POINT:
Should Oscillometry Be Used to Screen for Airway Disease? Yes

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ABBREVIATIONS: CAO = chronic airway obstruction; ECLIPSE = Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints; FOT = forced oscillation technique; FRC = functional residual capacity; WTC = World Trade Center

Detection of airway disease by physiologic testing was initially described using spirometry to determine vital capacity and expiratory airflow under maximal effort to distinguish obstructive from restrictive disease processes.[1] Subsequently, Dubois and colleagues[2] demonstrated direct assessment of airway resistance using plethysmography and in a separate publication described the precursor of the forced oscillation technique to measure respiratory system resistance.[3] This review addresses the question of whether direct assessment of resistance by forced oscillation provides diagnostic information equivalent or superior to standard assessment of airflow rates by spirometry.

The rationale and limitations of each technique are shown in Table 1. Spirometry measures airflow rates during forceful exhalation, but pressure remains unmeasured; thus, abnormalities in airway resistance are inferred based on the assumption of maximal effort. Ohm's law would dictate that assessment of airflow provides equivalent diagnostic information as direct assessment of resistance:

$$\left(Resistance = \frac{\Delta Pressure}{airflow} \right)$$

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CONFLICT OF INTEREST: None declared.

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Although this assumption is likely valid for a system comprising a single airway, its utility may be limited in lungs, which contain a complex branching system of airways. The multiplicity of airways in the periphery produces an increasing cumulative cross-section area such that disease localized in small airways may not be apparent on spirometry (ie, the quiet zone) until the extent of disease is severe.[4] This limitation of spirometry may preclude early diagnosis because many respiratory diseases originate in the small airways. Therefore, optimal screening for airway disease should include testing modalities sensitive to disease localized in the lung periphery.

Oscillometry is a noninvasive test performed during tidal breathing. Pressure fluctuations of small magnitude (2-5 cm H_2O) are applied at the mouth, and the reflections of airflow and pressure are measured.[5,6] The relationship between airflow and pressure is analyzed to derive the respiratory system resistance (Table 2). Two additional features provide information beyond that available from spirometry. First, a parameter (reactance) can be derived that reflects respiratory system dynamic elastance (distensibility) and inertia. Second, assessment of parameters at multiple oscillation frequencies allows identification of nonuniformities in airflow distribution.[6,7] Because nonuniformities may be the only manifestation of small airway dysfunction, these parameters may allow identification of early disease. Thus, oscillometry allows for the diagnosis of small airway disease on screening evaluation analogous to the "gold standard" demonstration of frequency dependence of compliance by esophageal manometry.

Oscillometry Provides Diagnostic Information Not Evident on Spirometry

Subtle markers available on spirometry suggest the presence of small airway dysfunction. Reduction in midexpiratory airflows and reduction in expiratory reserve volume may occur prior to reduction in FEV_1. Although abnormality in these parameters define the presence of airway dysfunction, the site of disease remains unclear (ie, mild large vs severe small airway). In addition, these parameters may vary when patient effort and completion of the expiratory maneuver are inadequate. Notably, numerous studies demonstrated

TABLE 1] Comparison Between Spirometry and Oscillometry

Variable	Spirometry	Oscillometry
Measurement	Airflow and volume Pressure not measured Resistance assessed indirectly by airflow rates	Pressure and airflow Impedance calculated as: • Resistance • Reactance (dynamic elastance + inertia)
Maneuver	Maximal effort	Tidal breathing
Obstructive abnormalities		
Large airway dysfunction	Identified by reduction in airflow	Identified by increase in resistance
Small airway dysfunction	Relatively insensitive	Assessed by indexes of nonuniformity: • Frequency dependence of resistance • Reactance at low frequencies
Expiratory flow limitation during tidal breathing	Inferred when tidal expiratory flow approaches maximal flow	Directly assessed: • Inspiratory and expiratory reactance
Restrictive abnormalities		
Parenchymal disease	Detectable by spirometry	Not distinguishable from obstruction
Neuromuscular disease	Detectable by spirometry	Not assessed
Chest wall disease	Detectable by spirometry	Not detectable or appears similar to obstructive disease

the detection of airway disease by oscillometry, even when these subtle spirometric markers were normal.[6,8,9]

