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Model-driven gas exchange monitoring in the critically ill

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Abstract

Understanding pulmonary gas exchange performance is a dynamic process which, depending on clinical context, exhibits different levels of complexity. Global tools such as tension-based indexes yield clinically crucial information under very specific conditions. Yet, accurate mechanistic insight can only originate in model-based tools. One-parameter models such as shunt or dead space are well established in clinical practice whilst two or three-parameter models have just been advanced and their role is yet to be delineated. Although the latter provide superior accuracy, this comes at the cost of increased complexity and possibly the need for invasive data sets. Modelling gas exchange enables a quantitative and physiologically-driven management of patients with lung failure. Assumptions are inherent to each tool and can clinically mislead if not accounted for. Thorough understanding of their subjacent theoretical construct is a prerequisite for their judicious use. This manuscript aims to describe current gas exchange monitoring tools, with special reference to their mathematical framework and constituent pitfalls. A unifying perspective on their clinical role is proposed.

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Key words: gas exchange, model; shunt; ventilation-perfusion mismatch; lung diffusion, dead space

Impaired respiratory function is common amongst critically ill patients; hence, insightful monitoring of gas exchange is paramount as it may translate into precise and objective therapeutic management.

Blood-gas relationships may be ascertained with a wide array of methods able to yield both qualitative and quantitative information, depending on clinical context. Outside the intensive care unit, clinicians may exhibit a "lumped" approach, such as merely reading system outputs (e.g. PaO_2, SpO_2 or SaO_2) or their interrelation to system input (e.g. PaO_2/F_iO_2). Although this may suffice when facing simple clinical scenarios, its limits often push intensivists to favour mechanistic information derived from a system model approach. Shunt and dead space calculations are examples of classical one-parameter system models to address blood gas data, described as early as 1950 [1, 2]. These are well entrenched in current practice and capable of guiding an individualized hemodynamic and ventilator support; an interesting perspective on their use came from authors investigating their ability to monitor the membrane lung [3]. Recently, two-parameter models have emerged as a more extensive method to identify and follow disturbances of pulmonary gas transfer. They dichotomize the oxygenation problem into shunt and a non-shunt compartment which is assigned to either diffusion limitation (Rdiff), alveolar dead space (Vdalv) or ventilation-perfusion (V/Q) mismatch. Although superior as to performance to fit data when FiO_2 is varied, they have yet to become routine clinical practice tools.

All models come with caveats which are to be acknowledged in order to avoid seriously consequential pitfalls. Correct interpretation and bedside implementation of model-derived data warrants understanding of their underlying mathematical construct and its inherent assumptions.

BASIC PRINCIPLES

This section aims to restate only those basic principles needed to allow a better understanding of the categorization and comparison of current tools to monitor pulmonary gas transfer.

Following a ubiquitous physiological principle such as mass conservation, a quantitative formulation of the ratio of alveolar ventilation to alveolar perfusion can be reached as previously described by Rahn and Riley [1, 2]:

$VA/Q = (CcO_2 - CvO_2)/(F_iO_2 - FAO_2)$ (equation 1)

where VA is alveolar ventilation; Q is total blood flow; Cc and Cv are pulmonary end-capillary and arterial blood concentrations; Fi and FA represent inspired and alveolar gas fractions; for simplicity, the Haldane transformation is neglected.

Diffusion, as stated by Fick, can be written as:

$VO_2 = DLO_2 \cdot (PAO_2 - PcO_2)$ (equation 2)

where DLO_2 is total diffusion capacity of O_2, PA is alveolar pressure and Pc is pulmonary end-capillary blood concentration .

After converting fractions to pressures ($FAO_2 = PAO_2/(PB - PH_2O)$ where PB is the barometric pressure and PH_2O is water vapour pressure) and by combining equation 1 with 2, this gives:

$\boldsymbol{VA/Q} = (CcO_2 - CvO_2)/[F_iO_2 - (VO_2/\boldsymbol{DLO_2} + \boldsymbol{PcO_2})/(PB - PH_2O)]$ (equation 3)

Equation 3 attests that main pulmonary factors modulating blood gas tensions (PcO_2) are the range of V/Q ratios and the quality of the lung capillary barrier (DLO_2). Extrapulmonary determinants represent another category subsumed in equation 3; total ventilation, haemoglobin (Hb), the composition of inspired gas and mixed venous blood, which in fact mirrors cardiac output and oxygen uptake, are the most relevant in daily practice [4]. Secondary extrapulmonary factors relate to the oxygen (ODC) and carbon dioxide (CO_2DC) dissociating curves. Both categories can move in perfectly opposite directions such that lumped parameters like PaO_2 or PaO_2/F_iO_2 can be both inaccurate and misleading. Depending on the clinical context and chosen therapeutic strategy, it may become crucial to discern between the two types of factors (principle 1).

