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Gas exchange indices — how valid are they?

André Coetzee, Justiaan Swanevelder, Giepie van der Spuy, Jaco Jansen

Objective. This study examined the arterial-alveolar oxygen tension difference ($AaDO_2$), arterial oxygen tension to inspired oxygen fraction ratio (PaO_2/FiO_2) and alveolar to arterial oxygen tension ratio (PAO_2/PaO_2) with regard to: (*i*) their correlation with the calculated pulmonary shunt in critically ill patients; and (*ii*) the influence of the inspired oxygen fraction on these indices before, during and after general anaesthesia.

Design. This study comprised two sections: (*i*) retrospective analyses of blood gas data retrieved from the intensive care computerised database; and (*ii*) analyses of arterial blood gases before, during and after abdominal and orthopaedic surgery in patients subjected to various inspired fractions of oxygen.

Setting. The study was conducted at an academic hospital.

Patients. The first section of the study was a retrospective analysis of blood gases retrieved from a computerised database from the surgical and respiratory intensive care units. Blood gases which indicated hypoxaemia (arterial haemoglobin saturation less than 90%) were collected from patients who suffered from adult respiratory distress syndrome. The calculated pulmonary shunt was correlated with the $AaDO_2$, PaO_2/FiO_2 and PAO_2/PaO_2. In the second section of this study, 15 patients of American Society of Anesthesiologists status 1, scheduled to undergo peripheral orthopaedic and intra-abdominal surgery, were exposed to various concentrations of inspired oxygen before, during and after general anaesthesia. At the end of a 15-minute period of exposure to a particular level of inspired oxygen (which was varied at random), arterial blood gases were analysed. A correlation was attempted between the inspired oxygen fraction and the various indices of pulmonary gas exchange.

Intervention. Patients were subjected to the various inspired fractions of oxygen before, during and after general anaesthesia. A radial artery cannula, inserted under local anaesthesia, allowed the researchers to collect arterial blood gas analysis.

Results. The correlation between the calculated pulmonary shunt and indices of gas exchange showed $r = 0{,}35$ for the $AaDO_2$, $r = 0{,}08$ for the PaO_2/FiO_2 and $r = 0{,}40$ for the PAO_2/PaO_2. Stepwise variable selection demonstrated that the FiO_2, $PaCO_2$, PAO_2 and shunt were the main components of the final models.

The inspired oxygen fraction had an effect on the indices of gas exchange inasmuch as they all varied directly with the change in inspired oxygen concentration. Furthermore, the slope of this relationship was less steep during anaesthesia than in the case of values obtained before and after anaesthesia.

Conclusions. The so-called non-invasive indices of pulmonary gas exchange do not correlate well with the calculated pulmonary shunt, which is regarded as the gold standard that reflects the various components of gas exchange. We speculate that the poor performance of these indices can be explained by the fact that they do not take into account the mixed venous saturation and, except for the alveolar to arterial oxygen tension ratio, ignore the effects of alveolar ventilation.

The effect of the inspired oxygen fraction on these ratios makes them difficult to interpret if similar inspired oxygen fractions are not used. The effect of the FiO_2 on these indices could possibly be explained by the denitrogenation and collapse of alveoli with low ventilation perfusion ratios.

The change in the slope of the FiO_2 and the indices that was demonstrated during anaesthesia could possibly be explained by the expected change in the mixed venous saturation that occurs during anaesthesia.

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The quest to define pulmonary gas exchange with relatively non-invasive measurements has led to the use of various indices such as the alveolar-arterial difference in oxygen tension ($AaDO_2$), arterial oxygen tension to inspired oxygen fraction ratio (PaO_2/FiO_2) and the alveolar to arterial oxygen tension ratio (PAO_2/PaO_2).

However, publications have demonstrated that the calculated shunt and $AaDO_2$ vary directly with the inspired oxygen fraction,[1-10] while there is controversy as to the effect the inspired oxygen fraction has on PaO_2/FiO_2 and PAO_2/PaO_2 ratios.[11-14]

This paper addresses the following issues: (*i*) how well do these indices correlate with the calculated pulmonary shunt (Qs/Qt) in patients with arterial hypoxaemia caused by adult respiratory distress syndrome (ARDS)?[15] and (*ii*) what is the effect of the inspired oxygen fraction and anaesthesia on these indices?

