Original article

Beyond PaO2: Relationships between Indices of Pulmonary Oxygen Transfer in Hospitalized Adults Undergoing Blood Gas Testing

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Abstract

The arterial partial pressure of oxygen in the arterial blood reveals limited information about pulmonary oxygen transfer. In 989 hospitalized patients undergoing arterial blood gas testing, we compared conventional indices of oxygen transfer: (1) P(A-a) O2 (A-a); (2) PaO2/PAO2 (a/A); and (3) the P/F ratio Nine hundred twenty-five of the patients were receiving supplemental oxygen therapy (FIO2 .24-1.00) and 65 were breathing room air. In patients receiving supplemental O2, the a/A ratio closely correlated with the P/F ratio (r = .98 to .99); the A-a O2 difference did not correlate as closely with the a/A ratio (r = -.77 to -.85) or with the P/F ratio (r = -.72 to -.80). In those breathing room air (FIO2 .21), the a/A ratio was closely and inversely correlated with the A-a difference (r= -.97 to -.98); correlations between the a/A and P/F ratios (r=.88 to .89) and between the P/F ratio and A-a O2 difference (r = -.78 to -.79) were less robust. We conclude that the a/A ratio is the preferred oxygen transfer parameter over the wide range of FIO2 levels encountered clinically.

Keywords: **alveolar oxygen pressure, arterial oxygen pressure, blood gases, hypoxemia, lung oxygen transfer, oxygen, carbon dioxide.**

Introduction

The PaO2 is sometimes used to determine how well the lungs are transferring oxygen to the circulation. Unfortunately, an isolated PaO2 measurement conveys limited O2 exchange information unless PAO2 is also considered.[1] A larger-than-expected difference between the PAO2 and the PaO2, the A-a O2 difference, provides a reliable indication of an abnormality of pulmonary O2 transfer.[1,2] A larger-than-expected A-a difference can be caused by a pulmonary ventilation-perfusion imbalance, a barrier to O2 diffusion across the alveoli, shunting of some deoxygenated venous blood through or past the lungs, or some combination of these factors.[1]

PAO2 is directly related to the alveolar ventilation rate, increasing when there is alveolar hyperventilation and decreasing when there is alveolar hypoventilation. Calculation of PAO2 (to determine A-a O2) is usually made by using the alveolar gas equation.[2] Use of this time-honored equation relies on numerous assumptions: (a) estimated FIO2 is accurately known; (b) ambient Pb is precisely known; (c) PICO2 is 0; (d) PaCO2 equals PACO2; (e) the water vapor pressure in the trachea and pulmonary alveoli is 47 mmHg; and (f) the respiratory exchange ratio is 0.8.[1,2] The A-a O2 difference increases with aging and also with use of supplemental

O2 therapy, and well-defined normal ranges for A-a are not known at all possible age and FIO2 combinations.[1]

The a/A ratio is an improvement on the A-a because it is unaffected by the FIO2. Thus, a/A can be assessed serially even when the FIO2 has changed over time. The a/A ratio may be the preferred index for quantitating O2 transfer by the lung.[3] However, a/A remains dependent on the validity of the numerous assumptions made to calculate PAO2. The a/A ratio is also age-related, being >0.75 in healthy older individuals and often >0.9 in younger people.

The P/F ratio is the simplest of the pulmonary O2 transfer indices and only requires an accurate estimate of FIO2. The P/F ratio calculation does not take into consideration the ambient Pb or the alveolar ventilation rate as reflected by the patient's PaCO2. If the ambient Pb is typical for the locale and the PaCO2 is close to normal, the P/F should be a very accurate reflection of O2 transfer by the lung. However, fluctuations in Pb or PaCO2 from typical or normal levels occur not uncommonly and can introduce inaccuracy if P/F is used as an index of lung oxygen transport. P/F can be estimated noninvasively by measuring using SO2 (%) and using tables that convert SO2(%) to estimated PaO2.[4] However, these tables require assumptions about arterial pH, body temperature, and erythrocyte 2,3-DPG levels.