The enhanced diagnostic capabilities of oscillometry are evident in numerous studies. Abnormal oscillometry may identify pediatric and adult subjects with symptoms suggestive of either asthma or COPD, even in the setting of normal FEV_1 and normal midexpiratory airflow.[6,8] In addition, for patients with established airway disease, respiratory symptom severity and quality-of-life measures may correlate with oscillometry parameters that reflect small airway function rather than FEV_1.[8] Moreover, the presence of small airway dysfunction predicts subsequent loss of symptom control in patients with asthma.[8] Finally, improvement in small airway function during therapy is frequently noted on oscillometry but is not evident on FEV_1 or midexpiratory airflows.[10] Despite the lack of change in spirometry, the improved small airway function correlates with improved symptoms, airway and alveolar inflammation, and bronchial hyperreactivity.[11-13]

Lower Respiratory Symptoms Are Attributable to Small Airway Dysfunction

Bronchoprovocation testing provides a unique opportunity to assess simultaneous development of respiratory dysfunction and lower respiratory symptoms. Inhalation of methacholine has been shown to predominately alter small airway rather than large airway function.[14,15] During methacholine challenge testing, changes in

TABLE 2] Commonly Used Oscillometry Parameters

Parameter	Definition	Interpretation
Resistance (R)		
R at lowest oscillation frequency (eg, R_5)	Respiratory system resistance	Total respiratory resistance
R at high oscillation frequency (eg, R_{20})	Respiratory system resistance	Resistance of larger airways
Frequency dependence of resistance (eg, R_{5-20})	Change in resistance with varying oscillation frequency	Nonuniform distribution of ventilation
Reactance (X)		
X at lowest oscillation frequency (eg, X_5)	Respiratory system elastance	Distensibility and nonuniformity
Resonant frequency (fres)	Oscillation frequency at which $X = 0$	Distensibility and nonuniformity
Reactance area (AX)	Area under reactance curve from X at lowest frequency to fres	Distensibility and nonuniformity

oscillometry variables precede and are more sensitive than spirometry variables for the detection of bronchoconstriction.[6] Importantly, symptom onset during methacholine challenge testing is more tightly linked to development of small airway obstruction than to changes in FEV_1.[15] Moreover, in some individuals, small airway dysfunction on oscillometry may be the only evidence for airway hyperreactivity, highlighting the diagnostic limitations of spirometry.[15]

Use of Oscillometry as a Screening Test

The foregoing discussion reflects physiologic studies and clinical trials; therefore, the relevance to using oscillometry to screen for airway disease remains uncertain. Screening for airway disease encompasses two different approaches: evaluation of patients with symptoms suggestive of airway disease and screening for disease in asymptomatic subjects.

The largest experience to date using oscillometry in routine practice has been in populations exposed to the World Trade Center (WTC) collapse on September 11, 2001. Small airway dysfunction demonstrated by both oscillometry and frequency dependence of compliance has been shown in a case series of subjects with WTC dust exposure.[9] Spirometry, including measures of midexpiratory airflow rates, remained within normal limits, suggesting that disease was localized to the small airways. Further analyses demonstrated that the magnitude of small airway abnormality was correlated to severity and frequency of wheeze. Attribution of symptoms to small airways dysfunction was confirmed during methacholine challenge.[15] The magnitude of small airway dysfunction was independently associated with the presence of systemic inflammation as assessed by serum C-reactive protein levels. Finally, small airway and distal lung injury was confirmed on histologic evaluation.[16] Taken together, these observations highlight that oscillometry overcomes the poor sensitivity of spirometry in the diagnosis of airway disease.

