AIRWAY OBSTRUCTION – HOW BAD IS IT?

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Over the years, performance of spirometry has become highly standardized with well established criteria for acceptability and repeatability. Equipment manufacturers have committed to recommendations of the ATS and ERS to produce spirometers that can measure FVC and FEV1 very accurately. But in spite of our best efforts to obtain accurate data, the diagnosis of airway obstruction is still somewhat contentious. There are two primary questions in this regard: Who is obstructed and how severe is the obstruction?

The first question about who has airways obstruction would seem to be easily answered by looking at the ratio of FEV1 to VC (or FVC). The ATS, the European Respiratory Society, the Global Obstructive Lung Disease group and others agree that a reduction in the FEV1 in relation to the VC typifies obstruction. The question arises as to how to best interpret the FEV1/VC ratio. The GOLD initiative and the ATS/ERS Committee for Standards for the Diagnosis and Treatment of Patients with COPD each suggest that a fixed ratio of 0.70 after bronchodilator is the threshold below which airway obstruction is present. There is, however, a significant body of evidence that the FEV1/VC ratio decreases with advancing age, and that height, race, and gender may also play a role in determining what is 'abnormal' in terms of this variable. Like most other spirometric parameters, the FEV1/VC ratio varies in healthy subjects. Hence, it is appropriate to describe a lower limit of normal (LLN) for the FEV1/VC ratio. Both the ratio itself and the LLN appear to decrease with increasing age. As a result, the LLN for the FEV1/VC ratio may be above 0.70 in young healthy adults and below 0.70 in older healthy adults.

The LLN for the FEV1/VC ratio also differs with gender and race, and may be dependent on height. The LLN is usually specified at the 5th percentile, or it may be calculated as 1.645 x the residual standard deviation (RSD) if the data is evenly distributed. In either case, using an LLN calculated for the patient's age will yield different results than using the fixed ratio of 0.70. Younger subjects who have an FEV1/VC below the LLN but above 0.70 may have airway obstruction that the fixed ratio does not address (false negatives). Similarly, in older healthy subjects, the LLN may be significantly less than 0.70; these individuals may be mislabeled as having obstructed airways (false positives) when in fact they are comparable to the group making up 95% of the normal subjects. Keep in mind that the 5th percentile refers to healthy subjects who are at the low end of the distribution; false positives that we accept in an attempt to gauge whether an individual has disease.

Assessment of FEV1 and VC (or FVC) should be performed after inhaled bronchodilator as suggested by the GOLD guidelines. Not doing so may misclassify a patient as having COPD when the problem is asthma. Some current/former smokers may have airway obstruction that is actually asthma (eosinophilic inflammation) rather than COPD (characterized by neutrophilic airway inflammation). Some of these subjects don't show a response to inhaled bronchodilators within 15 minutes, but do respond to appropriate asthma therapy in the long term. These subjects sometimes get labeled as COPD using the 0.70 cut-off for obstruction.

The FEV1/VC ratio may not tell the entire story of airways obstruction. Both the FEV1 and the VC (or FVC) may be decreased in subjects who have combined obstructive and restrictive processes, or more commonly in those who show poor effort on spirometry. Some healthy subjects, particularly young adults, may show a low FEV1/VC ratio while the FEV1 is within normal limits. This pattern may represent normal variation due to

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unequal development of airways and lung parenchyma ('dysynapsis'), or it may be indicative of airway narrowing because of asthma. The FEV1/VC ratio may be normal in upper airway obstructive patterns when flow limitation occurs primarily during inspiration. Inspection of multiple flow-volume curves may be needed to identify significant airway obstruction. An MVV out of proportion to the patient's FEV1 may also suggest inspiratory flow limitation.

A patient who has an FEV1/VC ratio of 0.80 and another with an FEV1/VC ratio 0.30 are diagnostically simple. The former likely has no obstruction while the latter most likely has significant obstruction. Those patients in whom the FEV1/VC ratio is near the LLN offer the greatest challenge. In this instance the pre-test probability of disease (signs, symptoms, previous history, other abnormal tests) becomes crucial in making the appropriate diagnosis.

No less controversial is the question of how to best describe the severity of the obstructive defect, once identified. The ATS, ERS, and GOLD groups are in agreement that the severity of obstruction should be determined based on the FEV1 percent of predicted. Classification of severe obstruction is similar among these three groups with FEV1 % predicted values of less than 50% associated with moderate or severe obstruction. Values less than 30-35% of predicted are termed 'very severe'. At the other end of the scale, however, there are some significant differences. The GOLD initiative suggests that an FEV1% predicted ≥ 80%, in the presence of a low FEV1/VC (<0.70) constitutes mild obstruction, with or without symptoms. The ATS/ERS interpretive strategies list percent predicted values for FEV1 > 70% as representative of mild obstruction. The classification of 'mild obstruction' is thus based on a percentage of the predicted FEV1, even though the same document (ATS/ERS) recommends against using fixed percentages for interpretation. The use of a percentage for purposes of classification may be further compromised by the choice of predicteds set. That is, a patient may be classified as mildly obstructed using one reference set, or moderately obstructed if a different set is chosen.

Alternatives to using a percent of predicted for the FEV1 include using Z scores (sometimes called the standard deviation score or SDS). The Z score is based on the difference between the measured and predicted value divided by the residual standard deviation (RSD). The Z score tells us how different a particular patient is from the population of normal reference subjects. A patient who has an FEV1 Z score less than -1.64 has an FEV1 that occurs in only 5% of the reference population. For a more detailed explanation, visit the web page of Philip Quanjer, MD, PhD at http://www.spirxpert.com/statistical.htm.

The classification, or misclassification, of patients who have borderline abnormal spirometry has serious consequences. It may indicate disease where none is actually present, resulting in additional testing and prescription of medications that are not indicated, along with the attendant financial and psychological consequences. A recent study commissioned by the Department of Health and Human Services (HHS) suggests that spirometry may be of limited value (for case finding or clinical management) in patients who have an FEV1 greater than 50% of predicted.

Even though performance of spirometry has become highly standardized, interpretation of the results has a way to go. Interpretation of spirometry in the very healthy or the very obstructed patient is easy. More difficult is making sense of values near the lower limits of normal for simple parameters such as the FEV1 and the FEV1/VC. Carefully selecting the reference set and defining the LLN are important steps, but the patient's history, physical presentation, and symptoms must all be considered. The old adage "Never mind the numbers, look at the patient" is appropriate in this context.