

Commentary

Assessment of gas exchange in lung disease: balancing accuracy against feasibility

Peter D Wagner

Division of Physiology, University of California, San Diego, California, USA

Corresponding author: Peter D Wagner, pdwagner@ucsd.edu

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Abstract

While the principles underlying alveolar gas exchange have been well-known for over 50 years, we still struggle to assess gas exchange in hypoxic patients. Unfortunately, simple measurements lack discrimination while complex measurements are infeasible in clinical care. The paper by Karbing *et al.* in this issue seeks a middle ground based on the arterial PO_2 (PaO_2)/inspired O_2 fraction (FiO_2) ratio measured at different FiO_2 s with the outcomes fed into proprietary software to account for both shunting and ventilation/perfusion inequality. Whether this is the optimal compromise between measurement difficulty and information available will have to be answered by those willing to test the approach in their own patients.

It never ceases to amaze me that the primary function of the lungs – gas exchange – can be accurately described by one simple mass conservation equation. Such cannot be said for any other organ. However, while this was well established over 50 years ago [1,2], we continue to struggle for ways to quantify abnormal gas exchange in patients with hypoxemia. The problem boils down to the complexity of gas exchange in diseased lungs, where hypoxemia can stem from, firstly, insufficient overall ventilation; secondly, shunting of blood through unventilated vascular channels; thirdly, non-uniform distribution of ventilation, perfusion, or both throughout the 300 million or so alveoli; and fourthly, diffusion limitation of O_2 exchange across the alveolar wall [3]. Added to these four well-known causes of hypoxemia is the also well-known modulation of arterial oxygenation by so-called extra-pulmonary factors: O_2 consumption, ventilation, cardiac output, acid/base state, Hb P_{50} and concentration, and body temperature [4]. Thus, when any of these extra-pulmonary factors change, so too will arterial oxygenation even if the lungs themselves remain unchanged. As if that were not enough, as inspired O_2 fraction (FiO_2) is altered, the arterial O_2 saturation changes, but the response is different depending on these various factors [5].

It should therefore come as no surprise that to fully assess gas exchange in any given patient, one really needs to be able to pin down each and every factor just mentioned. That of course is impractical (although technically feasible).

That leaves us wondering what the compromise should be. We want the most information at the least experimental cost. We want methodology that will quantify a gas exchange problem in a manner that allows reliable pulmonary pathophysiological insights and also filters out the “noise” from factors outside the lungs that, as mentioned above, affect gas exchange. Unfortunately, full understanding requires complex measurements – there is no short cut, and you get what you pay for.

At the simplest extreme, arterial PO_2 (PaO_2) or saturation do not do it, being sensitive to all the above factors: low experimental cost but poor discrimination between lung pathologies and between lung pathologies and the extra-pulmonary modulating factors. At the most complex extreme, the multiple inert gas elimination technique is currently the best tool to fully understand the nature of gas exchange [6,7], but the experimental cost is too high for routine clinical use.

The paper by Karbing *et al.* in this issue [8] tackles this optimization problem by re-examining the $\text{PaO}_2/\text{FiO}_2$ ratio, an index which has gained favor in recent years. They correctly point out that this ratio is NOT independent of FiO_2 despite its intent. They explore the behavior of this ratio under two common circumstances: two of the four causes of hypoxemia noted above – shunting and ventilation/perfusion ($\dot{V}\text{A}/\dot{Q}$) inequality. Applying this ratio to several sets of patients they show that while in some the ratio behaves as if the lung has a pure shunt, in others it behaves as if $\dot{V}\text{A}/\dot{Q}$ inequality is the problem. In others, both shunt and inequality are present. If

FiO_2 = inspired O_2 fraction; PaO_2 = arterial PO_2 ; $\dot{V}\text{A}/\dot{Q}$ = ventilation/perfusion ratio

$\text{PaO}_2/\text{FiO}_2$ is assessed at just one FiO_2 , one often cannot tell shunt from inequality. Many combinations of shunt and inequality can produce similar ratios at a given FiO_2 .

Their conclusion – to use $\text{PaO}_2/\text{FiO}_2$ as input to a model that includes both shunt and inequality to provide a more reliable view of the lungs than will be given by the ratio itself or by a model that allows only for shunt – should be self-evident. To do this will require measuring the ratio at more than one FiO_2 and using special software, so we are again at a crossroads. Is the information from this more sophisticated approach worth the extra effort of measurements over a range of FiO_2 coupled to use of a mathematical model? The authors say yes, and they have data to support this – a “confusion matrix” in which gas exchange severity classified by $\text{PaO}_2/\text{FiO}_2$ ratio changed less with FiO_2 when using their two-factor model than when using the shunt-only model. However, because the authors have a financial interest in commercial development of this methodology, it will be up to others to answer that question definitively.

Competing interests

The author declares that they have no competing interests.

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