Although its position as a gold standard has been questioned, the multiple inert gases elimination technique (MIGET) remains the reference tool to describe pulmonary factors [5]. It allows diffusion impairment to be discarded as a common cause of hypoxemia leaving only the full V/Q spectrum to account for gas exchange disturbances in the critically ill population [6]. Thus, from a lung perspective, hypoxaemia and hypercapnia are best explained by shunt, dead space and V/Q mismatch, all parts of a continuum. Partitioning the contribution of each mechanism would define the most comprehensive tool (principle 2).

TENSION-BASED PARAMETERS

Tension-based indexes are first-order monitoring tools. Although they make useful adjuncts to any scoring system, they are essentially devoid of mechanistic insight and fail to meet the above-stated principles. Under special circumstances (see below), they may allow mechanistic information to be qualitatively deduced.

1. ALVEOLAR-ARTERIAL PO_2 (A-APO_2)

The simplified alveolar gas equation corrects alveolar gas tensions for respiratory quotient and corresponding arterial tensions and serves to compute A-aPO_2:

$PAO_2 = P_iO_2 - PACO_2/R$ (equation 4)

where P_iO_2 is the O_2 pressure in the inspiratory gas, $PACO_2$ is the alveolar CO_2 pressure and R is the respiratory quotient. For simplicity, it is often assumed that $PACO_2$ is close to arterial CO_2 tension ($PaCO_2$) but coexistent shunt invalidates this approximation [7].

A-aPO_2 was originally devised to distinguish hypoventilation-related hypoxemia from that elicited by a V/Q inequality or a diffusion limitation [8]. It was later shown to be fallible exactly under these circumstances; given that hypercapnia varies inversely with A-aPO_2, a concomitant V/Q mismatch would tend to normalize this index and remain unaccounted for [9]. Meaningful yet qualitative information can be derived when F_iO_2 is varied; with increasing F_iO_2, A-aPO_2 is expected to rise proportionately if shunt is prevalent whereas it will describe an inverted V shape if V/Q inequalities prevail [10].

2. PAO_2/F_IO_2

PaO_2/F_iO_2 ratio is possibly the most popular tension-based tool to characterize gas exchange performance and a very strong predictor of mortality in the acute respiratory distress syndrome (ARDS). Its use is expected to extend outside critical care areas as arterial blood sampling is no longer obligatory for its determination. For peripheral oxygen saturations (SpO_2) lying on the bend of the ODC, nonlinear computation of PaO_2/F_iO_2 from SpO_2/F_iO_2 [11] or mathematical conversion of venous oxygen tensions (PvO_2) to arterial values (PaO_2) [12] can circumvent the need to directly measure PaO_2.

The amount of nonaerated lung can be tracked by the natural logarithm of PaO_2/F_iO_2 ($lnPaO_2/F_iO_2$) obtained during pure oxygen ventilation [13]. Bedside estimation of end-expiratory lung volume (EELV) [14], or the delivered volume after a recruitment manoeuvre [15], are complementary methods to weigh the "baby lung" and launch a protective ventilation strategy.

Limitations of the PaO_2/F_iO_2 ratio mainly stem from its nonlinear behaviour when F_iO_2 is varied. This relationship is actively and unpredictably modulated by the same intrapulmonary and extrapulmonary factors stated above, so that with fixed V/Q alterations an infinite number of PaO_2/F_iO_2 ratios becomes possible. A comprehensive mathematical formulation based on established gas transfer relations (see equation 7) has been derived [16] and simplifies to:

$f\ (FiO_2) = PaO_2$ (equation 5)

where $f\ (FiO_2)$ $f\ (FiO_2)$ comprises six physiological coefficients: PB, $PaCO_2$, R, Hb, S (shunt ratio), AVD (arterio-venous difference in oxygen content).

This translates the poor capacity of this index to specifically capture the magnitude of alveolo-capillary damage. Clinically, it is highly consequential as disease misclassification may ensue and cause treatment plans to neglect the true subjacent pathology [17].

