Josh Farkas MD (@PulmCrit)

Analysis of the relationship between arterial and peripheral venous blood gasses.

ABSTRACT

OBJECTIVE: To evaluate models for predicting arterial blood gas (ABG) values based on venous blood gas (VBG) values.

DESIGN: Meta-analysis

METHODS: Data from five original studies including matched ABG and VBG values were used to test three models relating ABG and VBG values. The direct correlation model involves linear regression equations directly relating arterial and venous blood gas values. The saturation model involves predicting ABG values from a combination of VBG values and arterial oxygen saturation. This model is based on approximating changes in pH and pCO_2 between arterial and venous blood as proportional to the change in oxygen saturation between arterial and venous blood. Finally, the simplified saturation model is derived from the saturation model by approximating arterial oxygen saturation as constant. Models were tested for consistency and accuracy across these studies in predicting ABG values.

RESULTS: Data were obtained from five studies that included [redacted] pairs of ABG and VBG values. The direct correlation model yielded inconsistent results across different patient groups. The saturation model revealed a consistent relationship between changes in oxygen saturation and changes in pH and pCO_2 across all patient groups. Based on two studies which defined the time interval between ABG and VBG sampling, the saturation model predicted ABG values with 95% confidence intervals for pH, pCO_2, and bicarbonate of ±.[redacted], ±[redacted] mm, and ±[redacted] mEq, respectively. The simplified saturation model predicted ABG values solely from VBG values with the same accuracy as the saturation model.

CONCLUSIONS: A series of approximations led to a simple, empiric model for estimating ABG parameters directly from VBG parameters. The accuracy of this model appears adequate for routine clinical use.

INTRODUCTION

Arterial blood gas (ABG) analysis is frequently used to assess respiratory function and acid-base status. When compared with venous phlebotomy, arterial puncture causes more pain, has a risk of arterial damage, and requires special training of those performing the procedure. For these reasons, there is ongoing interest in whether venous blood gas (VBG) analysis may be used as a surrogate for arterial blood gas analysis. Although many studies have been performed comparing ABG values with concurrent VBG values, no universal direct relationship has been established that is consistent across multiple studies. One theoretical model based on the difference in oxygen saturation between arterial and venous blood was successful, but the complexity of calculation required has hindered widespread use (1). The goals of this study were to test whether simple, empiric models incorporating the difference in oxygen saturation between arterial and venous blood could allow estimation of ABG values from VBG values.

MATERIALS AND METHODS

Subjects. The literature from 1995-2010 was reviewed for papers comparing >25 matched ABG and VBG measurements. This review included PubMed searches based on MESH keywords, a manual review of references, and a search using the Science Citation Index. In cases where multiple papers reported on the same data, the most recent and inclusive paper was selected. The corresponding authors of selected papers were contacted via e-mail to request paired ABG and VBG data of all study subjects. We defined a "patient group" as patients who were clinically similar in an individual study. Therefore, one study could potentially have multiple patient groups (e.g., control subjects and subjects with disease).

One data set did not include bicarbonate values, and other data sets recorded bicarbonate with varying degrees of precision. To establish consistency we re-calculated bicarbonate values for all subjects using the Henderson-Hasselbach equation. If there was substantial variation between our calculated values and the values within the data set, the data set was deemed unreliable and removed in its entirety. Subjects were censored if all necessary data was not available, or if the oxygen saturation in venous blood was >25% higher than the oxygen saturation in arterial blood.

Direct correlation model: This model is based on directly relating venous and arterial parameters for pH, pCO_2, and bicarbonate using linear regression equations. The venous parameters are designated as the independent variable, with corresponding arterial parameter as the dependent variable.

Saturation model. This model was based on two primary approximations (Figure 1). The first approximation was that the change in CO_2 partial pressure (ΔpCO_2) is proportional to the change in oxygen saturation ($\Delta O_2\%$). This was based on (a) the assumption that the respiratory

quotient (RQ) for tissues in the limb is constant, such that changes in total oxygen content are proportional to changes in total CO_2 content; and (b) the assumption that the total blood CO_2 content is proportional to the pCO_2 (neglecting, for example, the effect of fluctuating hemoglobin concentration on the CO_2 content of erythrocytes).

