demonstrated by the 6MWT or CPET.

In one study, PH patients who walked less than 300 m in 6 minutes had an increased likelihood of death or pretransplant hospital admission for continuous inotropic or mechanical support within 6 months.[37] In another study, poor exercise capacity (less than 10% of the predicted value) identified patients who died during or soon after cardiac catheterization.[8,38] Rhodes and coworkers[38] reported that the ability of exercise testing to identify patients with primary PH who were at high risk for right heart catheterization was superior to that of other noninvasive variables.

COST CONSIDERATIONS

The role of PFTs in clinical medicine continues to expand. The most

Table 5 – Survival rates in COPD patients based on FEV_1

		Cumulative survival rate (%)			
FEV_1 predicted (%)	Number of patients	At 2 years	At 5 years	At 10 years	At 15 years
< 20	9	44	11	11	0
20 - 29	40	65	30	10	3
30 - 39	43	83	47	21	7
40 - 49	26	92	89	39	30
50 - 59	21	95	95	57	32
≥ 60	9	100	89	89	67

COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second.
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CLINICAL HIGHLIGHTS

- ❑ Spirometry is recommended for all smokers aged 45 years and older as well as all patients who have respiratory symptoms.
- ❑ Be careful not to interpret pulmonary function test (PFT) results as "normal" or "abnormal" in the absence of a clinical context. For example, patients with primary pulmonary hypertension may have completely normal PFT findings—especially in the early stages of disease—whereas an obese patient may have a small-airway obstruction pattern with a decrease in expiratory reserve volume in the absence of significant pathology.
- ❑ Normal spirometric measurements may not be sufficient to exclude mild intermittent asthma when patients are asymptomatic. In this setting, bronchoprovocation testing may be the only way to establish the diagnosis of asthma.
- ❑ PFTs play a major role in determining the severity and prognosis of chronic obstructive pulmonary disease; obtain the results regularly as part of a comprehensive management plan.

important recent expansion is in screening smokers for the development of lung disease and the impact this may have on health care costs.

While PFTs have many benefits, they are expensive. If not indicated, PFTs can confuse the clinical picture and warrant unnecessary workups.[39,40] It is therefore important to use them on evidence-based grounds and to understand what PFTs can—and cannot—tell you about your patients' health. ■

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