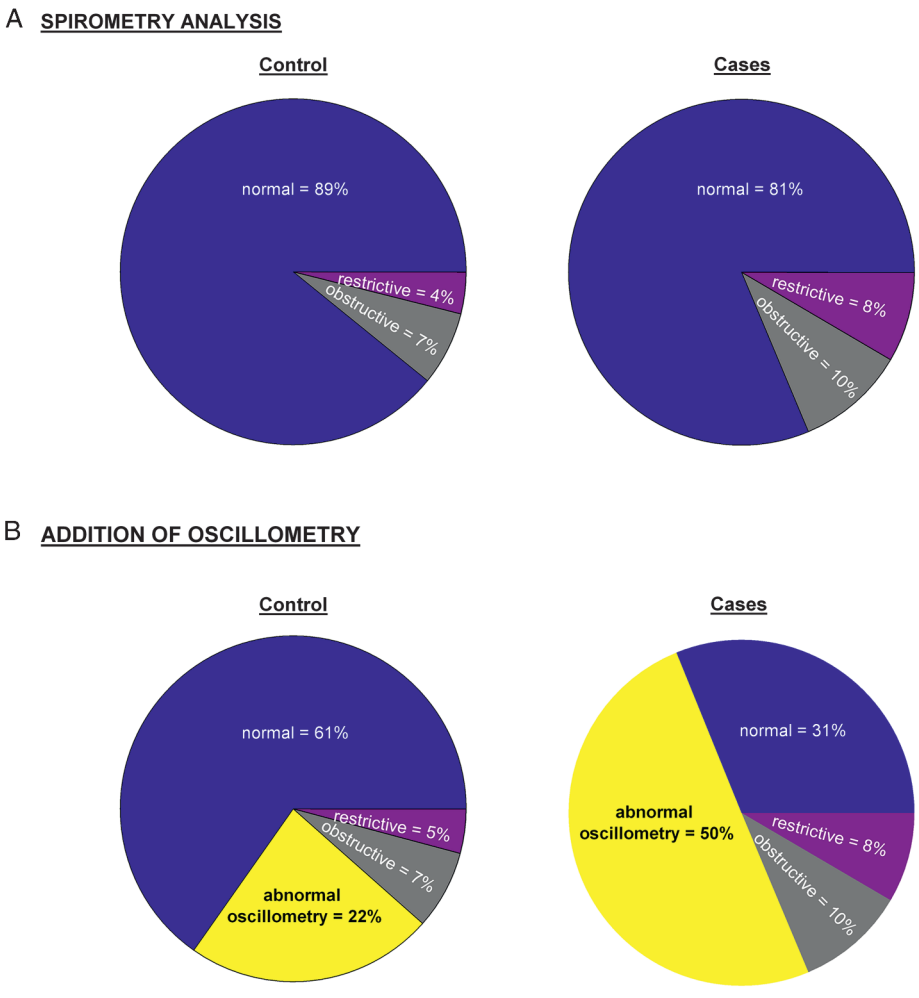

Figure 1 – *A, Spirometry results illustrated in asymptomatic vs symptomatic subjects following exposure to World Trade Center dust. The majority of cases demonstrated normal spirometry despite new-onset respiratory symptoms. B, Results when subjects with normal spirometry are classified by oscillometry data. Abnormal oscillometry was evident in the majority of symptomatic subjects despite normal spirometry. (Data adapted with permission from Friedman et al.[17])*

A case-control study based on these data was performed using oscillometry as a screening test in both symptomatic (case) and asymptomatic (control) subjects.[17] Spirometry was ineffective in identifying disease in symptomatic subjects because normal data were observed in the overwhelming majority (Fig 1A). Addition of oscillometry demonstrated elevated respiratory resistance in the majority of symptomatic cases, indicating dysfunction not detectable by spirometry (Fig 1B). Although oscillometry identified abnormalities in some asymptomatic subjects, they were predominately confined to those who were overweight or obese in accordance with prior observations in obesity.[18] Finally, additional analyses confirmed that lower respiratory symptoms were associated with intensity of WTC dust exposure and abnormal small airway function.[17] These associations were not related to spirometry measures.

Interpretation of Oscillometry Data

Several factors require consideration when interpreting oscillometry data. First, because oscillometry assesses respiratory system function, diseases of the parenchyma, pleura, and chest wall may produce abnormal data. However, positive results from these disease states are acceptable for a screening test because they can be diagnosed by routine clinical assessment. Second, obesity is associated with elevated airway resistance and heterogeneous distribution of ventilation on oscillometry evaluation.[18] Proposed mechanisms include small airway compression from mass loading, intrinsic airway inflammation, and vascular congestion. Although the precise mechanism remains unclear, identification of the airway dysfunction is clinically relevant because it is associated with respiratory symptoms and reversible following weight loss.[19]

Normative Data

Normative data for oscillometry have been published. Although each study used different equipment with differing pressure waveforms, the upper limits of normal for oscillometry were similar and match the values observed in the aforementioned clinical studies. Moreover, a multicenter study combined data from multiple devices to derive global predicted equations for oscillometry variables.[20] These equations account for the effects of sex, stature, age, and body weight (up to BMI of 35 kg/m^2).