Often, A-a, a/A, and P/F are reported by the laboratory to the care provider who ordered the blood gas measurement. The amount of detail provided may be confusing and redundant for a busy clinician. To what extent A-a, a/A, and P/F are interrelated in hospitalized patients undergoing blood gas measurements is unclear. We therefore analyzed 1,000 consecutive arterial blood gas patient samples that had been collected in our hospital and analyzed in our laboratory. Most patients were receiving supplemental oxygen therapy. A smaller subgroup breathing room air was included for comparison.

Methods

One thousand consecutive arterial blood gas samples collected in our hospital during March and April 2008 were evaluated for inclusion in the study. All samples had been obtained from adults (age 18 and above). To maintain patient confidentiality, samples were de-identified in the laboratory by assigning them a sequential study number from 1 to 1,000 before sending them to the investigator analyzing the data. Most samples were collected from patients who were receiving supplemental oxygen therapy (Table 1).

Table 1: FIO2 recorded at the time of collection of the arterial blood gas samples[a]

	FIO2	Number of patients/samples
Breathing Room Air (n=65)	.21	65
Receiving Supplemental O2 (n=924)	.24-.29	32
	.3-.39	80
	.4-.49	384
	.5-.59	73
	.6-.69	74
	.7-.79	95
	.8-.89	33
	.9-.99	9
	1	144

[a]11 of the original 1,000 blood gas samples (1.1%) were excluded due to quality control measures (see text). To calculate PIO2 in mmHg from FIO2, multiply FIO2 by (Pb-47).

The Abbott iStat[®]blood gas analyzer (Arbroath Angus, UK) was used to measure arterial PaO2, PaCO2, and pH in the samples. From these analytes and from the estimated FIO2 recorded at the time of sample collection, the following were calculated: (a) arterial SO2(%) from PaO2 using the Severinghaus formula;[5] (b) arterial HCO3 and base excess concentrations (mM) from the PaCO2 and pH using the Henderson-Hasselbalch and the Siggaard-Anderson equations,[6] respectively; and (c) PAO2 (mmHg) using the alveolar gas equation, which inputs PaCO2, Pb, and PIO2[1,2] Lastly, the laboratory calculated and reported three conventional oxygenation indices: A-a O2 difference (mmHg); a/A ratio (no units); and P/F ratio (mmHg).

Eleven of the 1,000 arterial samples (1.1%) were excluded if there was a negative A-a O2 difference (a/A ratio >1), implying an error in recording the true FIO2, or if the FIO2 was recorded as <0.21 or >1.00. The remaining 989 samples/patients were included for analysis.

Paired correlations of A-a, a/A, and P/F were calculated using the Pearson method (Excel, Microsoft Office Professional Plus 2013, Redmond, WA) and the Spearman rank-order correlation

method.[6] Linear regression analysis was performed to determine slopes and y-intercepts.[7] Group means (supplemental O2 vs. room air groups) were compared by unpaired t-tests, with 2-tailed P values < 0.05 considered significant.[8]

Results

Table 2 shows the laboratory's reference range for the arterial analytes (PaO2, PaCO2, and pH) and the derived values of SO2(%), HCO3, and base excess. There were highly significant differences between mean values in the two groups of patients for all six parameters. Compared to patients breathing supplemental O2, those breathing room air had lower mean values for all six parameters.