MODEL-BASED GAS EXCHANGE MONITORING

Gas exchange models merely approximate the real physiological picture. The ultimate test of model accuracy is its capacity to predict output (e.g. SaO_2, SpO_2 or expired fraction of O_2 – FeO_2) from a given input (e.g. FiO_2) (principle 3). This also turns out to be a good measure of its comprehensiveness in that a tool obeying principle 2 cannot but satisfy principle 3.

Classical one-parameter models (physiological dead space, venous admixture/shunt) and research tools such as the multicompartmental MIGET are based on forward modelling theory whereby a system structure is assumed and behaviour is predicted. Monoparametrical models often fail to see inside the "black box" and provide a poor fit to measured data. On the contrary, MIGET meets all three enunciated principles and shows the best fit although complexity itself disqualifies it as a routine clinical procedure.

An inverse modelling approach, whereby the least complicated but essential system structure is inferred from input-output linkages, indicates that the minimum number of parameters needed to appropriately depict gas exchange is two [18]. Models revolving around two parameters, although far from encapsulating all details of gas transfer, provide the next best fit to patient data after MIGET.

A detailed mathematical description is beyond our scope and can be found elsewhere [19]; instead, best clinical use of available models will be emphasized with special reference to their theoretical framework.

A. ONE-PARAMETER MODELS OF GAS EXCHANGE

In its simplest form, the oxygenation problem can be ascribed to a single cause: shunt, dead space, V/Q mismatch or diffusion limitation. Each model only satisfies principle 1. Of these, the first two are most clinically relevant and represent second-order monitoring tools.

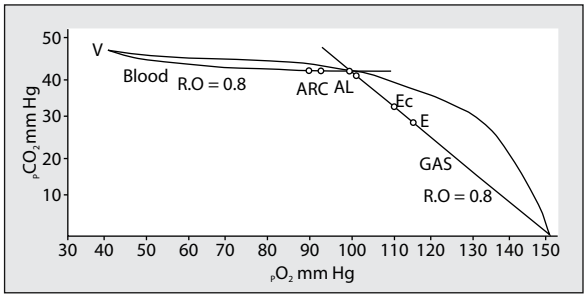

Figure 1. Classical O_2-CO_2 diagram showing all possible values for PO_2 and PCO_2 of alveoli with V/Q ranging from zero to infinity. Blood and gas R lines intersect in X. X — "ideal" alveolar air; C — mixed non-shunted alveolar capillary blood; AR — mixed arterial blood (after addition of shunt); AL — mixed alveolar air leaving all ventilated alveoli; E — mixed expired air; Ec — mixed expired air after correction for apparatus dead space; V — mixed venous blood; I — inspired air (reproduced with permission from Riley *et al.* [20])

1. SHUNT/VENOUS ADMIXTURE

Venous admixture may be thought of as the "alveolar dead space" of blood. It represents the deviation of arterial blood gas tensions towards mixed venous blood gas composition from that of an "ideal" alveolar blood-air interface which is defined by: 1) a local R equal to the respiratory quotient of the whole lung; and 2) a normal diffusion capacity (see Fig. 1) [20]. This "ideal" capillary–arterial gap is the result of alveoli with V/Q ratios less than " ideal" (lying at the left side of "X" in Fig. 1) and also includes true shunt (V/Q = 0). As theoretically predicted, when present, diffusion problems augment the gap as well.

A conceptual model consists of two alveolar compartments of which one provides "ideal" gas exchange and the other completely lacks ventilation (see Fig. 2). After writing mass balance equations for blood flow and oxygen content, the classical shunt equation of Berggren can be readily arrived at:

$$Shunt\ ratio\ (S) = (CcO_2 - CaO_2)/(CcO_2 - CvO_2)$$ (equation 6)

Resolution of the term CcO_2 requires the use of equation 4 and an ODC equation [21] to arrive at the corresponding pulmonary end-capillary saturation. Although computation of the denominator requires the use of a pulmonary artery catheter, this could be obviated by rewriting equation 6 and assuming a fixed AVD value (i.e. 4.3 mL dl^{-1}) [20]. This approach is sensitive to cardiac output oscillations.

$$S/(1-S) = (CcO_2 - CaO_2)/AVD$$ (equation 7)