The second approximation was that ΔpCO_2 is proportional to the change in pH between venous and arterial blood (ΔpH). The relationship between pH and pCO_2 is complex and nonlinear. However, a first-order approximation of any curve at a given point may be achieved via a linear regression equation. This linear approximation is reasonable because the ΔpH between venous and arterial blood is small.

Algebraic manipulation of these approximations indicated that ΔpH and ΔpCO_2 are both proportional to $\Delta O_2\%$ (Figure 1). The proportionality constants were derived empirically from patient data using proportional regression analysis. Once these constants were obtained, arterial pH and pCO_2 for any patient may be estimated from a combination of venous pH and pCO_2 and $\Delta O_2\%$. Bicarbonate may be subsequently calculated from estimates of pH and pCO_2 using the Henderson-Hasselbach equation.

Simplified saturation model. Most of the variability in $\Delta O_2\%$ derives from variability in venous oxygen saturation, such that $\Delta O_2\%$ may be approximated as $\Delta O_2\% \approx$ (mean arterial oxygen saturation for entire population – individual patient's venous oxygen saturation). The saturation model was simplified with the use of this approximation, allowing estimation of ABG parameters from VBG parameters alone (without the need for simultaneous arterial oxygen saturation).

Testing of each model: The saturation model and the direct correlation model were first tested for consistency by calculating model coefficients for each patient group using the method of least squares. Given variations in precision between different groups, coefficients from different

patient groups was combined using a weighted sample mean. The uniformity of coefficients between different groups was determined by comparing the coefficient from each group and its associated error to the weighted sample mean using a two-tailed Z-test.

The precision of each model was evaluated by calculating predicted ABG parameters for each patient and comparing these to actual ABG parameters. Arterial blood gas parameters change in real time, reflecting changes in a patient's condition. To obtain the most accurate estimate of error, only studies which explicitly defined the time interval between ABG and VBG sampling were used in this analysis. 95% confidence intervals were calculated by multiplying each standard deviation by 1.96. Statistical computations were performed using Microsoft Excel 2011.

RESULTS

Sixteen studies were identified from the literature search as relevant for consideration (2-17). Of these, five studies involving [redacted] subjects met requirements for analysis (Figure 1). Eleven studies were rejected for analysis for the following reasons: the corresponding author did not respond to our request to analyze their data (5), the corresponding author was unable to locate the data (4), the data did not contain oxygen saturation values (1), and the data was internally inconsistent with reported bicarbonate values that differed substantially from those calculated using the Henderson-Hasselbach equation (1). Since one of these five studies contained a control group, we designated this study as having two patient groups and, therefore, a total of six patient groups were analyzed. Data from two patients in two different studies were censored (in one case because pCO_2 was immeasurably high, and in another case because the venous oxygen saturation was >25% higher than the arterial oxygen saturation).

To test the validity of the direct correlation model, linear regression equations were calculated relating arterial and venous parameters of pH and pCO_2 within each group of patients (Table 2). Coefficients of the linear regression equations differed significantly from the weighted average of coefficients from all patient groups, implying that a direct correlation between ABG and VBG parameters could not be universally applied across the patient groups.

To test the validity of the saturation model, ΔpH and ΔpCO_2 were plotted against ΔO_2% and fit to proportional regression equations (Figure 1). Coefficients of proportional regression equations did not differ significantly from the weighted average of coefficients from all patient groups (Table 3). Correlation coefficients between ΔO_2% and ΔpH and between ΔO_2% and ΔpCO_2 were 0.49 and 0.61, respectively.

The error in estimated ABG parameters using various models is shown in Table 4. Given that ABG and VBG values change rapidly over time, error analysis focused on the studies which explicitly defined the interval between obtaining arterial and venous blood ([redacted] obtained both within [redacted], while [redacted]. obtained both within [redacted](2,3)). The saturation model estimated ABG parameters with more accuracy than the direct correlation model. More importantly, the saturation model estimates of ABG parameters were similar to the actual ABG values with 95% confidence intervals of ±.[redacted], ±[redacted] mm, and ±[redacted] mEq/L for pH, pCO_2, and bicarbonate, respectively.

