Journal of Veterinary Emergency and Critical Care

Original Study

Journal of Veterinary Emergency and Critical Care **23**(3) 2013, pp 280–285
doi: 10.1111/vec.12050

Preliminary evaluation of the utility of comparing SpO_2/FiO_2 and PaO_2/FiO_2 ratios in dogs

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Abstract

Objective – To determine whether the ratio of pulse oximetry saturation/fraction of inspired oxygen (SpO_2/FiO_2, [SF]) correlates with the ratio of partial pressure of oxygen in arterial blood/FiO_2 (PaO_2/FiO_2, [PF]) in dogs.
Design – Prospective, observational pilot study.
Setting – Urban tertiary veterinary referral center.
Animals – Thirty-eight client-owned dogs requiring assessment of oxygenation.
Interventions – None.
Measurements and Main Results – Arterial blood gas analysis with co-oximetry was performed on samples obtained from the dorsal pedal artery. Median SpO_2 was 91.5% (range 80–97%) and median PaO_2 was 70.1 mmHg (range 44.5–103.8 mmHg). Hypoventilation was uncommon and venous admixture was the predominant cause of hypoxemia in this population. Median SF was 435.7 (range 381.0–461.9) and median PF was 334.0 (range 211.9–494.3). Nine dogs (23.6%) had PF <300; no dogs had PF below 200. SF and PF were correlated ($\rho = 0.618$, $P < 0.01$).
Conclusions – SF and PF in dogs spontaneously breathing room air have good correlation, suggesting that SF may be a useful, noninvasive surrogate for PF when assessing oxygenation in canine patients. Further studies are warranted to confirm and validate this relationship in spontaneously breathing and mechanically ventilated dogs on varying levels of FiO_2 and to assess the ability of SF to predict outcome.

(J Vet Emerg Crit Care 2013; 23(3): 280–285) doi: 10.1111/vec.12050

Keywords: ARDS, ALI, blood gas analysis, noninvasive, pulse oximetry

Abbreviations

A-a gradient	Alveolar-arterial oxygen tension gradient
ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
AUC	Area under the curve
FiO_2	Fraction of inspired oxygen
OI	Oxygenation index
OSI	Oxygen saturation index
PaO_2	Partial pressure of oxygen in arterial blood
PAO_2	Partial pressure of oxygen in alveolar air
$PaCO_2$	Partial pressure of carbon dioxide in arterial blood
PEEP	positive end-expiratory pressure
PF	PaO_2/FiO_2 ratio
ROC	Receiver operating characteristic
SpO_2	Pulse oximetric oxyhemoglobin saturation
SF	SpO_2/FiO_2 ratio

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Dr. Prittie is an Assistant Editor for the journal and did not participate in the peer review process of this manuscript other than as an author.

The authors declare no other conflicts of interest.

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Submitted November 1, 2011; Accepted March 17, 2013.

Introduction

Tissue hypoxia is a major cause of morbidity and mortality in human and veterinary medicine. Arterial

blood gas analysis is the gold standard for assessing oxygenation, and the partial pressure of oxygen in arterial blood (PaO_2) is utilized in a number of indices of oxygenation.[1] Measurement of PaO_2 and other data from a single arterial blood gas sample represent one point in time. Although trends in arterial blood gas data provide more clinically relevant information than single measurements, repeated arterial puncture in small animals is often impractical and placement of indwelling arterial catheters to facilitate serial sample acquisition may be challenging. Complications associated with arterial blood sampling include laceration of the artery and subsequent hemorrhage or hematoma formation, arterial occlusion or thrombosis of distal structures, arteriospasm, pain, and infection.[2] Repeated puncture at a single site may lead to scarring,[2] and oversampling of small patients contributes to anemia. Additionally, contraindications to arterial sampling include hypoperfusion of the limb being considered for sampling, lesions over the sampling site, and coagulopathy or anticoagulant therapy.[2]

Pulse oximetry is a less invasive way of assessing oxygenation in patients. Changes in PaO_2 correlate well with changes in arterial oxygen saturation as measured by pulse oximetry (SpO_2) within the range of 80–97% on room air (fraction of inspired oxygen [FiO_2] of 21%) in people.[3–5] PaO_2 and SpO_2 are also correlated up to SpO_2 values of 98–99% in critically ill dogs and in healthy dogs utilized for laboratory experiments.[6–10] SpO_2 is therefore an acceptable surrogate for PaO_2 in normoxic or hypoxemic veterinary patients breathing room air. Pulse oximetry has become nearly ubiquitous in human medicine, and surrogate markers of oxygenation utilizing this modality are gaining more attention, as concerns about over-sampling and resultant anemia are contributing to decreased use of arterial blood gas analysis.[3,4]