Table 2: Comparison of arterial PaO2, PaCO2 and pH as well as derived SO2(%),HCO3 level and base excess levels in the two groups of patients

Parameter (RR)	Supplemental O2 (n=924) Mean ±SEM (Range)	Room Air (n=65) Mean ±SEM (Range)	P value
PaO2 (mmHg) (80-105[a])	134±3 (27-623)	78±3 (26-121)	<0.001
PaCO2 (mmHg) (35-45)	40±.4 (15-107)	36±1 (18-62)	0.009
pH (7.35-7.45)	7.40±.003 (6.88-7.68)	7.36±.01 (7.17-7.51)	0.006
SO2 (%) (96-100)	97±.1 (40-100)	92±2 (20-99)	<0.001
HCO3 (mM) (22-26)	24.7±.2 (4.6-50.9)	21.0±.9 (6.9-40.2)	<0.001
Base excess (mM) (-2-+3)	-0.1±.2 (-26 - +30)	-4.4±1.1 (-22 - +16)	<0.001

[a]based on breathing room air

Table 3 shows mean A-a O2 differences, a/A ratios, and P/F ratios in the two groups of patients.

Table 3: Calculated A-a, a/A and P/F in the two groups of patients

Index (RR)	Supplemental O2 (n=924) Mean± SEM (Range)	Room Air (n=65) Mean± SEM (Range)	P value
A-a (mm Hg) (4-25[a])	216±5 (0-644)	27±2 (0-80)	<0.001
a/A (≥0.75)	0.42±.007 (0.04-1.00)	0.74±.02 (0.25-1.00)	<0.001
P/F (mm Hg) (380-500)	257±49 (27-263)	369±12 (124-576)	<0.001

F, FIO2 expressed as a decimal; P, PaO2 in mmHg
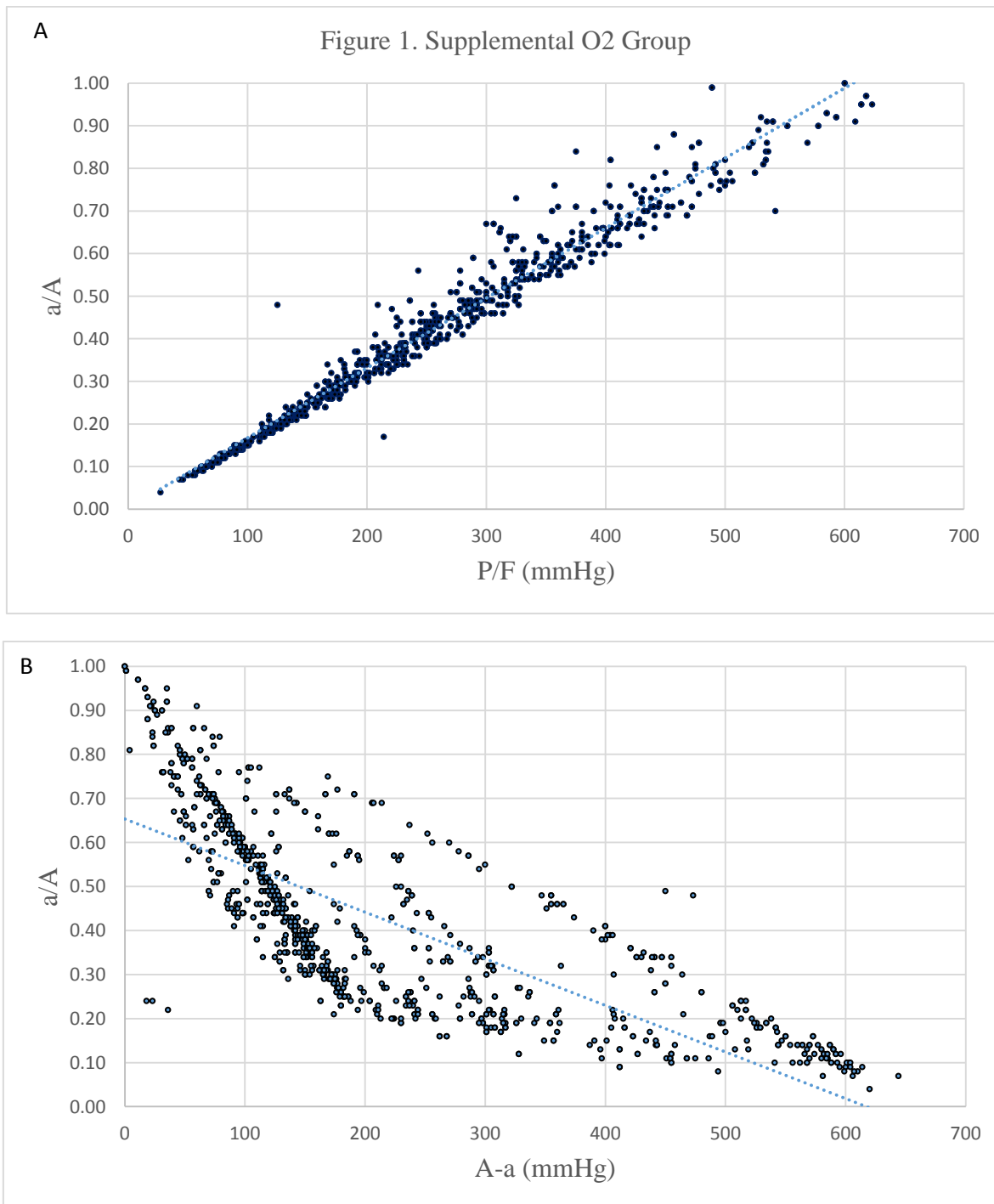
[a]based on breathing room air