Methods

Intensive care study

Data were gathered retrospectively from the surgical and respiratory intensive care units. As all blood gas data are

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stored on computer, a search was initiated of the most recent blood gas values in which the arterial oxygen tension (PaO_2) was less than 8 kPa and haemoglobin saturation for arterial blood (SaO_2) less than 90%. One hundred and four sets of data points (which included arterial and mixed venous gases as well as peripheral and central circulation parameters) were retrieved for analysis.

In the intensive care units, blood gases are collected anaerobically from an indwelling arterial cannula and proximal pulmonary artery catheter and analysed immediately in automated blood gas analysers (Corning 2500,288) in the laboratory of the respiratory unit.

Oxygen content (C) for arterial (a), mixed venous (v) and capillary (c) blood was calculated from the equation:

content = (haemoglobin*1,39*haemoglobin saturation/100)+ (0,0031*PO_2).

For calculation of CcO_2, it was assumed that the PcO_2 was similar to the alveolar oxygen tension (PAO_2) and that the latter was calculated from the alveolar gas equation:

$$PAO_2 = (P_B - P_{H2O})\ FiO_2 - PaCO_2[FiO_2 + (1 - FiO_2)/R],$$

where P_B = barometric [pressure and P_{H2O} = saturated water vapour pressure taken as 6,27 kPa at 37°C and R = respiratory quotient, which was accepted as 0,8. It was furthermore assumed that the haemoglobin saturation for capillary blood (ScO_2) was 100% as all the patients were on a FiO_2 in excess of 0,4. The pulmonary shunt was calculated from the shunt equation:

$$Qs/Qt = (CcO_2 - CaO_2)/(C\bar{v}O_2 - C\bar{v}O_2).$$

The $AaDO_2$ (in kPa) was calculated as the difference between the alveolar oxygen tension and the arterial oxygen tension. The PaO_2/FiO_2 ratio was calculated as the ratio of the PaO_2 (in kPa) and the FiO_2 and the PAO_2/FiO_2 ratio were determined using values in kPa.

Relationship of $AaDO_2$, PaO_2/FiO_2, and PAO_2/PaO_2 and FiO_2

Fourteen patients, 7 scheduled to undergo intra-abdominal operations and 7 peripheral orthopaedic surgery, of American Society of Anesthesiologists (ASA) status 1 were selected for this section of the study. Informed consent was obtained from each patient and they were subjected to the following protocol.

Patients were premedicated with oral diazepam 0,15 mg/kg 2 hours before surgery. In the induction room adjacent to the operating room, venous and radial arterial lines were placed under local anaesthesia. The patient then breathed various concentrations of oxygen (in air) through a Venturi-type oxygen mask with the correct oxygen flow. After 15 minutes at each new level of FiO_2, an arterial blood sample was taken and analysed as indicated in the previous section. The inspired oxygen concentrations were varied at random between 0,21, 0,28, 0,35 and 0,40 in every patient.

Anaesthesia was standard for all patients and consisted of thiopentone, fentanyl, vecuronium and mechanical ventilation (tidal volume 10 ml/kg) using air in oxygen. Ventilation rate was adjusted to ensure an expired CO_2 of 4,5 - 5%. Isoflurane was used to maintain anaesthesia. An ECG and capnograph were taken, and peripheral oximetry, airway pressure and FiO_2 were monitored in addition to invasive blood pressure.

During anaesthesia, the inspired oxygen fraction was again varied. The concentrations used were 30%, 40%, 50%, 60% and 70%; these were changed at random and the inspired fraction was continuously verified (Oxycheck, Criticon). Blood gases were determined 15 minutes after the inspired oxygen concentration was changed.

Before discharge from the recovery room, patients were again subjected to various inspired concentrations of oxygen, as was done before anaesthesia. the arterial cannula was removed before the patient left the recovery room.

Data were analysed by means of analysis of variance (ANOVA) (Tukey) and subsequently by multiple-range test. Regression analysis utilised the method of least squares. Data were only examined in respect of simple linear association, and non-linear models were not examined. The slopes of various regressions were compared using analysis of covariance. A probability of 0,05 was accepted as indicative of a significant difference between values.