A number of studies have recently demonstrated that the SpO_2/FiO_2 ratio (SF) is a reliable noninvasive surrogate marker for the PaO_2/FiO_2 ratio (PF) in critically ill adult and pediatric human patients.[3–5,11,12] Studies have demonstrated SF to be a valid diagnostic criterion for acute lung injury (ALI) and acute respiratory distress syndrome (ARDS),[3–5] and to be useful in assessing illness severity[11] and to be predictive of outcome.[12] A similar relationship between SF and PF may exist in veterinary patients suffering from ALI/ARDS and other forms of hypoxemic respiratory failure. Moreover, it would be useful to have a reliable, noninvasive surrogate for PF in dyspneic veterinary patients, as arterial blood gas analysis in small animal patients may be challenging.

Our primary objective in this pilot study was to assess whether a correlation exists between SF and PF in dogs presented to an urban tertiary veterinary referral hospital. A secondary objective was to determine whether SpO_2, PaO_2, partial pressure of carbon dioxide in arterial blood ($PaCO_2$), alveolar-arterial oxygen tension gradient (A-a gradient), SF or PF differed between survivors and non-survivors.

Materials and Methods

Animals

Any dog requiring assessment of oxygenation status was eligible for inclusion in the study. Exclusion criteria included carboxyhemoglobin > 4%, methemoglobin > 2%, SpO_2 < 80% or > 97%, a known or suspected coagulopathy, severe respiratory distress that precluded safe patient handling, clinical suspicion of anatomic right-to-left shunt, and incomplete data acquisition. We selected SpO_2 97% as the upper limit for inclusion in this study because the oxyhemoglobin dissociation curve is flat above this point.[3–5,14] The study protocol was approved by The Animal Medical Center's Institutional Animal Care and Use Committee and informed consent was obtained from owners prior to enrollment.

Samples and measurements

Arterial blood samples (approx 0.3 mL) were obtained from the dorsal pedal artery utilizing commercial arterial blood gas syringes[a] and run immediately in co-oximetry mode using a blood gas analyzer.[b] Co-oximetry mode was utilized to rule out concurrent carboxyhemoglobinemia or methemoglobinemia that might have confounded results. SpO_2 values, measured within 15 minutes of blood gas analysis, were recorded by a veterinarian or licensed veterinary technician.[c] Probe location was not standardized and lip, ear, tongue, and metacarpal/metatarsal regions were all utilized. Concordance with heart rate was verified prior to recording the value. All measurements were obtained on room air at sea level (FiO_2 21%). Alveolar-arterial oxygen tension gradient (A-a gradient, normal value < 10 mm Hg at FiO_2 21%),[13,14] SF and PF were calculated. Alveolar oxygen tension was determined using the alveolar gas equation: $PAO_2 = [(760\ mmHg - 47\ mmHg) \times FiO_2] - (PaCO_2/0.8)$.[13,14] SF was calculated as $SpO_2/0.21$ and PF was calculated as $PaO_2/0.21$.

If dogs were determined to be hypoxemic, the suspected cause of hypoxemia (eg, alveolar hypoventilation, diffusion impairment, or venous admixture) was recorded. Low FiO_2 was not considered as an etiology in this population, as all samples were taken from dogs spontaneously breathing room air. When available, thoracic radiographs obtained within 24 hours of sample acquisition were evaluated by a board-certified radiologist and the radiographic diagnosis was recorded. Outcome was noted as survival to discharge versus death