The supplemental O2 group (FIO2 .24-1.00), as expected, had markedly impaired O2 transfer as reflected by each of the oxygenation parameters (Table 3). In this group, there was a very close direct correlation (r= .98 and .99) between the a/A ratio and the P/F ratio (Table 4 and Figure 1A).

Table 4: Correlation coefficients (r) between pairs of oxygenation indices[a]

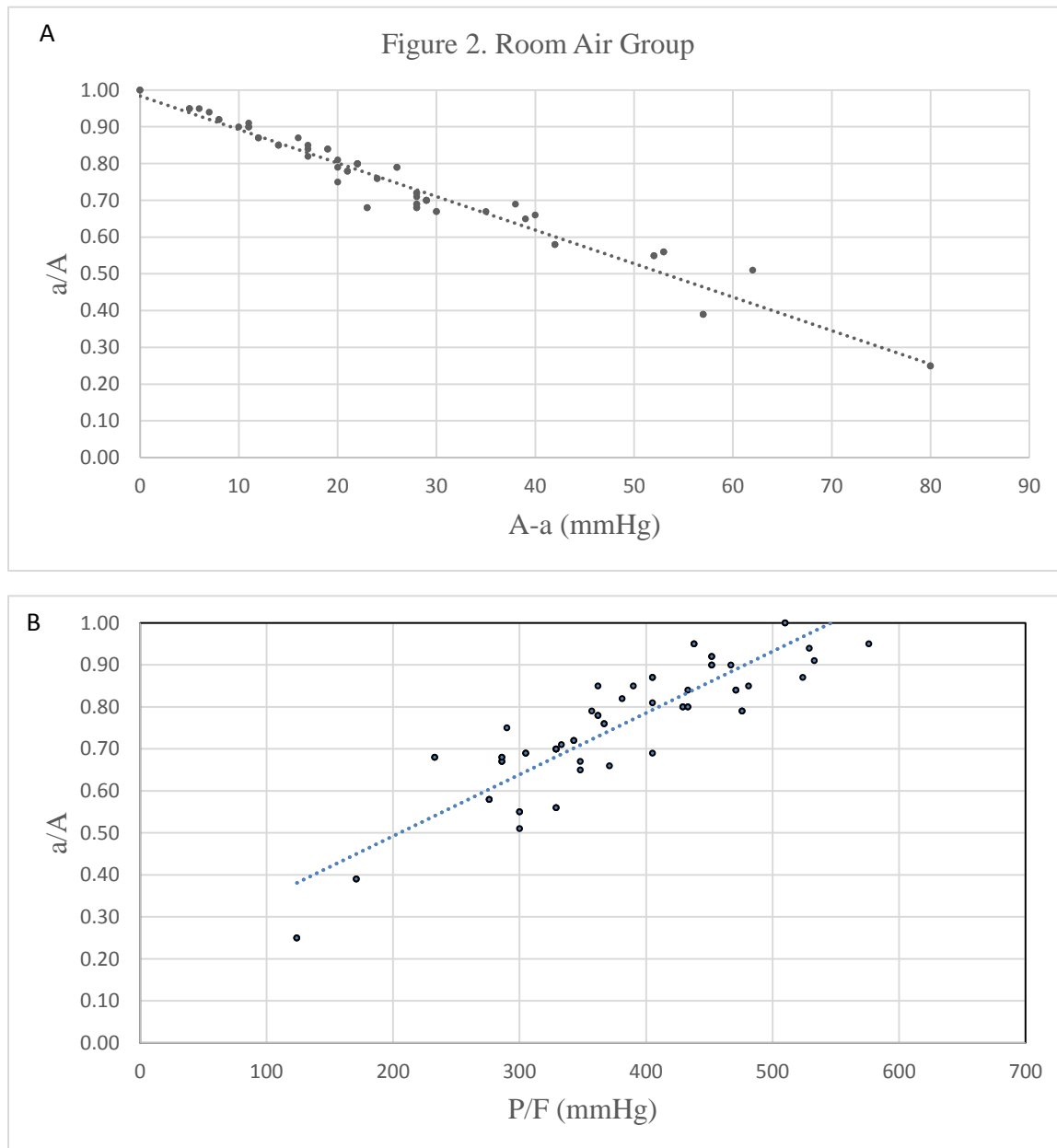| Supplemental O2 Group (n=924)			
Pearson (parametric)		Spearman (non-parametric)	
a/A vs. P/F	r= .98	r= .99	a/A vs. P/F
a/A vs. A-a	r= -.77	r= -.85	a/A vs. A-a
P/F vs. A-a	r= - .72	r= - .80	P/F vs. A-a
Room Air Group (n=65)			
a/A vs. P/F	r= .89	r= .88	a/A vs. P/F
a/A vs. A-a	r= -.98	r = -.97	a/A vs. A-a
P/F vs. A-a	r= -.78	r= -.79	P/F vs. A-a