Results

Relationship between the less invasive indices and Qs/Qt (Figs 1, 2 and 3)

When regression analyses were attempted for Qs/Qt, the independent variable, and $AaDO_2$, PaO_2/FiO_2 and PAO_2/PaO_2, the dependent variable, the following were obtained:

	Estimate	*SE*	*t*	*P-value*
$AaDO_2$				
Intercept	18,69	8,85	2,11	0,04
Slope	0,67	0,18	3,72	0,0003
F-ratio = 13,82, *P* = 0,00001, df = 1,102, *r* = 0,35, SEE = 21,49				
PaO_2/FiO_2				
Intercept	80,32	2,28	35,20	0,00001
Slope	0,04	0,05	0,83	0,4060
F-ratio = 0,69, *P* = 0,41, df = 1,102, *r* = 0,08, SEE = 5,54				
PAO_2/PaO_2				
Intercept	1,86	1,33	1,40	0,1640
Slope	0,12	0,02	4,46	0,00002
F-ratio = 19,85, *P* = 0,00002, df = 1,102, *r* = 0,40, SEE = 3,22				

Stepwise variable selection, with each of the three less invasive indices (PaO_2/FiO_2; $AaDO_2$; PAO_2/PaO_2), acting in turn as the independent variable, and FiO_2, PaO_2, SaO_2, PvO_2, $S\bar{v}O_2$, $PaCO_2$ and calculated pulmonary shunt the dependent variables, the following variables were included in the models:

$AaDO_2$. The r^2 for FiO_2 was 0,988 and the model thereafter only improved slightly with the addition of $PaCO_2$ (r^2 = 0,996), PaO_2 (r^2 = 0,999) and shunt (r^2 = 0,999).

PaO_2/FiO_2. The r^2 for FiO_2 in the model was 0,471. This improved to 0,888 after addition of $PaCO_2$ and 0,896 when SvO_2 was also included.

PAO_2/PaO_2. The initial model included FiO_2 (r^2 = 0,816), and this improved to r^2 = 0,949 with the addition of PaO_2; r^2 = 0,956 when $PaCO_2$ was included and finally r^2 = 0,959 when SaO_2 was included.

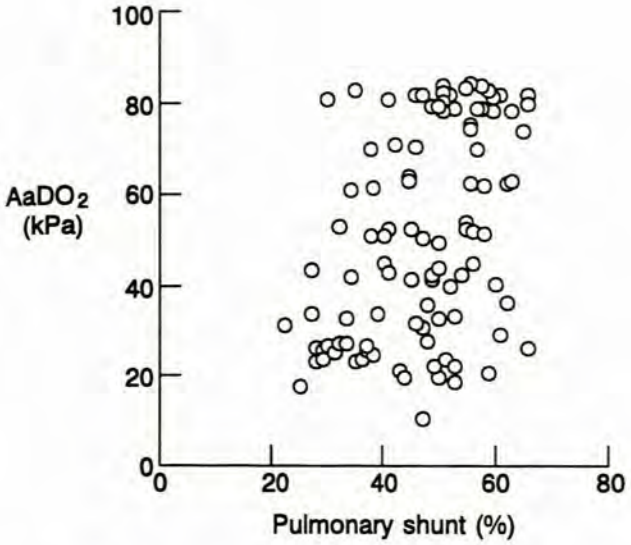

Fig. 1. Relationship between Qs/Qt and the $AaDO_2$.

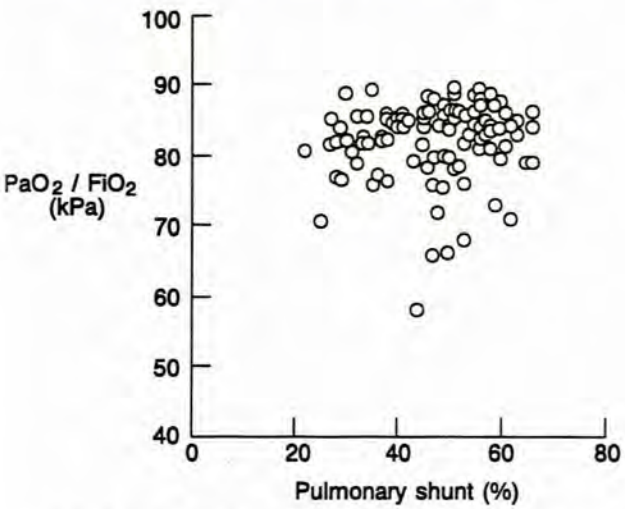

Fig. 2. Relationship between Qs/Qt and PaO_2/FiO_2 ratio.

