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Why we should never ignore an "isolated" low lung diffusing capacity

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BACKGROUND

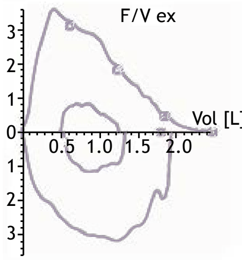
Different diseases causing "opposite" consequences on lung function tests (obstruction vs. restriction) frequently coexist, thereby modifying the pattern that is typical of each disorder. Untangling the underlying physiological disturbances is invariably useful to the pulmonologist.

OVERVIEW

A 72-year-old smoker (80 pack-years) was referred to advanced functional assessment due to "out-of-proportion" dyspnea relative to a normal spirometry performed by her family physician. Our spirometry results were also unremarkable; moreover, lung volumes were within

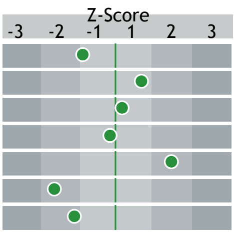
(A) Spirometry

	Pred	Pred LL	Pre	Pre % Pred
FVC	2.19	1.54	2.46	112
FEV_1	1.68	1.19	1.79	106
FEV_1/FVC	78	63	73	94
FEV_1/VC	77.77	63.21	72.87	94
FEF 25-75	1.44	0.61	1.33	93
FEF 50	2.71	2.24	1.83	67
FEF 75	0.31	0.10	0.48	157
PEF	4.85	1.68	3.62	75



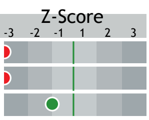
Body plethysmography

	Pred	Pred LL	Pred UL	Pre	Pre % Pred
TLC	4.21	3.25	5.17	3.72	88
VC	2.19	1.54	2.87	2.46	112
IC	1.43	0.98	1.89	1.47	103
FRCpl	2.32	1.54	3.09	2.25	97
ERV	0.71	0.48	0.93	0.87	124
RV	1.88	1.25	2.50	1.26	67
RV%TLC	42	30	55	34	80



Lung diffusing capacity

	Pred	Pred LL	Pre	Pre % Pred
DLCO Single...	16.1	12.0	5.0	31
DLCO/VA	4.3	3.2	1.6	37
VA Single...	3.81	3.01	3.19	84



(B)

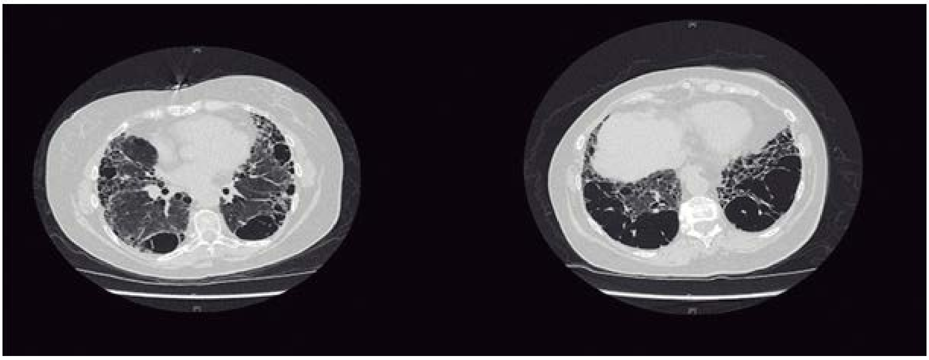


Figure 1. Pulmonary function test results (in A) and high-resolution CT scans of the chest (in B) in a 72-year-old female with "out-of-proportion" dyspnea. Pred: predicted value; Pred LL: lower limit of predicted value; pred UL: upper limit of predicted value; IC: inspiratory capacity; FRCpl: functional residual capacity by plethysmography; ERV: expiratory reserve volume; RV: residual volume; and VA: alveolar volume.

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normal limits with a trend to restriction. Of note, these results contrasted with severely reduced DLCO and carbon monoxide transfer coefficient [K_{CO} = DLCO/alveolar volume (V_A); Figure 1A]. She terminated an incremental exercise test at only 20 W due to severe dyspnea. Despite moderate hypoxemia and hypocapnia, neither hyperinflation nor critical inspiratory constraints were observed.[1] The dead space (V_D)/tidal volume (V_T) ratio was markedly increased at rest (0.60) and during exercise (0.50) in association with severe ventilatory inefficiency (V_E/VCO_2 nadir = 62). HRCT scanning uncovered combined pulmonary fibrosis and emphysema (CPFE; Figure 1B).

Why were spirometry and body plethysmography insensitive to the profound structural abnormalities of the patient? It is apparent that the lung parenchyma with no emphysema was heavily infiltrated by fibrosis (Figure 1B). Thus, opposite mechanical abnormalities canceled out each other, the net result being "normal" flows and volumes. The restrictive abnormalities seem to be physiologically more relevant than the enlarged airspaces—despite the CT scans suggesting otherwise. Notably, low DLCO exposed the ominous effect of both diseases on gas exchange.[2]

Exercise V_E was excessive for metabolic demand because a large fraction of the breath was "wasted" in the V_D, and the patient hyperventilated (low $PaCO_2$).[3] These phenomena might be inter-related: an enlarged V_D/V_T ratio is expected to increase overall (i.e. whole-lung) ventilation; thus, hyperventilation of areas with still preserved ventilation-perfusion would lead to hypocapnia—particularly in the presence of hypoxemia and other sources of increasing chemosensitivity.[4] Of note, V_A was close to TLC (V_A/TLC > 0.80), indicating that the tracing gas used in the single-breath DLCO measurement did gain access to most of the enlarged airspaces seen in Figure 1B.[5] In other words, they were still ventilated but likely not perfused, an important source of "wasted" V_E. Owing to preserved inspiratory capacity, V_T and V_E increased markedly. In contrast, patients with such severe emphysema—but no pulmonary fibrosis—are usually hyperinflated, mechanically constrained, and hypercapnic.[6] Thus, CPFE, paradoxically, gave her a ventilatory mechanical advantage as she could breathe from a "safe" distance from her TLC.[1] Unfortunately, her heightened drive fueled by "wasted" V_E and the vigorous efforts to keep $PaCO_2$ at a low value provoked severe breathlessness.

CLINICAL MESSAGE

Preserved spirometric parameters and lung volumes in symptomatic patients with an interstitial or obstructive lung disease should raise the suspicion of coexistent disorders. An out-of-proportion decrease in DLCO is frequently valuable to expose the severity of functional impairment and track the progression of the underlying diseases.

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