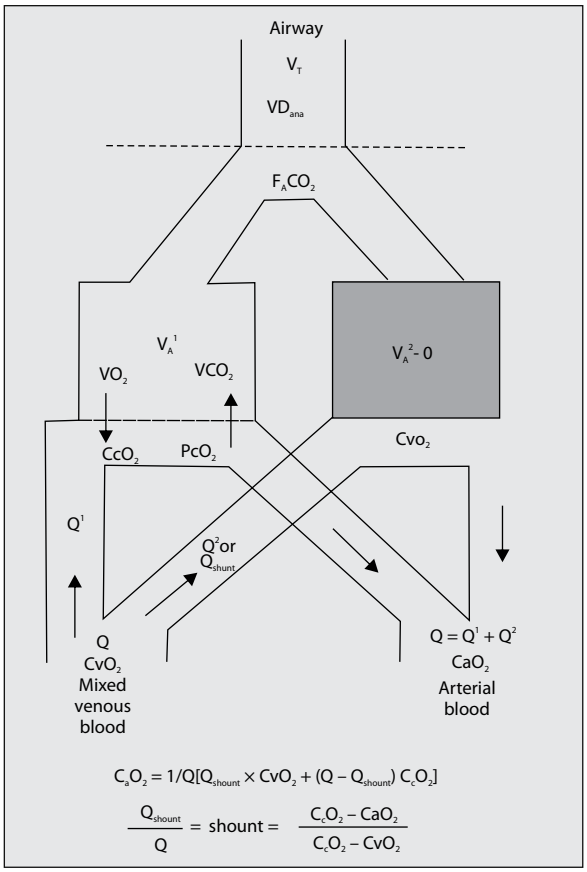

Figure 2. One-parameter, two-compartment model of shunt. Alveolar ventilation is absent in one compartment, leaving gas exchange to occur in the other one according to "ideal" conditions (see text for "ideal" definition). See Figure 5 for abbreviations

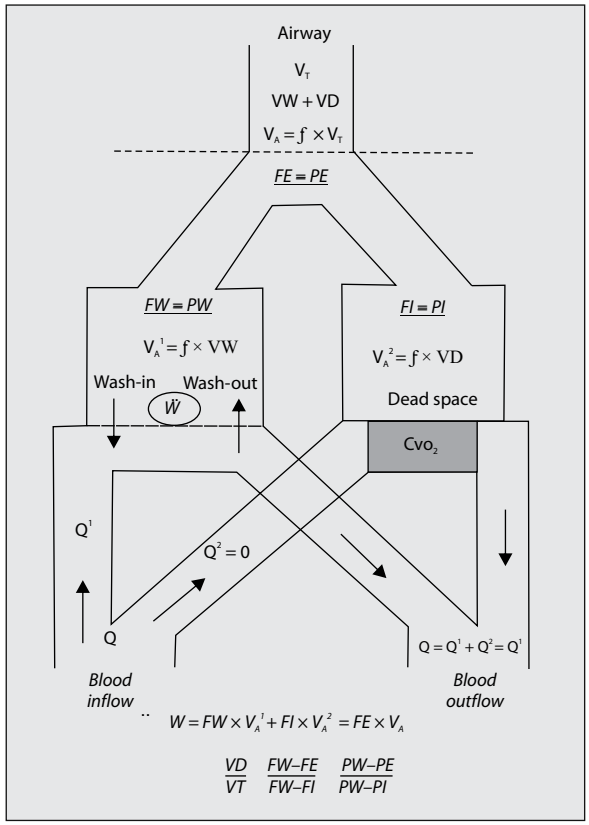

Figure 3. One-parameter, two-compartment model of dead space. Perfusion is absent in one compartment leaving gas exchange to occur in the other one according to "ideal" conditions. $\dot{W}$ is the wash-in/wash-out rate of any tracer gas; FE, FW, FI are tracer gas fractions in mixed expiratory air, compartment W and the non-perfused compartment respectively. PE, PW, PI are corresponding pressures of the same tracer gas; equivalency of pressures with fractions is shown. VW, VD are tidal volumes of compartment W and dead space respectively. Breathing frequency is ***f*** and minute alveolar ventilation is shown in each compartment

With increasing FiO_2, V/Q inequalities wane and equation 6 will approximate true shunt. Any pure oxygen-related atelectasis may be successfully negated, or at least minimized, if sufficient positive end-expiratory pressure is already applied [22]. Measurement of shunt during 100% oxygen predicts the amount of nonaerated lung and becomes a useful bedside method to track recruitment/derecruitment episodes [13].