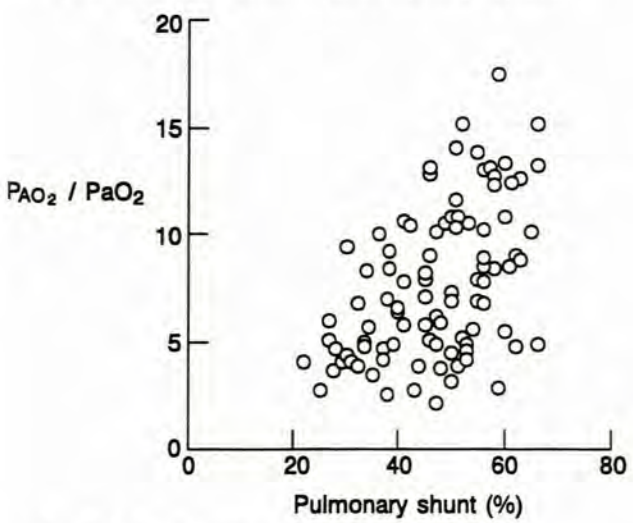

Fig. 3. Relationship between Qs/Qt and PAO_2/PaO_2.

Relationship between FiO_2 and $AaDO_2$ and PaO_2/FiO_2, PAO_2/PaO_2 (Fig. 4)

Initially a comparison was made between data obtained from the group subjected to abdominal procedures and peripheral orthopaedic surgery. Comparison of pre-operative, intra-operative and postoperative slopes for the relationship between FiO_2 and $AaDO_2$ failed to demonstrate any differences between the groups (pre-operative: $t = 2,50$, $P = 0,06$; intra-operative: $t = 1,75$, $P = 0,13$; postoperative: $t = 0,60$, $P = 0,58$). Data for the two populations were therefore pooled and analysed as a single group.

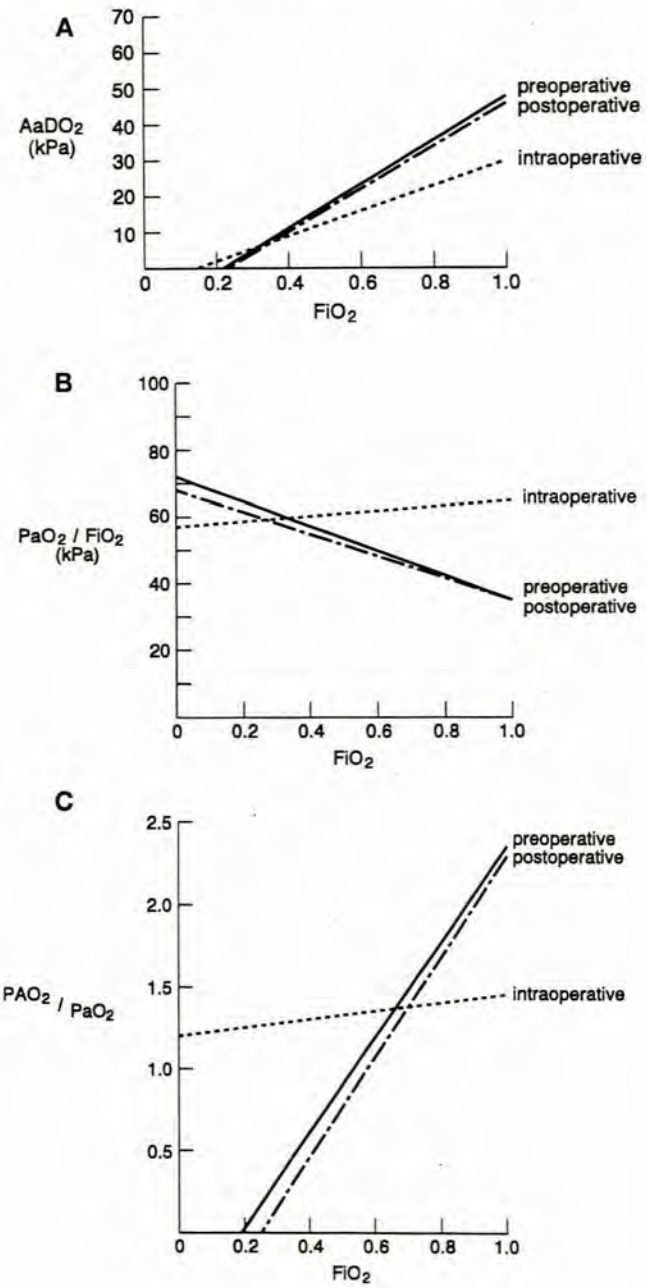

Fig. 4. Relationship between the less invasive indices and FiO_2 pre-, intra- and postoperative for $AaDO_2$ (A); PaO_2/FiO_2 (B); PAO_2/PaO_2 (C).

