Is this asthma, COPD, or both?

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BACKGROUND

Asthma and COPD are the commonest respiratory diseases followed by pulmonologists. Due to shared clinical features, discriminating between the two diseases can be challenging; moreover, there might be asthma-COPD overlap (ACO).[1] Symptomatic patients are often referred for pulmonary function tests (PFTs), because their physicians hope that such tests will provide clear-cut diagnostic information.

OVERVIEW

Patient "A" was a 61-year-old woman, former smoker (18 pack-years), who was referred for PFTs "to confirm asthma," because a previous spirometry had shown a large FEV_1 response (0.55 L) to bronchodilator. Repeated PFTs showed a moderate and proportional decrease in FEV_1 and FVC (FEV_1/FVC = 0.72) with a large post-bronchodilator volume response (ΔFVC = 0.81 L), leading to a commensurate increase in FEV_1, that is, pre- and post-bronchodilator FEV_1/FVC ratios were similar. Gas trapping was detected on body plethysmography (RV/TLC = 0.59), with preserved TLC; of note, DL_{CO}, carbon monoxide transfer coefficient (K_{CO}), and alveolar ventilation (V_A)/TLC ratio were all moderately reduced. These results combined were more consistent with COPD than asthma; in fact, a chest CT showed moderate-to-severe centrilobular emphysema and diffuse airway thickening. Patient "B" was a 73-year-old gentleman previously diagnosed with COPD, on the basis of a heavy smoking history and airflow limitation on remote spirometry. Repeated PFTs confirmed moderate airflow limitation (FEV_1/FVC = 0.58; FEV_1 = 64% of the predicted value). Following the use of inhaled bronchodilator, FEV_1 and mid-expiratory flows normalized. Lung volumes, DL_{CO}, K_{CO} and V_A/TLC ratio were within normal limits, as was a chest CT. Collectively, these data were deemed more consistent with asthma than COPD.

Table 1. Ten misconceptions regarding the value of pulmonary function tests in discriminating asthma from COPD.[a]

False statement	Comment
1. Normal baseline spirometry (i.e., with no previous use of a BD) excludes airway disease	Some patients with airway disease present with ΔFEV_1 > day-to-day variability seen in normal subjects (up to 12% and 200 mL) despite normal spirometry, suggesting increased bronchomotor tone
2. Normal spirometry excludes smoking-related lung disease	Smokers with imaging (airway disease and emphysema) and other functional ($\Downarrow DL_{CO}$ and/or $\Downarrow K_{CO}$) abnormalities may present with "preserved" spirometry
3. An isolated decrease in mid-expiratory flows ($\Downarrow FEF_{25-75\%}$) is not relevant from a symptomatic standpoint in subjects with suspected airway disease	$FEF_{25-75\%}$ < LLN (60% of predicted), particularly in a subject with preserved FVC (i.e., $\Downarrow FEF_{25-75\%}$/FVC ratio), increases the likelihood of dynamic gas trapping and exertional dyspnea in patients with airway disease
4. SVC does not add value to FVC	In the right clinical context, $\Downarrow FEV_1$/SVC ratio despite preserved FEV_1/FVC ratio may uncover airflow limitation both in asthma and COPD
5. A significant "flow" response to inhaled BD (e.g., $\Delta FEV_1 \geq$ 12% and ≥ 200 mL) signals asthma	A sizeable fraction of patients with COPD (~2/3) may present with a "flow" response at some point
6. Large ΔFEV_1 (e.g., ≥ 20% and ≥ 400 mL) indicates asthma	Such large changes in FEV_1 may occur in a patient with COPD showing a "volume" response, i.e., ΔFVC ≥ 12% and ≥ 200 mL leading to similar pre- and post-BD FEV_1/FVC ratios
7. A significant "volume" response to inhaled BD (e.g., ΔFVC ≥ 12% and ≥ 200 mL) signals COPD	A "volume" response may occur in patients with asthma showing gas trapping and extensive small airway disease
8. Lack of normalization of a baseline spirometry showing airflow limitation signals COPD	~1/3 of the patients with moderate-to-severe persistent asthma may present with "fixed" airflow limitation
9. A negative methacholine challenge test excludes asthma	A negative test only indicates the absence of "active" hyperresponsiveness at a given point in time
10. Normal DL_{CO} excludes COPD	COPD patients showing features of the chronic bronchitis phenotype may present with preserved DL_{CO}

BD: bronchodilator; K_{CO}: lung diffusing coefficient for carbon monoxide (DL_{CO}/alveolar volume); LLN: lower limit of normal; and SVC: slow vital capacity. [a]Δ indicates the changes promoted by a short-acting BD.

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The list of scenarios in which PFTs are ambiguous about the presence of asthma or COPD (Table 1) is considerably larger than is that describing the few "diagnostic" situations provided above. For instance, even if a large increase in post-bronchodilator FEV_1 (ΔFEV_1 ≥ 20% and ≥ 400 mL) is more commonly associated with asthma, this is not necessarily the case when the increase in FEV_1 is largely driven by volume recruitment (Patient "A"; Table 1, scenario 6). In practice, no cutoff value has provided excellent performance to differentiate asthma from COPD clearly.[1] The spirometric pattern designated Preserved Ratio Impaired Spirometry, also seen in Patient "A," has been described in both diseases.[2] Low DL_{CO} and K_{CO} speak against asthma (Patient "A"), but low DL_{CO} may occur in non-anemic patients with asthma if V_A is a low fraction of TLC.[3] Conversely, preserved (or increased) DL_{CO} is more consistent with asthma, but it may occur in COPD patients with a predominance of chronic bronchitis (Table 1, scenario 10).[4] Establishing the presence of ACO is even more challenging. Given the seven definitions of ACO,[5] spirometry-based criteria were the least reliable and stable over time.

CLINICAL MESSAGE

In various circumstances, PFTs alone are unable to definitively establish asthma and/or COPD (Table 1). Relating functional data with additional clinical information (pre-test likelihood of disease, potentially including eosinophil counts) is crucial to this endeavor. A cautious, noncommittal approach is recommended: even if the results do suggest one of the diseases, it is safer (and more honest) to state that "in the right clinical context," the results are "consistent with" asthma and/or COPD.

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