

Optimal asthma diagnosis: A destination or a process?

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Asthma is a common and complex disorder with a variety of manifestations. The variability of the condition complicates the diagnosis because the criteria can be historical but not confirmable at the time of care. Spirometry is essential for confirming a diagnosis of asthma.¹⁻⁵ However, spirometry has problems and limitations. Change in FEV₁ is the measurement most frequently used, with an increase of more than 200 mL or a 12% to 15% change, usually after some dose of a bronchodilator, generally accepted as evidence of sufficient reversibility to support, but not prove, the diagnosis of asthma. There are questions about whether the absolute increase, the percentage of baseline FEV₁, or FEV₁ percent predicted is the best indicator of reversibility.⁶ Limitations are that patients are not always able to perform spirometry, particularly in the very young and chronically or acutely ill.⁷ Spirometry requires a commitment of the health professional to vigorously encourage the patient because spirometry is effort dependent. Normal values for spirometry differ depending on the criteria used, and select ethnic groups, notably populations from southern Asia and Africa,⁷⁻⁹ might not have reliable normative data. Reversibility is not specific for asthma, and asthmatic patients do not always exhibit diagnostic reversibility. Other quantifiable tests that support a diagnosis of asthma include biomarkers, such as the presence of serum eosinophilia, bronchial provocation studies, sputum eosinophilia, increased total IgE levels, clinically significant specific-IgE, and increased fraction of exhaled nitric oxide values.¹⁰ However, spirometry remains king in the world of asthma diagnosis.

How can the measurement of airflow obstruction be improved? Techniques that do not require as much effort, such as impulse oscillometry, have advocates, but the overall effect of such testing is currently limited.¹¹ Increased information from the current spirogram is another strategy.^{12,13} Variability or decrease in forced vital capacity (FVC), forced expiratory flow between 25% and 75% of FVC, and FEV₁/FVC ratio have all been suggested. FEV₁/FVC ratio is of particular interest because this

ratio helps distinguish airflow limitation caused by obstructive disease from that caused by restrictive pulmonary disease, with obstruction defined as an FEV₁/FVC ratio of less than 0.70. The figure of 0.7 has problems because the FEV₁/FVC ratio varies with age.

An article in the current issue of the *Journal of Allergy and Clinical Immunology* by Lambert et al¹⁴ provides evidence for the value of the FEV₁/FVC ratio not solely as a binary response variable with the presence or absence of obstruction based on a value of 0.7 but also the magnitude of decrease compared with the age-adjusted predicted normal value (z score). The authors used data from a variety of clinical trials of the American Lung Association/National Institutes of Health/National Heart, Lung, and Blood Institute Clinical Research Centers. The specific studies from which subjects were analyzed included well-defined asthmatic populations with mild or moderate-to-severe disease. Age- and sex-adjusted normal values for the FEV₁/FVC ratio were obtained from the published National Health and Nutrition Examination Survey data from 1999.¹⁵ The authors statistically evaluated test accuracy for the FEV₁/FVC z score for pretest asthma probabilities of 5%, 25%, and 50%. An SD was converted to the percentage difference from age-matched normal values. For a pretest asthma probability of 5%, an FEV₁/FVC z score decrease of 3 SDs provided maximum discrimination, whereas a pretest asthma probability of 50% only required an FEV₁/FVC z score threshold of a 1-SD decrease. The authors suggested that the optimal FEV₁/FVC z score for population screening is -2.0 SD, a 12% mean decrease, and for a symptomatic clinic patient with a pretest probability of approximately 50%, the optimal FEV₁/FVC z score is -1.0 SD, a 6% mean decrease. The authors also applied statistical methods to assess the accuracy of diagnosis in populations with variable asthma control. They found similar data for optimal performance in the FEV₁/FVC z score, with a 6% and 12% mean decrease predicting asthma in those with high and low pretest probabilities, respectively.

These findings have significant limitations, which are stated in the article.¹⁴ The basis for the analysis are data from well-defined asthmatic populations compared with those from a healthy population. Will the FEV₁/FVC z score perform as well in a population of clinic patients with a variety of diagnoses? Spirometric normal values are debated as well, with several predicted normal values used. Which is the best: the National Health and Nutrition Examination Survey, Polgar, Quanjer, Knudson, or Crapo? Should different normal values be used in different situations? Therefore what is the most accurate normal FEV₁/FVC ratio? Children are a challenging population in which to make a diagnosis of asthma, but they were not included in the analysis. The article by Lambert et al¹⁴ investigated optimal diagnostic accuracy but did not explore false-positive and false-negative values. Finally, the ethnic mixture of patients in the current article does not permit an answer to the question of determination of the FEV₁/FVC z score in Asian or other

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populations, in which normal data might not be as accurate and spirometric results might be more difficult to interpret.

Despite these limitations, the FEV₁/FVC *z* score is likely another useful parameter that can be applied to the interpretation of spirometry, along with FEV₁ percent predicted, absolute FEV₁, change in FEV₁, change in FVC, and possibly forced expiratory flow between 25% and 75% of FVC. No single value is sufficiently sensitive or specific to apply in all clinical situations for the diagnosis of asthma. All of these numbers are important but do not replace clinical judgment coupled with a thorough history and complete physical examination. The nonspecific nature of asthma symptoms and the inherent variability of the disease, with limited findings on physical examination, increase the importance of measurable parameters, now including the FEV₁/FVC *z* score. However, as with most chronic diseases, unbiased observations over time are critical in arriving at an accurate diagnosis. The secret of the care and diagnosis of asthma requires caring for the asthmatic patient, just as Francis Peabody¹⁶ pointed out almost 90 years ago. No test replaces caring and good clinical judgment.

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