The variation in ΔO_2% (standard deviation of 20%) derives primarily from variation in the venous oxygen saturation (standard deviation of 20%) rather than the arterial oxygen saturation (standard deviation of 7%). Therefore, the simplified saturation model may account for the vast majority of variation in oxygen saturation by approximating the arterial oxygen saturation as fixed and equal to the average arterial oxygen saturation among all patients, in this series 93% (Table 5). The correlation coefficient between (arterial oxygen saturation – venous oxygen saturation) and (93% - venous oxygen saturation) was 0.94, supporting the validity of this approximation. The accuracy of the simplified saturation model was equivalent to the saturation model (Table 4). Bland-Altman plots of the simplified saturation model demonstrate low error across a wide range of ABG values (Figure 3).

DISCUSSION

Although many studies have been performed comparing ABG and VBG parameters, there is no consensus as to whether the latter is a reliable surrogate for the former. The goal of this investigation was to analyze the performance of various models which predict ABG parameters from simultaneous venous measurements.

The usual method of comparing ABG and VBG parameters is by direct comparison with linear regression (direct correlation model). However in terms of the studies that we analyzed, linear regression coefficients from different patient populations differed to a significant degree (Table 2). This variation is also evident in studies not included in this analysis (11-18). Thus, linear relationships relating VBG and ABG parameters may not be valid across different populations.

The parameters of the saturation model were consistent across all patient groups (Table 3). Given the diversity of patient groups (Table 1), this model appears robust and may allow for universally applicable equations relating ABG and VBG values.

An important issue concerning the estimate of ABG parameters from VBG parameters is the amount of error which is clinically acceptable or relevant. Arterial blood gas parameters fluctuate substantially in real time. Studies on clinically stable patients have defined standard deviations for variation in pH and pCO_2 over one hour to be 0.015-0.02 and 1.5-3 mm, respectively (19-21). We observed standard deviations for estimated pH [redacted]) and pCO_2 ([redacted]) well within these limits, suggesting that the error in estimated pH and pCO_2 is not substantially greater than spontaneous variations in these parameters over time. Therefore, pH and pCO_2 parameters calculated from VBG parameters using our model could be considered as a surrogate for ABG pH and pCO_2 measurement.

Given the current practice of monitoring oxygen saturation noninvasively and aggressively treating hypoxemia, it is uncommon for hospitalized patients to be significantly hypoxemic for any duration of time. Therefore, the vast majority of variability in $\Delta O_2\%$ derives from variability in the venous oxygen saturation. This explains why the simplified saturation model performs as well as the saturation model (Table 4). The simplified saturation model is not expected to perform well for patients with untreated or refractory severe hypoxemia, but these conditions are rare among monitored hospitalized patients. The simplified saturation model has the advantage that it does not require a simultaneous measurement of oxygen saturation (which often will not be available), but rather provides a method of converting directly from VBG to ABG parameters.

Our study has many limitations. First, the saturation model is based on a series of first-order approximations and does not exclude that a more sophisticated model would have higher precision. However, we have demonstrated that the error of our estimates were within the natural variation of the measurements themselves. Second, the amount of error in the saturation model was based on two studies performed by the same group of investigators, and requires further validation. Third, this was a retrospective analysis and, therefore, subject to possible selection bias. Finally, the selection of studies we included was retrospective and required exclusion on the basis of several factors.

CONCLUSIONS

We have developed a simple, empiric model for estimating ABG parameters directly from VBG parameters. The accuracy of this model was confirmed in a subset of patients where the timing of the ABG and VBG measurements was clearly documented. This model has the potential to accurately estimate ABG parameters by less invasive and less expensive means. Given the retrospective nature of this study, further validation is needed.

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TABLE 1 Characteristics of subjects in source studies.

Study	Location	*n*	Subjects
Ak et al.	Turkey	132	Emergency department patients with acute exacerbation of COPD
Ibrahim et al.	Singapore	122	Emergency department patients
O'Connor et al.	Ireland	60	30 patients with acute exacerbation of COPD (inpatients and emergency department patients) 30 preoperative patients admitted electively with no history of respiratory disease
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

TABLE 2 Direct Correlation Model: Coefficients of linear regression equations relating pH and pCO_2 in arterial and peripheral venous blood. Probabilities compare each coefficient from a single patient group and its associated error with the weighted average of that coefficient when combining all patient groups.