Data for the individual $AaDO_2$, PaO_2/FiO_2 and PAO_2/PaO_2 measurements at the various FiO_2s for the pre-, intra- and postoperative periods are summarised in Table I. Statistical analysis compared the various indices for the pre-, intra- and postoperative periods separately. No attempt was made to compare the three periods with each other.

Table I. Response of various indices to change in FiO_2

FiO_2	$AaDO_2$ (kPa)	PaO_2/FiO_2 (kPa)	PAO_2/PaO_2
Pre-operative			
0,21	0,41 ± 1,75	60,50 ± 16,62	0,99 ± 0,27
0,28	2,46 ± 1,74	64,79 ± 6,35	1,15 ± 0,11
0,35	6,56 ± 3,28	59,19 ± 8,98	1,35 ± 0,21
0,40	9,13 ± 4,03	57,06 ± 9,07	1,44 ± 0,28
F	29,68	3,37	13,97
P	0,0001	0,024	0,0001
Intra-operative			
0,30	3,91 ± 2,12	63,17 ± 7,47	1,22 ± 0,14
0,40	7,41 ± 3,12	62,54 ± 8,64	1,32 ± 0,19
0,50	9,54 ± 3,74	64,60 ± 8,04	1,32 ± 0,16
0,60	12,89 ± 6,40	63,99 ± 11,09	1,38 ± 0,24
0,70	13,48 ± 5,08	67,64 ± 7,00	1,30 ± 0,15
F	9,95	0,50	1,41
P	0,0001	0,70	0,35
Postoperative			
0,21	1,11 ± 1,98	58,84 ± 9,56	1,11 ± 0,16
0,28	3,05 ± 2,73	60,15 ± 8,76	1,21 ± 0,24
0,35	8,02 ± 3,38	53,31 ± 8,57	1,48 ± 0,32
0,40	9,96 ± 4,27	52,73 ± 10,23	1,53 ± 0,32
F	21,68	13,97	7,43
P	0,00001	0,0001	0,0003

Mean ± SD. Statistical analyses refer to data directly above the F and *P*-value. $P < 0,05$ confirms statistically significant differences between values for that particular phase of the study.

Regression analysis was performed with average FiO_2 the independent variable and average $AaDO_2$ the dependent variable ($N = 14$). Results indicate a significantly linear relationship during the three stages of the experiment:

	Estimate	*t*	*P*
Pre-operative			
Intercept	–9,67	6,75	0,02
Slope	47,05	10,16	0,0009
$r = 0,99$, $P = 0,009$ ($N = 4$)			
Intra-operative			
Intercept	–2,9	2,9	0,13
Slope	24,7	8,9	0,02
$r = 0,98$, $P = 0,002$ ($N = 5$)			
Postoperative			
Intercept	–9,75	5,01	0,003
Slope	49,3	8,11	0,01
$r = 0,98$, $P = 0,01$ ($N = 4$)			

Analysis of covariance demonstrated that the slope of the pre-operative data differed significantly from that of the intra-operative data ($t = 3,66$, $P = 0,019$) but was similar to that of the postoperative data ($t = 0,28$, $P = 0,78$). The intra-operative slope differed significantly from the postoperative slope ($t = 3,71$, $P = 0,01$).

The relationship between the average FiO_2 and the average PaO_2/FiO_2 ratio ($N = 14$) was as follows:

	Estimate	*t*	*P*
Pre-operative			
Intercept	68,9	9,8	0,01
Slope	–27,1	1,2	0,3
$r = -0,54$, $P = 0,5$ ($N = 4$)			
Intra-operative			
Intercept	60,4	24,0	0,0001
Slope	8	1,68	0,19
$r = 0,87$, $P = 0,05$ ($N = 5$)			
Postoperative			
Intercept	67,7	11,7	0,007
Slope	–38,8	2,13	0,20
$r = -0,86$, $P = 0,13$ ($N = 4$)			

Analysis of covariance indicated that the postoperative and intra-operative slopes were significantly different ($t = 3,60$, $P = 0,01$), while the pre-operative and intra-operative as well as pre- and postoperative slopes did not differ significantly ($t = 1,98$, $P = 0,104$; $t = 0,56$, $P = 0,60$).