[a]The r values can vary from -1 to +1. All r values reported here are significant (P<0.001).

The linear regression equation relating a/A to P/F was: (a/A)=.0017(P/F)+.0027. The 95% confidence interval for the .0017 slope of this relationship was .0016 to .0017. Thus, for every 100-mmHg increase (or decrease) in P/F, a/A increased (or decreased) by 0.16-0.17. In this supplemental O2 group, there were less robust inverse correlations between a/A and A-a (Table 4 and Figure 1B) and between P/F and A-a (Table 4).

Figure 1. Supplemental O2 Group

In patients breathing room air, the indices of oxygenation were close to the reference ranges (Table 3), implying that the blood gas sample had been ordered more to assess pH or $PaCO_2$ than PaO_2 (see also Table 2). In this group there was a very close inverse correlation between a/A and A-a (r = -.98 and -.97) (Table 4 and Figure 2A.The linear regression equation relating them was: (a/A)=0.984-.009(A-a). The 95% confidence interval for the -.009 slope of this relationship was -.0086 to -.0096. Thus, for every 100 mmHg increase in A-a, a/A would fall by approximately 0.09. There were more modest correlations between a/A and P/F (Table 4 and Figure 2B) and (inversely) between P/F and A-a in this group (Table 4).

Figure 2. Room Air Group

Discussion

Results of this study varied depending on the group of hospitalized patients analyzed. In the larger group receiving a wide range of supplemental O2 doses (FIO2 0.24-1.00), a/A correlated very closely with P/F, but not nearly as well with A-a. This finding was not entirely unexpected, as a/A is independent of FIO2, whereas the A-a O2 difference is highly FIO2-dependent. The close correlation between a/A and P/F implies that the parameters used to calculate PAO2 are not as critical is assessing oxygen transfer by the lungs in patients receiving supplemental O2 as they might be in people breathing room air. These parameters include the ambient Pb and the patient's PaCO2. The 0.0017 slope of the line relating P/F to a/A with its narrow confidence interval and its y-intercept close to zero (Figure 1A) indicate that a/A can be easily and closely estimated from P/F and vice versa for inpatients receiving O2 therapy.

