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Out-of-proportion dyspnea and exercise intolerance in mild COPD

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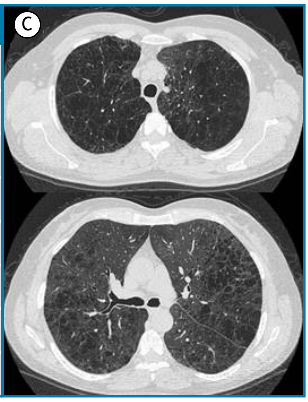
BACKGROUND

Most patients with COPD show only mild airflow limitation on spirometry. Despite FEV_1 normalcy, however, dyspnea on exertion is a frequent complaint. Structural and functional investigations in dyspneic patients with mild COPD showed important abnormalities in gas exchange efficiency, caused by a complex interaction among small airway disease, emphysema, and microvascular dysfunction.[1] Cardiopulmonary exercise testing is invariably useful to indicate whether patients presenting with out-of-proportion dyspnea can or cannot be ascribed to mild COPD.[2]

OVERVIEW

A 47-year-old woman (smoking history of 15 pack-years) was referred to a pulmonary clinic due to chronic dyspnea (modified Medical Research Council scale score = 2) and progressive exercise intolerance. Lung function tests revealed a mild obstructive ventilatory defect, preserved FEV_1, lung hyperinflation (↑functional residual capacity), gas trapping (↑RV), and $↓DL_{CO}$ (Figure 1A). Excess ventilation, as shown by high minute ventilation ($\dot{V}_E$)/carbon dioxide output ($\dot{V}CO_2$), was observed at rest and throughout the incremental cardiopulmonary exercise test (Figure 1B, first graph). These findings were associated with ↑Borg dyspnea scores as a function of work rate (Figure 1B, second graph). Conversely, dyspnea scores regarding heightened $\dot{V}_E$ were initially within the expected range for women of same age.[3] However, $\dot{V}_E$ at ~ 35 L/min caused an upward inflection in dyspnea scores (Figure 1B, third graph; red arrow) concomitant to critical constraints to V_T expansion (V_T/inspiratory capacity ~ 0.70). She subsequently stopped exercising at low peak O_2 uptake (69% of the predicted value) and work rate (48% of predicted) despite preserved "breathing reserve" (peak

(A)	Pre BD	Z score	% pred	Post BD	% pred
FVC	3.49	0.79	117	3.43	115
FEV_1	2.24	−0.41	90	2.19	88
FEV_1/FVC	0.64	−2.23	77	0.63	77
TLC	5.69	2.29	128		
RV	2.29	2.00	153		
FRC	3.63	2.21	149		
IC	2.05	0.53	106		
DLco	5.15	−1.96	69		



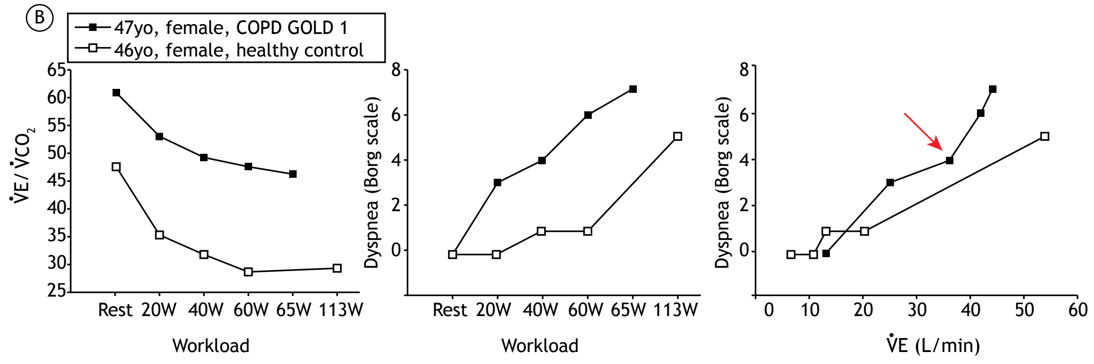


Figure 1. Data of a 47-year-old female smoker with out-of-proportion dyspnea and mild COPD. In A, lung function results with the patient at rest, In B, ventilatory response and dyspnea perception during incremental cardiopulmonary exercise testing. In C, chest CT scans showing extensive emphysema. BD: bronchodilator; FRC: functional residual capacity; IC: inspiratory capacity; yo: years old; GOLD 1: $FEV_1 \geq 80\%$ of predicted; $\dot{V}_E$: minute ventilation; and $\dot{V}CO_2$: carbon dioxide output.

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$\dot{V}_E$/estimated maximum voluntary ventilation ~ 0.6). Echocardiography was unremarkable, but a chest CT unveiled extensive emphysema (Figure 1C).

The efficiency of the lungs as gas exchangers improves on exercise since a lower fraction of V_T is "wasted" in the alveolar dead space (VD). Their efficiency as gas movers is maintained because end-expiratory lung volume decreases, and V_T occurs over the most compliant portion of the pressure-volume relationship of the respiratory system. In patients with mild COPD and dyspnea, enlarged areas of high alveolar ventilation-capillary perfusion relationship leads to a high VD/V_T.[4] Such impairment in gas exchange efficiency is frequently reflected on ↓DL_{CO} (Figure 1A).[5] The excess ventilation is associated with a high drive to the respiratory muscles, leading to increased dyspnea at a given exercise intensity (Figure 1B, second graph). Because the ventilatory pump can still respond to such a high drive, dyspnea remains proportional to the heightened $\dot{V}_E$. As $\dot{V}_E$ further increases and the expiratory time becomes progressively shorter, acute (dynamic) gas trapping ensues; thus, V_T eventually occurs too close to TLC. At that point onwards, dyspnea increases faster than does $\dot{V}_E$ because the ventilatory pump can no longer translate the high drive into the mechanical act of breathing (Figure 1B, third graph).[2]

CLINICAL MESSAGE

Although spirometry is useful for the diagnosis and gradation of airflow limitation, it provides an incomplete view of the functional abnormalities that are germane to a key, patient-centered outcome in COPD: physical activity-related dyspnea. ↓DL_{CO}, and ↑exertional $\dot{V}_E/\dot{V}CO_2$ signal gas exchange inefficiency in mild COPD, establishing a causal link between mild COPD and exercise intolerance in individual patients.

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