Computation of shunt is the most cited technique to characterize native and membrane lungs of patients on extracorporeal membrane oxygenation (ECMO) [3]. It has been successfully implemented in a mathematical model of oxygenation during veno-venous ECMO which can be accessed online (www.ecmomodel.unimi.it) to help start up a preemptive therapeutic strategy [23].

2. DEAD SPACE

Similar to venous blood eluding gas exchange, air leaving non-perfused territories can be thought of as a "shunt". Regardless of whether it originates in conducting airways (VDana) or in alveoli (VDalv), dead space causes the composition of mixed alveolar air to diverge from that of an "ideal" compartment towards that of the inspired air (see Fig. 1).

Quantification of any dead space volume (VD) can be reduced to a two compartment model analysis: a ventilated but non-perfused compartment and one capable of gas exchange (W) (see Fig. 3). Mass balance relationships can be combined to obtain the following generalized formulation:

(PW–PE)/(PW–PI) = VD/(VD + VW) (equation 8)

where any tracer gas is characterized by: PW as the partial pressure inside compartment W; PE as the partial pressure in the mixed expired air flowing from both compartments; PI as the partial pressure in inspired air; VW is the volume of compartment W; and VD is the volume of the non-perfused compartment (V/Q = ∞). The absolute principle of this is that PW must only reflect the gas within W and cannot account for the gas within the dead space (V/Q = ∞) (principle 4).

For the particular case of VDana and CO_2 as a tracer gas, equation 8 becomes:

$(PAmCO_2 - PECO_2)/PAmCO_2 = VDana/VT$ (equation 9)

where $PAmCO_2$ is the mean CO_2 pressure of mixed alveolar air (approximated by end-tidal CO_2 ($PETCO_2$) if time-constants are perfectly homogeneous across the lung) and $PECO_2$ is CO_2 pressure of mixed expired air which can be derived from a volumetric capnogram (Vcap) or classically measured with a Douglas bag; VT is tidal volume.

Being ascribed to Bohr, equation 9 conveys one very important message: mean CO_2 pressure of all ventilated alveoli can only determine anatomical VD. Indeed, equation 9 was originally conceived to derive $PAmCO_2$ based on known VDana which had been measured on cadaver airways [24].

When compartment W is taken to represent an alveolar sector with "ideal" characteristics, equation 8 translates to the classical physiological dead space (VDphys) computation:

$(PAiCO_2 - PECO_2)/PAiCO_2 = VDphys/VT$ (equation 10)

where $PAiCO_2$ is the alveolar CO_2 tension of an "ideal" territory as already defined. VDphys will include not only anatomical dead space and true alveolar dead space (V/Q = ∞) but also territories with V/Q values higher than "ideal" (lying at the right side of "X" in Fig. 1). Most confusion stems from defining $PAiCO_2$ as this will establish the V/Q range of what actually constitutes dead space.

Approximation of $PAiCO_2$ with $PaCO_2$ as originally suggested by Riley, is referred to as Enghoff's physiological dead space (VDe).

$(PaCO_2 - PECO_2)/PaCO_2 = VDe/VT$ (equation 11)

This is the favoured method to assess wasted ventilation and has recently been applied to artificial lungs as well [3]. Coexistent shunt, especially when larger than 40%, will erroneously elevate VDe [25]. This may turn out to be clinically useful when an inclusive index of lung state is called for as in prediction of mortality [26]. Dynamic monitoring of VDe detects lung collapse [27] and indicates the best positive end expiratory pressure (PEEP) [28] or the optimum inspiratory flow pattern [29]. On the contrary, a single value may not allow a differentiated ventilator strategy, as it may indicate both atelectasis and overdistension [30], each triggering a totally opposite action. Correction for shunt seems justified and has been achieved by several authors, with the most direct method provided by Kuwabara *et al.* [31]. As oxygen content is simplistically equated to oxygen pressures, the following results from equation 6:

$PcCO_2 = PvCO_2 - [PvCO_2 - PaCO_2/(1-S)]$ (equation 12)

Concordant with Riley's model, $PcCO_2$ is taken to represent $PAiCO_2$ and thus equation 10 is combined with 12 to yield a corrected VDphys.

