Normal Routine Spirometry Can Mask Chronic Obstructive Pulmonary Disease and Emphysema and Asthma in Symptomatic Patients

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This editorial will address the issues raised in the article by Qin et al1 entitled: “FEF25-75% is a more sensitive measure reflecting airway dysfunction in patients with asthma: a comparison study using FEF25-75% and FEV1%,” which is published in the current issue of JACI: In Practice. The isolated abnormal forced expiratory flow at 25% to 75% of forced vital capacity (FEF25-75%) was associated with higher spinae cosinophils, higher dosage of inhaled corticosteroid, and greater airway hyper-responsiveness. Qin et al1 noted that only 4.6% of the asthmatics studied had an isolated abnormal FEF25-75% despite both a normal forced expiratory volume in 1 second (FEV1)% and FEF25-75%. Similar issues have been raised by Bonini et al,2 Almeshari et al,3 and Postma et al,4 concerning earlier detection of suspected small airway obstruction in symptomatic asthmatics with otherwise normal routine spirometry including FEV1 (L), forced vital capacity (FVC) (L), and FEV1/FVC%. We have previously noted that symptomatic nonsmoking patients with suspected small airway obstruction, including asthmatics, can be identified by isolated abnormal expiratory airflow at low lung volume, FEF80%, despite normal routine spirometry and normal FEF25-75%.2

Furthermore, there also has been increasing interest in earlier physiologic detection of chronic obstructive pulmonary disease (COPD) in symptomatic smokers despite normal spirometry. Our recent COPD study6 that included high-resolution thin-section lung computed tomography and lung pathology confirmed our earlier observations7 that detection of small airway obstruction and emphysema in symptomatic smokers with normal routine spirometry requires analysis of expiratory airflow at low lung volumes, including FEF75%.8 Despite normal spirometry, including FEV1, FVC, and FEV1/FVC%, measuring airflow at FEF75% detected only 8 of 16 patients, maximal expiratory flow % only 4 of 16, residual volume (RV) 4 of 16, and RV/totall lung capacity % only 2 of 16, but all had abnormal FEF75%. Dependence on normal routine spirometry may result in clinical and physiologic delay in the diagnosis and treatment in symptomatic smokers with emphysema and small airway obstruction.

However, the ATS issued an official technical statement that concluded that FEF75% and FEF25-75% have not demonstrated added value for identifying obstruction in adults and children with normal routine spirometry.8 Unfortunately, this ATS statement is in contrast to published data in asthma and COPD/emphysema, as noted previously, that identify small airway obstruction despite normal routine spirometry by abnormal FEF25-75% and especially FEF75%. We also have emphasized that when the FEV1/FVC% is equal to or greater than 75%, the FEF25-75% is always normal.9 However, if the FEF25-75% is reduced, the FEV1/FVC% is always less than 75%, although not always outside predicted limits.10

Sentinel pathophysiologic studies by Macklem and Mead10 demonstrated that the resistance offered by the peripheral, small airways without cartilage, upstream from 10 to 12 divisions and <2.0 mm in internal diameter, normally contributed <20% of total airway resistance. Moreover, Hogg et al11 reported that in the presence of COPD, with or without emphysema, the distal quiet small bronchiolar zone was the major site of increased airway resistance. These studies were performed in postmortem lung specimens when the larynx was excluded. When all upper airway resistance is included, the contribution of small airway resistance to total airway resistance is probably ≤15%.10,11 This paradigm could be further obscured by normal expiratory spirometry measurements consistent with “preserved pulmonary function” as previously reported.

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