Patient group	Intercept	*p-value*	Slope	*p-value*
Arterial vs. Venous pH values				
Ak et al.	0.18 +/- 0.26	0.001	0.98 +/- 0.04	0.001
Ibrahim et al.	0.91 +/- 0.33	0.66	0.88 +/- 0.04	0.69
O'Connor et al. - Control patients	5.72 +/- 0.72	10^{-10}	0.23 +/- 0.10	10^{-10}
O'Connor et al. - COPD patients	2.98 +/- 0.75	0.01	0.60 +/- 0.10	0.01
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weighted average	1.05		0.86	
Arterial vs. Venous PCO_2 values				
Ak et al.	-2.03 +/- 1.96	0.009	0.91 +/- 0.04	0.047
Ibrahim et al.	3.40 +/- 2.46	0.90	0.85 +/- 0.05	0.79
O'Connor et al. - Control patients	32.95 +/- 4.25	10^{-12}	0.16 +/- 0.09	10^{-14}
O'Connor et al. - COPD patients	1.73 +/- 3.86	0.73	0.86 +/- 0.07	0.72
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weighted average	3.09		0.84	

TABLE 3 Saturation model: Coefficients of proportional regression equations which relate ΔpH and ΔpCO_2 to ΔO_2%. Probabilities compare each coefficient from a single patient group and its associated error with the weighted average of that parameter when combining all patient groups.

Patient group	**Slope**			***p-value***
pH				
Ak et al.	0.0011	+/-	0.0001	0.74
Ibrahim et al.	0.0009	+/-	0.0002	0.41
O'Connor et al. - Control patients	0.0009	+/-	0.0002	0.37
O'Connor et al. - COPD patients	0.0012	+/-	0.0002	0.47
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weighted average	0.0011			
pCO_2				
Ak et al.	0.234	+/-	0.011	0.15
Ibrahim et al.	0.175	+/-	0.023	0.063
O'Connor et al. - Control patients	0.183	+/-	0.022	0.10
O'Connor et al. - COPD patients	0.222	+/-	0.022	0.86
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Weighted average	0.218			

TABLE 4 Error in predictions of pH, pCO2, and bicarbonate based on different models. Errors are presented as average error (bias) plus or minus the standard deviation. The last row describes an analysis of the combined data from [redacted]

	Error in pH calculation			Error in pCO_2 calculation			Error in bicarbonate calculation		
Patient Group	Direct correlation model	Saturation Model	Simplified saturation model	Direct correlation model	Saturation model	Simplified saturation model	Direct correlation model	Saturation model	Simplified saturation model
Ak et al.	-0.014 ± 0.013	-0.002 ± 0.025	0.004 ± 0.029	1.5 ± 5.3	0.7 ± 4.1	-0.4 ± 4.6	0.2 ± 2.1	0.3 ± 2.0	0.1 ± 2.1
Ibrahim et al.	0.006 ± 0.069	0.014 ± 0.064	0.011 ± 0.065	-0.8 ± 10.0	-2.7 ± 8.7	-2.1 ± 8.8	-0.1 ± 2.9	-1.0 ± 3.0	-0.7 ± 2.9
O'Connor et al.	-0.018 ± 0.039	0.004 ± 0.037	0.003 ± 0.037	1.6 ± 6.2	-1.1 ± 5.1	-0.8 ± 5.0	-0.2 ± 2.0	-0.7 ± 1.9	-0.5 ± 1.9
[redacted]									

TABLE 5 Equations involved in the saturation model and simplified saturation model, including coefficients and error. Coefficients are based on analysis of all patients, whereas error is based on two studies [redacted]

5A: The saturation model:

$$\text{Estimated Arterial pH} = \text{Venous pH} + (0.0011)[\text{Arterial oxygen saturation} - \text{Venous oxygen saturation}]$$ [redacted]

$$\text{Estimated Arterial } pCO_2 = \text{Venous } pCO_2 - (0.22)[\text{Arterial oxygen saturation} - \text{Venous oxygen saturation}]$$ [redacted]

5B: The simplified saturation method:

$$\text{Estimated Arterial pH} = \text{Venous pH} + (0.0011)[93\% - \text{Venous oxygen saturation}]$$ [redacted]

$$\text{Estimated Arterial } pCO_2 = \text{Venous } pCO_2 - (0.22)[93\% - \text{Venous oxygen saturation}]$$ [redacted]

FIGURE 1 Saturation model for relating ABG and peripheral VBG data. k_1 and k_2 are constants derived empirically from patient data using proportional regression analysis.