Carbon dioxide kinetics will probably play an increasing role as a routine clinical decision tool with the advent of respiratory monitors capable of continuously tracking Vcap. With $PaCO_2$ superimposed on a CO_2-VT plot, the graphical determination of VDe becomes possible and reproduces equation 11 [32]. The most common way to derive VDana is according to Fowler's equal area method which is, in fact, a geometrical representation of equation 9. In order to standardize Vcap, a mathematical function was recently applied to the raw CO_2 waveform, allowing a more robust measurement of VDana and other curve specifics [33]. The same author group foregrounded the use of a mean alveolar CO_2 pressure ($PA_{BOHR}CO_2$) to calculate "true" alveolar dead space (VD_{BOHR}), uncontaminated by shunt effects [30]. It was commented that this approach merely equates to equation 9 [34]: using the mean of "all" alveoli as a substitute for PW (see equation 8) will undoubtedly encapsulate units with high V/Q ratios (e.g. V/Q = ∞) and therefore principle 4 is violated — VDalv/VDphys just cannot be inferred, only VDana can. This contrasts with the proven ability of VD_{BOHR} to actually track VDalv in a cardiac surgery patient [34], or detect overdistension during a PEEP trial [35]. To clarify this discrepancy, it is useful to consider the proposed determination of the "airway-alveolar" interface which is different from Fowler's method. As the authors clearly show, under most circumstances, Fowler's method will underestimate the VDana calculated by their method [33]. The net result is that $PA_{BOHR}CO_2$ will lie at the right side of $PAmCO_2$, which is closer to a virtual $PAiCO_2$ (i.e. $PaCO_2$ according to Riley). Conveniently, this means that, under most circumstances, $PA_{BOHR}CO_2$ will not be the "true mean" as it fails to represent all alveoli and VD_{BOHR} will then be able to capture VDalv.

Measured together, VDe and VD_{BOHR} cover the entire continuum of V/Q ratios, provide complementary data and can act in concert to enable a lung-protective ventilatory strategy.

Lastly, the information obtained from Vcap could extend beyond the assessment of CO_2 volumes. Waveform morphology distorts specifically with alveolar recruitment and reflects acinar gas mixing and perfusion [36, 37]. The translatability of these findings into clinical practice is yet awaited.

B. TWO-PARAMETER MODELS OF GAS EXCHANGE

These are third-order tools to monitor pulmonary gas exchange as they meet both principles 1 and 3. Their conceptualization originates in Riley's work (see Fig. 1) [20]. Between ideal capillary and arterial blood, two virtual oxygen gaps can be delineated: one caused by "pure" shunt (distance between AR and C) and a second represented by

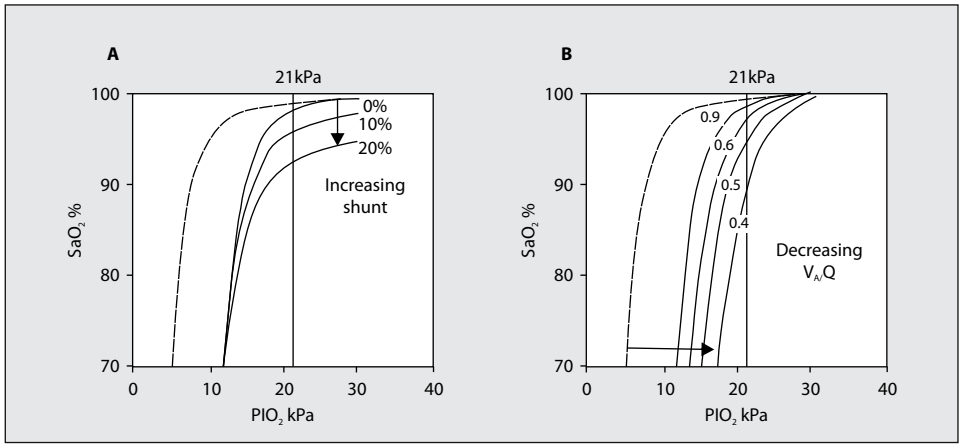

Figure 4. Effects of increasing shunt or reducing ventilation — perfusion (V/Q) ratio on a plot of PiO_2 versus SaO_2. The dashed line identifies the oxygen dissociation curve (reproduced with permission from Rowe *et al.* [39])

the difference between ideal capillary and mixed capillary blood (ΔPO_2 is distance from X to C). The latter could be attributed to either Rdiff, V/Q mismatch (any V/Q > 0) or a mixture of these but , with Rdiff cast off as a common cause of hypoxemia in the critically ill (see above), ΔPO_2 can be entirely attributed to the V/Q state.