Summary

Our arguments in favor of using oscillometry as a screening test include the following:

1. Requirement for early diagnosis when only the small airways may be involved
2. Observation that spirometry markers of small airway dysfunction are unreliable
3. Enhanced capability to detect small airway dysfunction when spirometry remains normal
4. Oscillometry abnormalities that can be related to respiratory symptoms even when spirometry remains normal
5. Disorders other than airway disease that may produce abnormal oscillometry but are usually identifiable by clinical evaluation.

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COUNTERPOINT:
Should Oscillometry Be Used to Screen for Airway Disease? No

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Pulmonary physiologists at the Mayo Clinic used a large loudspeaker to measure respiratory system resistance the year I was born (Fig 1).[1] My first research project used a forced oscillator to measure bronchodilation during exercise in children with asthma.[2] Joe Rodarte, MD, from whom I learned pulmonary physiology at the Mayo Clinic, said about the technique in 1990 that "one man's noise is another man's signal." After five generations and 65 years of improvements in forced oscillation technique (FOT) instrumentation and software, I remain cautiously optimistic that this test will eventually find clinical value.

The holy grail of pulmonary physiologists during my lifetime has been a test that will reliably detect early chronic airway obstruction (CAO). The most common example of a disease that starts in the silent zone of small airways is COPD due to cigarette smoking. Clinically important airway obstruction develops in only one in 10 smokers, yet currently available tests cannot reliably detect this subset of susceptible smokers during the first 20 or so years of their disease progression. FOT enthusiasts believe that the silent zone is making noise (or at least reflecting it back toward the mouth).[3]

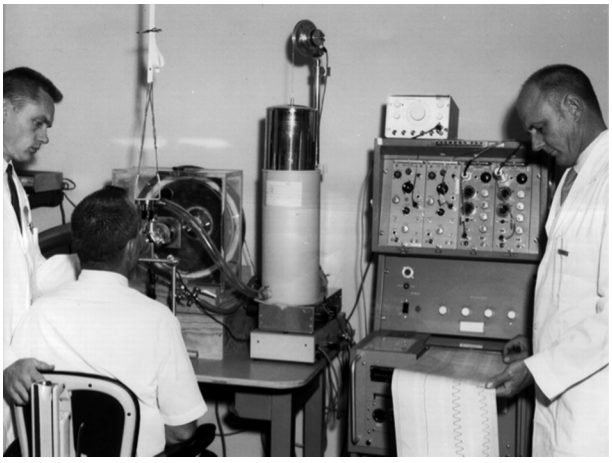

Figure 1 – *Pulmonary physiologists at the Mayo Clinic using the forced oscillation technique in 1950. Note the 15-in subwoofer loudspeaker used to generate the low-frequency sounds (from Mayo Clinic archives).*

The use of spirometry to measure airway obstruction is clinically valuable because it (1) helps with the diagnosis of asthma and COPD, (2) is an index of disease severity (or lack of control for asthma), (3) is an independent predictor of morbidity and disease progression, (4) objectively measures response to bronchodilator therapy, and (5) predicts all-cause and COPD-related mortality. However, these benefits have not yet been proven for FOT indexes.

For children with respiratory symptoms who cannot reliably perform spirometry, FOT (or specific airway resistance measured in a body box) may be helpful for diagnosing asthma and response to therapy, but an experienced and motivated technologist can coach > 90% of school-aged children and people aged > 65 years (including patients with severe lung disease) to meet guidelines for acceptable and repeatable spirometry tests.[4]

Longitudinal studies of smokers have not been done to determine whether FOT indexes measured during baseline examinations add to models that predict progression of CAO, all of which have included spirometry.[5] On the other hand, diffusing capacity of lung for carbon monoxide tests have this ability[6,7] probably because a low diffusing capacity of lung for carbon monoxide is an index of the emphysema phenotype of COPD. In adult smokers, FOT indexes are modestly

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CONFLICT OF INTEREST: P. L. E. has been reimbursed for travel expenses by professional societies during the past 3 years for giving talks at international meetings about pulmonary function testing. These societies were often given funding for these talks by ndd Medical Technologies, Inc, which does not make a forced oscillation technique instrument.
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