Regression analyses for average FiO_2 and average PAO_2/PaO_2 ($N = 14$) showed the following:

	Estimate	*t*	*P*
Pre-operative			
Intercept	0,47	12,16	0,007
Slope	2,46	19,6	0,002
$r = 0,99$, $P = 0,003$ ($N = 4$)			
Intra-operative			
Intercept	1,19	13,74	0,008
Slope	0,22	1,31	0,28
$r = 0,66$, $P = 0,22$ ($N = 5$)			
Postoperative			
Intercept	2,41	6,38	0,02
Slope	0,58	4,88	0,04
$r = 0,97$, $P = 0,02$ ($N = 4$)			

Analysis of covariance indicated that the slope of the FiO_2 and PAO_2/PaO_2 differed significantly between the pre-operative and intra-operative periods ($t = 6,78$, $P = 0,001$). There was, however, no difference between the pre- and postoperative data ($t = 0,06$, $P = 0,95$). The intra-operative and postoperative slopes also differed significantly ($t = 5,348$, $P = 0,03$).

Discussion

Results from this study indicate that the so-called less invasive indices of gas exchange do not adequately reflect the pulmonary shunt in patients with ARDS. Although the correlation between the $AaDO_2$ and PAO_2/PaO_2 and Qs/Qt was significant, the wide scatter of data around the regression in all probability invalidates the prediction of shunt from these indices as most of the data points were outside the 95% confidence intervals. Of the three indices tested, the PaO_2/FiO_2 had the worst association with calculated pulmonary shunt.

The importance of the FiO_2 in all three indices can be gauged from the stepwise variable selection, where FiO_2 was always the first and significant inclusion in the final model. As was to be expected, factors reflecting alveolar ventilation, such as the $PaCO_2$, also feautured in all models, given that

these indices either directly or indirectly include alveolar gas composition in the calculations.

The inability of these indices to reflect the true Qs/Qt could, on theoretical grounds, most probably be explained by the fact that the indices do not incorporate the role of mixed venous oxygen content as the shunt equation does. The derivation of the shunt equation adequately explains the fact that CaO_2 is the weighed sum of $C\bar{v}O_2$, shunt flow, $C\acute{c}O_2$ and the difference between total and shunt blood flow. The inclination to accept the arterial-venous oxygen difference (and hence venous oxygen tension and content) as a constant, cannot be accepted in the critically ill patient. In this particular sample, the average $P\bar{v}O_2$ was 5,05 ± 0,94 kPa and average $S\bar{v}O_2$ was 62,34 ± 11,64% (mean ± SD). This serves to illustrate the wide scatter of data in a group of critically ill patients.

Data from the second part of this study indicate that the $AaDO_2$ changed as the FiO_2 was changed and, indeed, was linearly dependent on the FiO_2. This has been reported in previous publications.[4,7] Furthermore, the slope of the regression $AaDO_2$ and FiO_2 decreased during general anaesthesia relative to values obtained before and after anaesthesia.

The PaO_2/FiO_2 ratio demonstrated the weakest association with FiO_2. Previous publications failed to agree on whether this index was insensitive to the inspired oxygen fraction, given that some authors demonstrated a relationship and others failed to show an association with the FiO_2.[12-14] This index could be regarded as more robust inasmuch as it was less affected by the FiO_2, but it must be kept in mind that it was also quite insensitive in predicting the calculated pulmonary shunt fraction.

The PAO_2/PaO_2 ratio varied in direct relation to the FiO_2 during the pre- and postoperative phases of the experiment. However, intra-operatively there was little variation in the index as the inspired oxygen concentration was changed.

The slope of FiO_2 and $AaDO_2$ or PaO_2/FiO_2 became less marked during anaesthesia compared with the pre- and postoperative values. The authors speculate that this could be explained by a number of factors. The denitrogenation of the alveoli with low ventilation-perfusion ratios resulted in a loss of alveolar volume but the raised $P\bar{v}O_2$ probably offset the effect of the denitrogenation. Although we did not measure the $P\bar{v}O_2$ of the patients in this trial, there is evidence to suggest that the reduction in oxygen consumption associated with anaesthesia and mechanical ventilation,[16] combined with the decrease in body temperature of patients under anaesthesia,[17,18] results in an increased $P\bar{v}O_2$ provided the cardiac output is not excessively depressed. In the light of the previous argument, which explains the effect of the mixed venous gases on the total PaO_2 in the presence of a shunt, this predicted increase in $P\bar{v}O_2$ during anaesthesia could explain the limited effect of the FiO_2 on the less invasive indices during general anaesthesia.