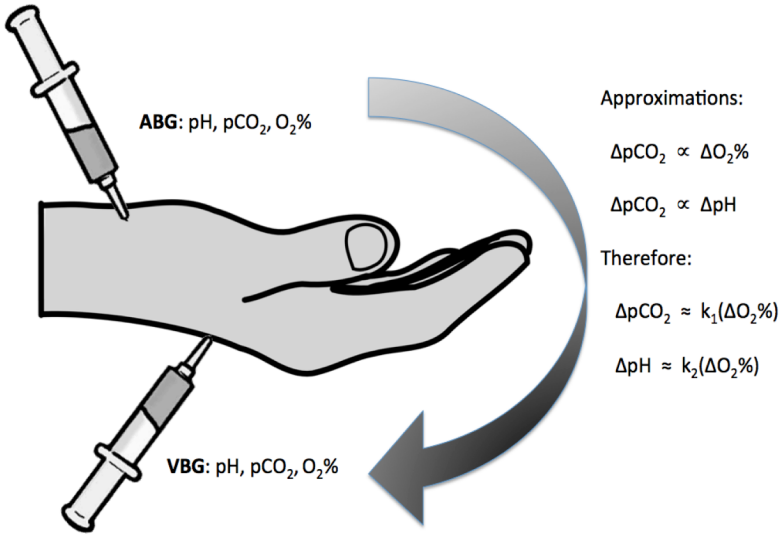

FIGURE 2 Plots of the difference between arterial and venous oxygen saturation ($\Delta O_2\%$) versus differences between venous and arterial pH (ΔpH) and pCO_2 (ΔpCO_2). Lines represent proportional regression equations.

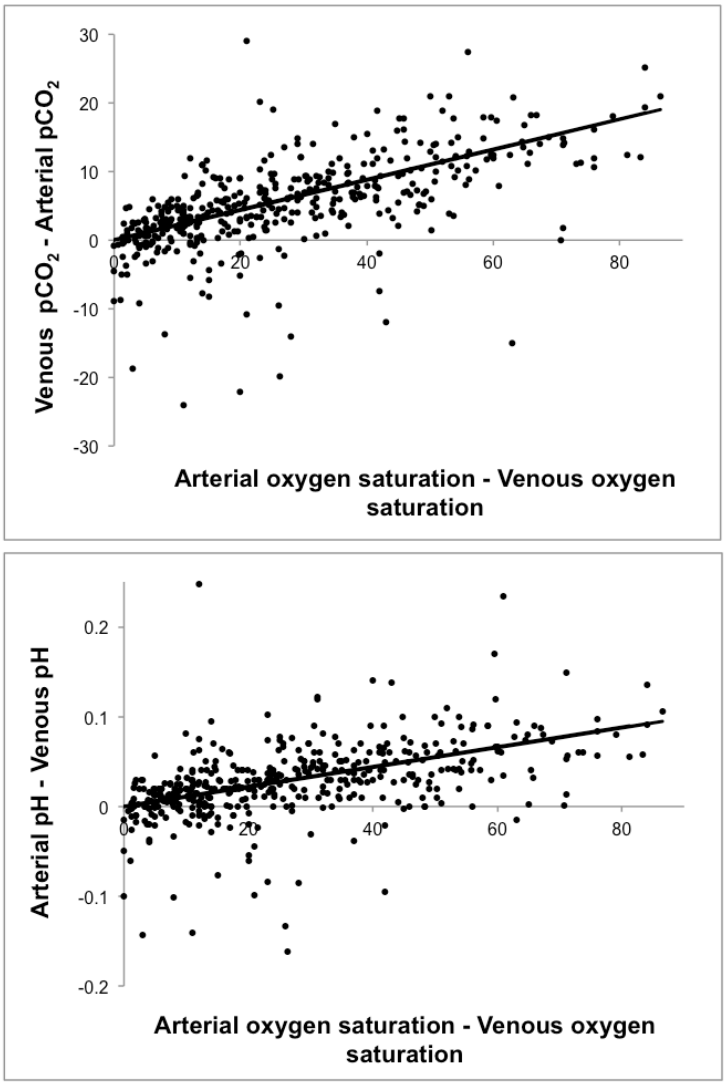

FIGURE 3 Bland-Altmann plots of the error in the simplified saturation model applied to data from [redacted] Horizontal lines represent 95% confidence estimates.

[REDACTED]