Integrating measurements of pulmonary gas exchange to answer clinically relevant questions

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BACKGROUND

The human body is primarily concerned with the stability of pH. The lungs are the organs responsible for maintaining an adequate $PaCO_2$ for the level of CO_2 production ($\dot{V}CO_2$) while avoiding critical decrements in PaO_2. Most of the pulmonary function tests, however, explore potential abnormalities in a step that precedes alveolar gas exchange, i.e., ventilation ($\dot{V}E$). Of note, arterial blood gases are influenced not only by the integrity of the alveolar-capillary membrane but also by hemodynamic factors (e.g., poor peripheral tissue perfusion leading to low mixed venous O_2 pressure) and changes in ventilatory drive (e.g., hypoventilation leading to hypercapnia and hypoxemia) among others.[1] Due to the ominous systemic consequences of impaired pulmonary gas exchange, tests addressing its multifaceted features are germane to the practice of Pulmonology.

OVERVIEW

A 71-year-old current smoker woman was referred to the pulmonology clinic due to progressing exertional dyspnea (modified Medical Research Council score = 3/4) despite normal spirometry, lung volumes, and contrast-enhanced chest CT results. Her dyspnea has been ascribed to sedentary lifestyle and severe anemia in the context of multiple myeloma. A six-minute walk test confirmed poor exercise tolerance with high dyspnea burden and exertional hypoxemia. Tests assessing gas exchange showed: a) low hemoglobin-corrected DL_{CO}

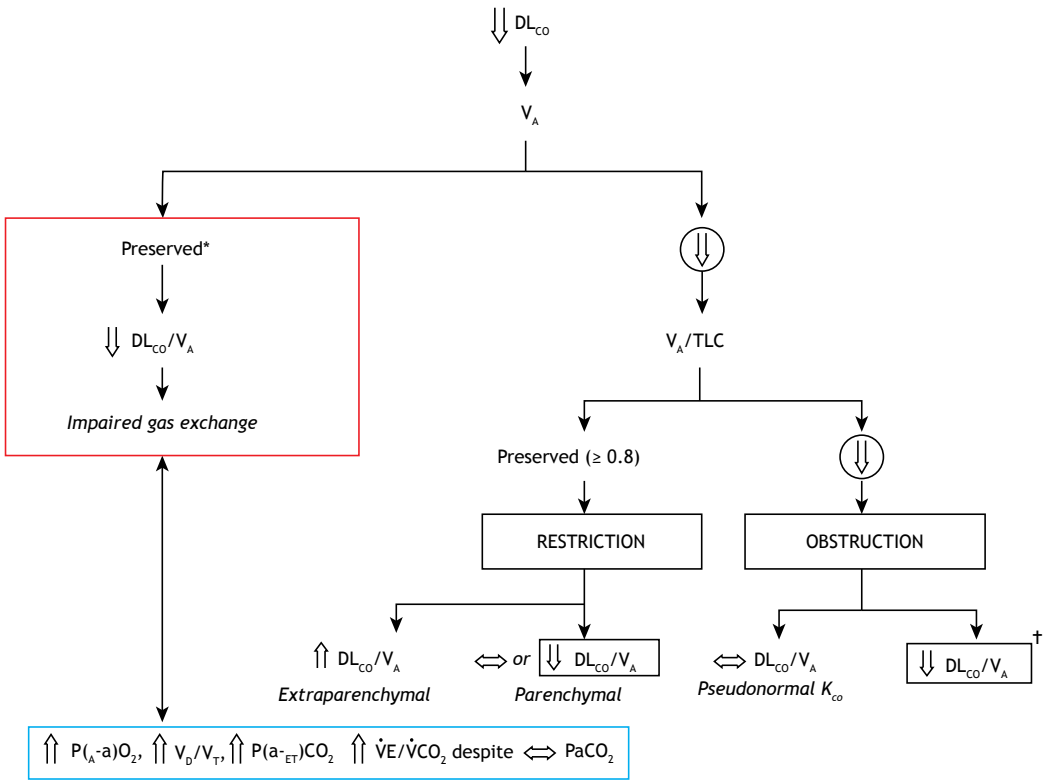

Figure 1. A simplified framework for an integrative analysis of pulmonary gas exchange based on routine pulmonary function tests. See text for further elaboration. Modified, with permission from the publisher.[3] V_A: alveolar ventilation; K_{CO}: carbon monoxide diffusion (transfer) coefficient; $P(A\text{-}a)O_2$: alveolar-arterial gradient pressure of O_2; V_D: dead space ventilation; V_T: tidal volume; $P(a\text{-}ET)CO_2$: arterial to end-tidal carbon dioxide gradient; $\dot{V}E$:ventilation; and $\dot{V}CO_2$: carbon dioxide production. *A normal V_A may coexist with airflow obstruction in a subject with mild airflow limitation in whom the distributive abnormalities are not severe enough to decrease V_A. †V_A may still lie in the normal range despite a low V_A/TLC in a severely hyperinflated patient (high TLC).

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and carbon monoxide transfer coefficient (K_{CO}) with normal alveolar ventilation (V_A) and V_A/TLC ratio; b) mildly reduced PaO_2 and eucapnia; and c) high alveolar-arterial gradient pressure of O_2 [$P(_A\text{-}a)O_2$], shunt fraction (on 100% O_2), physiological dead space, arterial to end-tidal carbon dioxide gradient [$P(a\text{-}_{ET})CO_2$], and resting o $\dot{V}E/\dot{V}CO_2$ratio. The pattern of impaired pulmonary gas exchange (Figure 1, in red), shunt and preserved $\dot{V}E$ distribution in the absence of emphysema or pulmonary arterial-venous fistulas raised concerns of poor pulmonary perfusion secondary to an extrapulmonary shunt. In fact, a transesophageal echocardiogram with microbubbles showed a small patent foramen ovale whose dimension markedly increased even with mild exertion. Absence of pulmonary hypertension at rest did not preclude right-to-left shunt (putative mechanisms in the study by Vitarelli).[2]

The rate of alveolar gas exchange can be substantially impaired despite preserved lung parenchyma. If hypoxemia cannot be explained by hypoventilation—high $PaCO_2$ and alveolar partial pressure of CO_2 (P_ACO_2), leading to low alveolar partial pressure of O_2 (P_AO_2)—or low inspired O_2 pressure (e.g., high altitude), impaired pulmonary perfusion should be considered as the most likely explanation. In the present case, right-to-left shunt diminished pulmonary perfusion thereby decreasing the functional surface for alveolar-capillary gas transfer (↓ DL_{CO}).[3] As VE was relatively well distributed (normal V_A/TLC ratio),[4] K_{CO} decreased. High $\dot{V}E$/perfusion ratio increased P_AO_2—and $P(_A\text{-}a)O_2$ as PaO_2 was low—and the fraction of tidal volume "wasted" in the dead space.[5] Thus, end-tidal CO_2 tension ($P_{ET}CO_2$) was substantially lower than P_ACO_2 (estimated by $PaCO_2$), because it was diluted by the PCO_2 from alveoli which were not properly exposed to CO_2-rich venous blood [↑$P(a\text{-}_{ET})CO_2$].[6] Higher $\dot{V}E$ was then needed to keep alveolar ventilation (↑$\dot{V}E/\dot{V}CO_2$ ratio; Figure 1, in blue).

CLINICAL MESSAGE

An integrated analysis of arterial blood gases (with indirect measurements of $\dot{V}E$ distribution and $\dot{V}E$-perfusion matching) and lung transfer capacity—in the light of clinical data—is invariably useful to untangle the mechanisms and consequences of impaired pulmonary gas exchange.

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