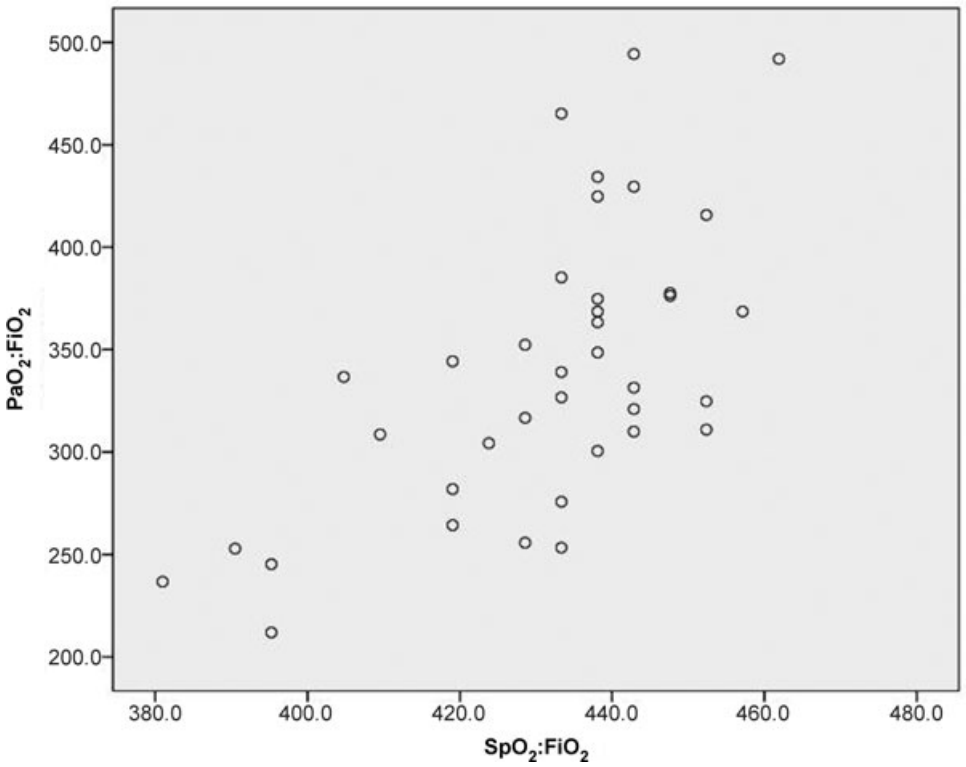

Figure 1: Scatterplot of SpO_2/FiO_2 (SF) ratios versus PaO_2/FiO_2 (PF) ratios in dogs ($\rho = 0.618$, 2-tailed significance < 0.01).

or euthanasia in the hospital. Any interventions were performed at the discretion of the primary clinician and were not recorded for the purposes of this study.

Data Analysis

Data were analyzed using a standard software package.[d] Descriptive statistics (eg, mean, SD, median, range) were generated for patient age, weight, $PaCO_2$, PaO_2, SpO_2, A-a gradient, SF, and PF. Normal distribution was assessed using the Shapiro-Wilk test. A two-way scatterplot was generated for SF versus PF and Spearman's correlation coefficient was calculated. The Mann-Whitney test was used to compare age, weight, $PaCO_2$, PaO_2, SpO_2, A-a gradient, SF, and PF in survivors versus nonsurvivors.

Results

Fifty dogs were considered for inclusion in this pilot study. Thirty-eight dogs were enrolled, and 12 dogs were excluded for a variety of reasons ($SpO_2 < 80\%$, $n = 2$; $SpO_2 > 97\%$, $n = 1$; carboxyhemoglobin $> 4\%$, $n = 3$; methemoglobin $> 2\%$, $n = 1$; and failure to utilize co-oximetry mode or malfunction of blood gas analyzer resulting in incomplete co-oximetry readings, $n = 5$). Median body weight was 30.0 kg (range 3.1–41.7 kg) and median age was 11 years (range 0.5–17 y of age). There were 21 males (6 intact, 15 neutered) and 17 females (1 intact, 16 spayed).

Median SpO_2 was 91.5% (range 80–97%), and median PaO_2 was 70.1 mm Hg (range 44.5–103.8 mmHg). Venous admixture was the most common cause for hypoxemia in this study, with a median A-a gradient of 39.3 mm Hg (range 4.4–64.9 mm Hg). Hypoventilation, defined as $PaCO_2 \geq 50$ mm Hg,[15] was not a common cause of hypoxemia in this population, as median $PaCO_2$ was 31.4 mm Hg (range 17.3–52.6 mm Hg) and $PaCO_2$ exceeded 50 mm Hg in only 2 dogs (both with A-a gradients $>$ 28 mm Hg).

Median SF was 435.7 (range 381.0–461.9). Median PF was 334.0 (range 211.9–494.3); 9 dogs had PF < 300 and no dogs had PF below 200. PaO_2 values and PF were normally distributed ($P = 0.863$ for both values), however SpO_2 values and SF were not normally distributed ($P = 0.007$ for both values). The SF and PF were correlated ($\rho = 0.618$, $P < 0.01$ [2-tailed], Figure 1).