The observed change in the Qs/Qt as the FiO_2 is changed was addressed in a theoretical analysis by Dantzker and colleagues.[4] In alveoli with a sufficiently small ventilation-perfusion ratio, the total uptake of oxygen by the capillary blood could exceed the ventilation to that alveolus with the result that the alveolar volume would be reduced and alveoli may even collapse. This concept of denitrogenation, as an explanation for the observed change in Qs/Qt and $AaDO_2$ when the FiO_2 is changed, is supported by the calculations showing that if a less soluble gas is used with oxygen (such as SF_6), alveolar collapse would not occur. If a more soluble gas is used (e.g. N_2O), the tendency to collapse would be enhanced.

In theory, there seems to be a critical level of denitrogenation that will collapse a particular alveolus. This critical point is determined by a combination of the ventilation-perfusion ratio and the inspired oxygen fraction (alveoli with a ventilation-perfusion ratio in excess of 0,5 will, in theory, not be prone to collapse, irrespective of the inspired oxygen concentration). In principle, the lower the ventilation-perfusion ratio, the lower the level of inspired oxygen at which the alveolar volume would be reduced.[4] This critical point is further altered by the $P\bar{v}O_2$. If the mixed venous blood oxygen tension is raised, the gradient for diffusion of oxygen from the alveolus to the capillary blood is reduced.

Historically, it was accepted that the release of the pulmonary hypoxic vasoconstriction effect associated with the raised alveolar oxygen tension also contributed to the observed increase in the Qs/Qt and $AaDO_2$ as the FiO_2 was raised.[5] However, in their theoretical approach, Dantzker *et al.* do not agree with this concept.[4] They argue that alveoli with the greatest stimulus-effect curve for hypoxic vasoconstrictors are those with a PAO_2 less than 100 mmHg. The lung units that will therefore show the greatest change are those with moderately low ventilation-perfusion ratios. Given that the total cardiac output remains stable (and may even decrease) as the inspired oxygen fraction is increased, blood will be 'stolen' from alveoli with lower or higher ventilation-perfusion ratios. The maximum amount of blood will be diverted from units with low ventilation-perfusion ratios because their PAO_2 remains close to the venous PO_2.

However, although there are explanations and theoretical evidence for an increase in Qs/Qt when the inspired oxygen is increased, this does not necessarily explain, for instance, the $AaDO_2$ increase given the poor correlation between, for example, the $AaDO_2$ and pulmonary shunt demonstrated in our study. The alveolar gas equation defines the factors that will be important in determining the PAO_2 part of the $AaDO_2$, while the rearranged shunt equation gives the variables which will affect the PaO_2: $CaO_2 = C\acute{c}O_2 - Qs/Qt (C\acute{c}O_2 - C\bar{v}O_2)$.

In this equation the $C\acute{c}O_2$ is, for theoretical purposes, a constant and the Qs/Qt purports to reflect the parenchymal function (or dysfunction) of the lung and is hence also a constant for a particular patient at a particular time. The variable which has to be considered is the $C\bar{v}O_2$ and experience in the intensive care unit does not justify its acceptance as a constant. The $C\bar{v}O_2$ is dependent upon a number of variables best illustrated by the rearranged Fick equation: $C\bar{v}O_2 = CaO_2 - \dot{V}O_2/CO$, where $\dot{V}O_2$ = oxygen consumption and CO = cardiac output.

The $\dot{V}O_2$ will change as body temperature changes.[18] The CO is dependent upon the loading conditions of the heart, contractility and heart rate. In the light of the number of changing variables which could affect $P\bar{v}O_2$, the $P\bar{v}O_2$ is a changing (and often undefined) variable in, for example, the $AaDO_2$. If the $P\bar{v}O_2$ increases, alveoli will be more stable according to the theoretical analysis of Dantzker and colleagues.[4] Also, changes in the CaO_2, such as could occur when the haemoglobin concentration changes, could affect

the $C\bar{v}O_2$. Although a change in FiO_2 will only have a small effect on the $C\acute{c}O_2$ and hence oxygen delivery, an increase in the inspired fraction of oxygen from 0,21 to 1 will translate into an approximately 10% increase in $C\acute{c}O_2$. Given that the CaO_2 is a mathematical combination of the $C\acute{c}O_2$ and $C\bar{v}O_2$, this will lead to modest increases in total oxygen delivery. At a constant $\dot{V}O_2$ this will result in an increase in the $P\bar{v}O_2$ and therefore affect the $AaDO_2$. This theoretical view has been confirmed by Douglas *et al.*[8]