A smaller group of patients underwent arterial blood gas testing while breathing room air, many of whom had a metabolic acidosis with respiratory compensation (Table 2). In this group, the a/A ratio better correlated with A-a than with P/F. However, in this group FIO2 was constant (0.21), unlike in the supplemental O2 group where FIO2 varied >4-fold. Thus, in hospitalized patients breathing room air, a/A and A-a (which use the same parameters) are highly inversely correlated and give essentially identical information. The -0.009 slope of the line relating A-a and a/A, with its narrow confidence interval and its y-intercept approaching 1, indicate that a/A can be easily and closely estimated from A-a and vice versa. In contrast to the supplemental O2 group, the a/A ratio in the room air group was not as highly correlated with the P/F ratio, probably because inclusion of the ambient Pb and PaCO2 in the a/A calculation, but not the P/F calculation, provided less precise information for P/F than for a/A in this group of subjects.

Conclusion

We agree with an editorial opinion expressed nearly 35 years ago by Hess and Maxwell that the a/A ratio is the preferred parameter of oxygenation and lung O2 transfer whether patients are breathing room air or receiving supplemental O2. For the former group, the A-a O2 difference is a suitable alternative to a/A, while for the latter group, the P/F ratio provides a suitable alternative to a/A. Another advantage of relying on the a/A ratio is that it has no units.

Both A-a and P/F can be expressed in different pressure units globally (e.g., mmHg, torr, or kilopascals), which can lead to confusion when comparing results across institutions or groups of investigators. Our conclusions apply to patients admitted to the hospital in whom arterial blood gases were ordered by their care provider regardless of diagnosis. For certain known diagnoses (e.g., pneumonia, pulmonary embolism, acute respiratory distress syndrome), PaO_2 alone, the P/F ratio or the A-a O_2 difference might perform equally or even superiorly to the a/A ratio. Additional studies may shed further light on this issue.

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Figure Legends

1A. Direct and generally close linear relationship between a/A and P/F in 924 patients receiving supplemental O2. Correlation coefficients were .98 (Pearson) and .99 (Spearman) (Table 4). Linear regression equation was: (a/A)= 0.0017(P/F) + 0.0027. The 95% confidence interval for the slope was 0.0016 to 0.0017. 1B. Nonlinear relationship between a/A and A-a in these same patients. Correlation coefficients were only -.77 and -.85 (Table 4). Trendlines are shown.

2A. Inverse linear relationship between a/A and A-a in 65 patients breathing room air. Correlation coefficients were -.98 (Pearson)and -.97 (Spearman) (Table 4). Linear regression equation was: (a/A)= 0.984-0.009(A-a). The 95% confidence interval for the slope was - 0.0086 to - 0.0096. 2B. Direct, moderate linear relationship between a/A and P/F in the same patients. Correlation coefficients were only .88 and .89 (Table 4). Trendlines are shown.

Abbreviations

A-a, PAO2-PaO2

a/A, PaO2/PAO2

2,3-DPG, 2,3-diphosphoglycerate

FIO2, fraction of inspired oxygen

HCO3, bicarbonate

PACO2, alveolar carbon dioxide pressure

PaCO2, arterial carbon dioxide pressure

PAO2, alveolar oxygen pressure

PaO2, arterial oxygen pressure

Pb, barometric pressure

P/F, PaO2/FIO2

PICO2, inspired carbon dioxide pressure

PIO2, inspired oxygen pressure

RR, reference range

SEM, standard error of the mean

SO2(%), percentage oxygen saturation of hemoglobin