Underlying etiologies for venous admixture in this cohort were variable. Primary respiratory diseases included pneumonia ($n = 8$), chronic lower airway disease ($n = 6$), neoplasia ($n = 5$), suspected pulmonary fibrosis ($n = 3$), pulmonary contusions ($n = 1$), and suspected pneumonitis versus ALI following smoke inhalation ($n = 1$). Other disease processes included congestive heart failure ($n = 1$) and multiple organ dysfunction

syndrome ($n = 3$). We suspected atelectasis in 5 recumbent dogs recovering from anesthesia and underlying disease was unclear in 5 dogs, including 2 postseizure patients with no evidence of noncardiogenic pulmonary edema on thoracic radiographs.

Six of thirty-eight (15.8%) patients died and 2 of 38 (5%) were euthanized in the hospital for an overall mortality rate of 21%. There were no significant differences detected in age, weight, $PaCO_2$, PaO_2, SpO_2, A-a gradient, SF, or PF between survivors and nonsurvivors.

Discussion

This pilot study demonstrated reasonable correlation between SF and PF in a heterogeneous population of dogs with a variety of underlying diseases, most of which resulted in venous admixture. The SF has been utilized as a noninvasive substitute for PF in several human patient populations.[3–5,11,12] It has been used in critically ill adult and pediatric patients as a viable surrogate for PF in the diagnosis of ALI and ARDS[3–5] and in the calculation of illness severity scores and mortality prediction indices.[11,12] This study suggests that SF might also be a useful surrogate for PF in veterinary patients.

Normal PaO_2 in human and canine patients breathing room air (FiO_2 21%) at sea level (atmospheric pressure 760 mmHg) is 80–100 mmHg.[13–16] Patients with chronic respiratory compromise may adapt to lower-than-normal PaO_2,[16] however, acute hypoxemia with PaO_2 < 60 mm Hg is critical and requires intervention.[15,16] PaO_2 is utilized in a number of indices for oxygenation, most notably the alveolar-arterial oxygen tension gradient (A-a gradient, or PAO_2-PaO_2) and PF. The A-a gradient is normally 5–10 mm Hg on room air.[13–16] Pulmonary diseases that impair transfer of alveolar oxygen to pulmonary capillary blood and result in venous admixture cause decreased PaO_2 relative to PAO_2, thereby increasing the A-a gradient.[13–16] A normal A-a gradient in a hypoxemic patient is suggestive of hypoventilation.[15,16] The PF ratio has well-documented utility as an indication of disease severity. It is used to stratify human and veterinary ALI/ARDS patients: PF $\leq$ 300 mm Hg is consistent with ALI and PF $\leq$ 200 mm Hg is consistent with ARDS.[17–19] It may also be used to assess the degree of respiratory compromise in human patients with other causes for hypoxemic respiratory failure, for example, chronic obstructive pulmonary disease,[20] pulmonary contusions,[21] and hepatopulmonary syndrome.[22]

Pulse oximetry permits noninvasive assessment of oxygenation in human and veterinary patients and correlates well with PaO_2.[3–10] Arterial oxygen saturation >95% typically corresponds with a PaO_2 > 80 mm Hg, while SpO_2 < 90% typically corresponds with a PaO_2 < 60 mm Hg in patients breathing room air.[15] SpO_2 and PaO_2 are correlated in critically ill and healthy dogs up to SpO_2 98–99%.[6–10] Furthermore, pulse oximeters are inexpensive, readily available, and probe placement is generally well tolerated.

The SF ratio has recently been evaluated as a surrogate for PF in human clinical patients by several investigators.[3–5,11,12] Rice et al[3] utilized data from human patients enrolled in a prospective National Heart, Lung and Blood Institute ARDS Network trial evaluating low tidal volume ventilation in adults to explore the correlation between PF and SF.[3] All patients were mechanically ventilated and FiO_2, adjusted to target SpO_2 88–92%, varied from 21–100%. Sample size was large, with 2,673 data points from 672 patients in the data set used to derive the relationship and 2,031 data points from 526 patients in the data set used to validate the relationship. In the derivation data set, these investigators demonstrated a linear correlation between SF and PF that did not change with ventilation strategy (ie, high versus low tidal volume) or FiO_2. Level of positive end-expiratory pressure (PEEP) had a slight but statistically significant effect on the relationship between SF and PF. These authors determined that SF <315 corresponded with PF <300 and SF <235 corresponded with PF <200. Receiver operating characteristic (ROC) curve analysis demonstrated that SF provided excellent discrimination between patients with and without ALI or ARDS. Rice et al[3] subsequently validated these surrogate ratios with the validation data set from the same ARDS Network trial and documented analogous discriminatory ability. Area under the curve (AUC) for ROC curves were 0.878 and 0.928, respectively, for patients with ALI and ARDS. The SF threshold of 315 was 91% sensitive and 56% specific for ALI and the SF threshold of 235 was 85% sensitive and 85% specific for ARDS.[3]