The effect of positive end-expiratory pressure (PEEP) on the increase in $AaDO_2$ as the FiO_2 increased, has not been directly examined.[5,6] When the effect of PEEP on the Qs/Qt was examined, conflicting results were reported. One study demonstrated that PEEP prevented the increase in Qs/Qt[6] as the FiO_2 was increased while another failed to confirm this observation.[5] First impressions suggest that the stabilising effect of PEEP should overcome the tendency of alveoli to collapse. One can, however, speculate that the alveoli with the lower ventilation-perfusion ratios (lower alveolar volume) are the least compliant and will therefore only benefit at a later stage of PEEP application, compared with the more compliant alveoli which will absorb the early PEEP. If this speculation is correct, then the alveoli with low ventilation-perfusion ratios at risk of collapse during denitrogenation are the alveoli that will benefit the least from PEEP. Also, PEEP could impede cardiac output and have an effect via the decrease in $P\bar{v}O_2$.

Data from this study seem to indicate that the commonly used indices do not accurately reflect the Qs/Qt of the injured lung. Also, the FiO_2 had an effect on some of these indices. The so-called less invasive indices should therefore be applied with the necessary circumspection and comparison should, at least, be made at a similar FiO_2.

REFERENCES

1. Wagner P, Lavaruso R, Uhl R, West JB. Continuous distribution of ventilation perfusion ratios in normal subjects breathing room air. *J Clin Invest* 1974; **54:** 54-68.
2. McAslan TC, Matjsko-Chui J, Turney S, Cowley RA. Influence of inhalation of 100% oxygen on intrapulmonary shunt in severely traumatized patients. *J Trauma* 1973; **13:** 811-821.
3. Dery R, Pelletier J, Jaques A, Clavet M, Houde J. Alveolar collapse induced by denitrogenation. *Can Anaesth Soc J* 1965; **12:** 531-544.
4. Dantzker D, Wagner P, West JB. Instability of lung units with low ventilation/perfusion ratios during oxygen breathing. *J Appl Physiol* 1975; **38:** 886-895.
5. Shapiro B, Cane R, Harrison R, Steiner M. Changes in intrapulmonary shunting with administration of 100% oxygen. *Chest* 1980; **77:** 138-141.
6. Oliver A, Abinader E, Bursztein S. Influence of varying inspired oxygen tensions on intrapulmonary venous admixture (shunt) of mechanically ventilated patients. *Crit Care Med* 1980; **8:** 99-101.
7. Torda TA. Alveolar-arterial oxygen tension difference: A critical look. *Anaesth Intensive Care* 1981; **9:** 326-350.
8. Douglas M, Downs J, Dannemiller F, Hodges M, Munson E. Changes in pulmonary venous admixture with varying inspired oxygen. *Anesth Analg* 1976; **55:** 688-693.
9. Fahri LE, Rahn H. A theoretical analysis of the alveolar-arterial O_2 difference with special reference to the distribution effect. *J Appl Physiol* 1955; **7:** 699-704.
10. Suter P, Fairley H, Schlobohm R. Shunt, lung volume and perfusion during short periods of ventilation with oxygen. *Anesthesiology* 1975; **43:** 617-627.
11. Gilbert R, Keighley J. The arterial/alveolar oxygen tension ratio. An index of gas exchange applicable to varying inspired oxygen concentrations. *Am Rev Respir Dis* 1974; **109:** 142-145.
12. Peris L, Boix J, Salom J, Valentin V, Garcia D, Arnau A. Clinical use of the arterial/alveolar oxygen tension ratio. *Crit Care Med* 1983; **11:** 888-891.
13. Gilbert R, Auchinocloss J, Kuppinger M, Thomas M. Stability of arterial/alveolar partial pressure ratio. *Crit Care Med* 1979; **7:** 267-271.
14. Doyle D. Arterial/alveolar oxygen tension ratio. A critical appraisal. *Can Anaesth Soc J* 1986; **33:** 471-474.
15. Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. *Am Rev Respir Dis* 1988; **138:** 720-723.
16. Viale JP, Annat GJ, Ravat F. Oxygen uptake and mixed venous oxygen saturation during aortic surgery and the first three operative hours. *Anesth Analg* 1991; **73:** 530-535.
17. Hall GM. Body temperature and anaesthesia. *Br J Anaesth* 1978; **50:** 39-44.
18. Sessler D, McGuire J, Moayeri A, Hynson J. Isoflurane induced vasodilatation minimally increases cutaneous heat loss. *Anesthesiology* 1991; **74:** 226-232.
19. De las Alas V, Geddes LA, Voorhees WD. Oxygen uptake and mean blood pressure as indicators of induced hypothermia. *J Clin Monit* 1990; **6:** 186-188.

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