Shunt and ΔPO_2 are embedded in plots of PiO_2 versus SpO_2 such that, after adjustment for their effect and correction for alveolar air (equation 4), complete identity between ODC and the $P_iO_2 - SpO_2$ diagram is mathematically demonstrable [38]. An increasing shunt will produce a specific downward shift of the original ODC whereas ΔPO_2 relates to a rightward displacement of the curve (see Fig. 4); ultimately, a unique $P_iO_2 - SpO_2$ plot inclosing all synchronous gas exchange abnormalities is ready to be deciphered.

The first mathematical formulation of these models was generated by Sapsford and Jones.[38] Simplistically, it can be restated as:

$f\,(PiO_2) = f\,(PiO_2) = SaO_2$ (equation 13)

where f (PiO2) f (PiO2) comprises two unknowns (shunt and ΔPO_2) and several physiological coefficients of which haemoglobin and cardiac output result in the largest sensitivity. Correct identification of system parameters requires at least two P_iO_2/SaO_2 data sets which should range over the maximal downward curvature of the $P_iO_2 - SpO_2$ plot to ensure optimum model fit (i.e. close to SaO_2/SpO_2 of 96%) [40]. The implicit assumption hereof is that multiple F_iO_2 steps will not alter lung physiology; this may be valid only as long as an upper limit of 0.8 is respected [41].

A refinement came from Kjaergaard *et al.* [19] who advanced a three-compartment, two-parameter model (see Fig. 5). Data sets belong to a plot of F_eO_2 versus SpO_2/SaO_2. A fixed perfusion split ($f_2 = 0.9$) is assigned to the non-shunted blood serving two alveolar compartments ventilated according to a variable fraction (fA_2) which indirectly becomes a measure of V/Q heterogeneity. Optimum gas exchange is simulated at zero shunt and fA_2 equal to 0.9 ($\Delta PO_2 = 0$kPa). Although far from fulfilling principle 2, this "minimal" model fits with acceptable accuracy MIGET data sets [42] and significantly outperforms one-parameter models (i.e. shunt in equation 7 or 5) in predicting the PaO_2/FiO_2 behaviour to varying FiO_2 [17]. Improved accuracy, but at the cost of increased complexity, comes with the addition of a third free parameter (f_2 as the fractional perfusion distributor) and the writing of alveolar and blood mass balance equations for both O_2 and CO_2 [43].

Clinical use is yet to be defined. Non-invasive determination of parameters will probably enable wider application of these models [44], as will the free distribution of simple, intuitive bedside tools (http://www.noranaes.org/shuntcurves/).

Failure to differentiate between shunt and V/Q mismatch precludes a flexible and advised therapy. Such a dichotomized view has been shown to inform on the risk of postoperative hypoxemia, the impact of anticongestive therapy, lung recruitability or PEEP selection and could be envisaged to assess any drug-related (e.g. nitric oxide) or mechanically-induced V/Q alteration [19, 45, 46]. "Minimal" models of gas exchange have been assimilated to advanced model-based decision supports, such as the Intelligent Ventilator (INVENT) project [47] or non-invasive cardiac output estimators [48]. In addition, because a stepwise variation in FiO_2 simply imitates a tracer gas (oxygen as in Weissman's LUFU system [49], or nitrogen as described by Stenqvist *et al.* [50]), functional residual capacity (FRC) or EELV would be readily attainable and overall lung strain may be calculated from sequential EELV determinations [14]. The extent of local inhomogeneities is imprinted in oxygen washout curves which could provide yet another useful index [51]. Overall,