Khemani et al[4] replicated the study by Rice et al[3] in pediatric patients in two tertiary care pediatric ICUs. Their study was also large, with 1,298 data pairs in the derivation data set and 1,845 data pairs in the validation data set. FiO_2 in this study ranged from 40% to 90%. ROC analysis demonstrated that SF had good discriminatory capability for patients with and without ALI and ARDS.[4] Threshold values in this data set differed slightly from those in the earlier study in adults[3,4]; SF <263 predicted ALI and SF <201 predicted ARDS.[4] These threshold values were subsequently evaluated in the validation data set. Sensitivity and specificity values were 86% and 47% for ALI and 68% and 84% for ARDS, respectively.[4] We based the methodology for our pilot study upon the studies by Rice et al[3] and Khemani et al[4] however, our sample size was too small to support ROC analysis or to establish surrogate SF values for PF <300 or PF <200. Correlation between SF and PF was stronger in these human studies than in our study, which

could be the result of our limited sample size or patient population.

Thomas et al[5] conducted a similar study in children. They utilized data from 2 large randomized controlled trials that enrolled children with severe acute pulmonary disease. Threshold values were comparable to those in the study by Khemani et al[4]: SF <253 predicted ALI and SF <212 predicted ARDS.[5] To determine the impact of airway pressures on these surrogate diagnostic markers, these investigators also evaluated oxygenation index (OI) using the formula OI = FiO_2 × mean airway pressure/PaO_2 and oxygen saturation index (OSI) using the formula OSI = FiO_2 × mean airway pressure/SpO_2. ROC analysis demonstrated good to excellent discriminatory ability for SF, OI, and OSI for patients with and without ALI or ARDS. Area under the ROC curve for SF was 0.87 for ALI and 0.88 for ARDS, AUC for OI was 0.95 for ALI and 0.93 for ARDS, and AUC for OSI was 0.84 for ALI and 0.84 for ARDS.[5] We did not enroll mechanically ventilated dogs, precluding measurement of airway pressures and the use of OI or OSI; however, effects of airway pressure on surrogate markers for ALI and ARDS represent interesting avenues for further study.

This pilot study had a number of limitations. The study population was small and heterogeneous. Alterations in patient signalment and underlying disease process could have influenced the degree of SF and PF correlation. Patient body position and anatomic location for SpO_2 readings were not standardized and there may have been significant interoperator variability in acquiring readings. This variability could be limited if future investigators standardize SpO_2 probe location and body position for sample acquisition, incorporate efforts to limit the number of personnel recording SpO_2 readings, and analyze plethysmographic waveforms to validate SpO_2 readings. We enrolled dogs with both acute and chronic pulmonary disease and the correlation between SF and PF may differ between these patient populations due to potential shifts in the normal oxyhemoglobin dissociation curve. Investigators might consider separating patients with acute versus chronic disease in future studies. Our patients were all spontaneously breathing room air, precluding comparison of SF and PF at varying FiO_2 or analysis of other surrogate diagnostic criteria, such as the OI or OSI, that incorporate airway pressure. Finally, we did not enroll enough patients to perform ROC analysis or to determine SF cutoff values that could serve as surrogates for PF <300 or PF <200. Despite these limitations, we believe that our data suggest that SF may prove to be a reasonable surrogate for PF in dyspneic small animal patients. Further studies are needed to validate correlation between SF and PF in larger populations of small animals at varying levels of FiO_2 and to assess SF as a marker for disease severity or a predictor of outcome.

Footnotes

[a] Marquest MicroBAG syringes, Vital Signs, Inc., Englewood, CO.
[b] Siemens Rapidlab1265, Siemens, Inc., Tarrytown, NY.
[c] Cardell 9403, Midmark Corp., Versailles, OH.
[d] SPSS, IBM Corporation, Armonk, NY.

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