Does Global Lung Initiative Obviate the Need for Lung Volume Measurements?

Establishing the diagnosis of restrictive lung disease is often difficult and requires extensive testing not only to diagnose but also to accurately classify the underlying disease. Current clinical practice often involves an initial screening with spirometry and a subsequent measurement of the vital capacity and lung volumes to confirm or exclude the diagnosis. Several clinical studies have failed to demonstrate a robust correlation between a low FVC and a low total lung capacity (TLC). Fewer than 50% of patients with an FVC below the lower limit of normal also have a reduced TLC.[1] In this issue of RESPIRATORY CARE, Vaz Fragoso et al[2] set out to determine whether the age-adjusted Global Lung Initiative (GLI) equations for spirometry would better identify those individuals with true restrictive lung disease. Their work demonstrated a high correlation between subjects with GLI restrictive-pattern spirometry and a decreased TLC. However, it remains unclear whether these findings are clinically important, accurately identifying patients with pathologically reduced lung volumes, and whether they truly represent a higher incidence of restrictive lung disease. Without these data, the article offers no concrete clinical evidence to suggest that isolated spirometry without lung volumes is adequate to establish the diagnosis of restricted lung disease.

Vaz Fragoso et al[2] show that those with GLI restrictive-pattern spirometry have a lower TLC than those without restrictive indices. However, all lung volume reference sets were eschewed due to disproportional racial and generational representation. Instead, the authors opted to show the relative differences in lung volumes between the different GLI spirometric categories. Although on average those with restrictive-pattern spirometry had lower lung volumes, it is unclear how many would have met the traditional definition of restrictive lung disease or had clinical evidence of disease. Interestingly, the demographics of

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the subjects in the Vaz Fragoso et al[2] study were roughly similar to the middle-aged and white populations that compose many of the standard reference values.[3,4] The lack of reference values in the study detracts from its clinical importance and applicability because it is difficult to assess whether these lower lung volumes truly signify a ventilatory restriction or a normal variant. Comparison with traditional equations and TLC reference values would have established clinical relevance and could have lent additional credibility to the study.

Being able to diagnose restrictive disease from simple spirometry is an alluring proposition that has been frequently investigated.[1,5-8] These studies use the traditional definition of restrictive lung disease and were designed to identify spirometric features that readily detect patients with restrictive patterns. Defining restrictive lung disease as a TLC less than the fifth percentile of standard reference values, Bruel Tronchon et al[8] showed in a population of elderly subjects that the GLI fared no better than the standard European Respiratory Society reference equations in predicting patients with restrictive lung disease. Although the positive predictive value of these reference values may be as low as 35%,[8] modifying the inclusion criteria may more accurately predict restrictive lung volumes. Vandevoorde et al[6] showed a 96% probability of identifying pathologic spirometric restriction by changing the definition of restrictive spirometry to FVC $<$55% predicted and a having a preserved FEV_1/FVC; however, they could not rule out restriction with equal certainty until the FVC was $>$100% predicted. The probability of accurately identifying restrictive spirometry is additionally augmented by accounting for a normal to elevated FEV_1/FVC.[2] In these studies, the accepted standard for determining restrictive disease remained the measurement of lung volumes, and the diagnostic algorithms were used as adjuncts to determine the need for lung volumes, not as a substitution for lung volume measurements. Spirometry as a

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single quick test to diagnose restrictive disease has been shown to be imprecise and has continued to require confirmatory lung volume testing.

Multiple methodologies have been investigated in the search for a more streamlined and accurate diagnosis of restrictive lung disease. Low-dose computed tomography has been closely correlated in normal and COPD cohorts,[9,10] and it may be helpful in classifying severity of disease in the absence of spirometry and static lung volumes. However, the volumetric estimation does not appear to correlate well with measured lung volumes in restrictive lung disease. In patients with systemic sclerosis, there is poor correlation in low-dose computed tomography lung volume measurements and traditional spirometry and static lung volumes, making it an unreliable methodology to track disease progression or establish severity of disease.[11] This further suggests the continued need for static lung volumes in patients with restrictive ventilatory defects.

Another consideration in this study by Vaz Fragoso et al[2] includes their use of single-breath-hold helium dilution to measure the TLC, and whereas their study demonstrated generally lower lung volumes in those subjects who exhibited restricted pattern on spirometry by GLI equations, single breath-hold helium dilution may underestimate overall lung volumes, especially in the areas of poor ventilation in the setting of underlying lung disease. The single-breath-hold technique is further flawed by a patient's frequent inability to exhale to residual volume,[12] which may be more pronounced in patients with lung pathology.

The patient population in this study is also worth noting because nearly 80% of the participants in the study were current or former smokers, probably with a high prevalence of underlying lung disease and possibly inaccurate lung volumes. Second, the patient population was significantly overweight, with nearly half of the subjects being in the obese category. Although the body mass index was accounted for in the multivariate analysis, obesity has been associated with spirometric restriction without decreased TLC, also termed a nonspecific pattern.[13] This nonspecific pattern is not uncommon in routine spirometry, and classifying all patients with a nonspecific reduced FVC as restrictive lung disease is premature and potentially dangerous.

The use of the GLI equations accounts for a nonlinear decrease in lung function, and it may be more accurate at advanced ages and better account for racial and ethnic physiologic differences than standard equations and could demonstrate a more accurate reflection of lung function. However, without TLC reference ranges and a comparison with current standards, it is impossible to truly determine whether restriction exists or to estimate to what degree it is present based on spirometry measurements alone. Although the authors ambitiously suggest that measurement of TLC for diagnosis of restrictive lung disease is no longer needed, without better and more concrete evidence, the use of spirometry to diagnose restrictive disease is not ready for clinical practice.

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