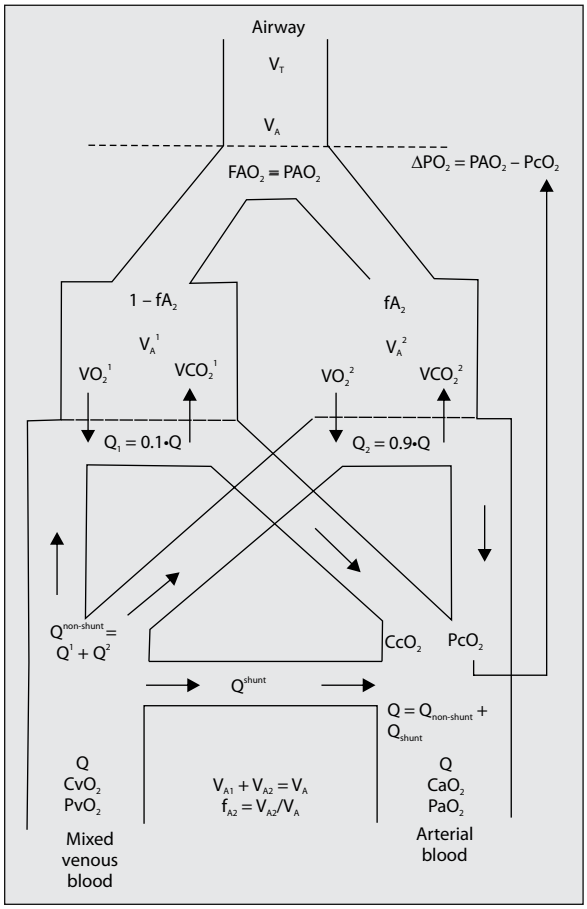

Figure 5. Minimal model of gas exchange with three compartments and two parameters: a pulmonary shunt compartment and two others ventilated according to a fractional ventilation distributor (fA_2). V_A — alveolar ventilation; V_A^1 and V_A^2 — alveolar ventilation of the ventilated compartments; Q — overall cardiac output; PvO_2 — mixed venous pressure of oxygen; CvO_2 — oxygen content in mixed venous blood; PaO_2 — systemic arterial pressure of oxygen; CaO_2 — oxygen content in systemic arterial blood; Q^{shunt} — shunted venous blood flow; Q^1 and Q^2 — blood flows corresponding to ventilated compartments; PcO_2 — non-shunted end-capillary oxygen pressure; CcO_2 — oxygen content in non-shunted end-capillary blood; PAO_2 — mixed alveolar air oxygen pressure; $VO_2^{1,2}$ and $VCO_2^{1,2}$ compartmental O_2 consumption and CO_2 production respectively (adapted after Karbing *et al.* [42])

a simple bedside manoeuvre such as FiO_2 variation could coordinate a highly personalized, physiologically-oriented stress-free ventilation strategy.

DISCUSSION

Deciding which monitoring test to use is clinically consequential. It is tempting to define the ideal tool as that which offers the most exhaustive description of gas exchange. MIGET could then emerge as the ultimate choice were it not for its cumbersome and costly preparation. Hierarchically, three-parameter models followed by two-parameter models would come next. Could these be the optimum tools to monitor pulmonary gas exchange?

Critical illness offers a diverse array of challenges, ranging from a simple dichotomous decision of whether to turn prone an ARDS patient to a dynamic, quantitative assessment of lung state following a change in ventilator settings. Physicians will face situations which call for a pragmatic and undifferentiated approach devised to set out a timely therapeutic plan. The necessity for a low tidal volume strategy should rely on the clinical context and elementary tools such as the PaO_2/FiO_2 ratio. Likewise, Enghoff's VD may serve as a very strong predictor of mortality in ARDS patients and this is probably due to its global nature resulting from the failure to separate shunt from dead space. An accurate split-view of these two mechanisms may turn out to be advantageous when an informed open lung strategy is considered. The solution thereof is a combination of VD_{BOHR} and the computation of equation 6 during a short episode of pure oxygen ventilation. Alternatively, discriminating between shunt and V/Q imbalance with third-order monitoring tools may generate an even more inclusive and reproducible picture, one closer to patient physiology and remarkably accurate when set against MIGET.

Thus, it appears that appropriateness in context may be the correct descriptor of the ideal tool. If weighed carefully, clinical settings will advise one of the right balance between the information yield and the complexity of a test. An optimum, but often different monitoring method will then ensue within each clinical scenario. To answer the question above, any tool may be ideal but only when used in the right context.

CONCLUSION

Model-based quantification of pulmonary gas exchange merely approximates the complexity of real physiological processes. If limits inherent to their underlying mathematical construct are thoroughly acknowledged, these tools enable rational, uniform and physiologically-oriented clinical decision making. Optimum use rests in each clinician's ability to tune the right model to the appropriate context and patient in a timely fashion.

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