

Repeatability of Blood Gas Parameters, Pco_2 Gap, and Pco_2 Gap to Arterial-to-Venous Oxygen Content Difference in Critically Ill Adult Patients

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Abstract: The objective of this study was to examine the repeatability of blood gas (BG) parameters and their derived variables such as the central venous-to-arterial carbon dioxide tension difference (ΔPco_2) and the ratio of ΔPco_2 over the central arteriovenous oxygen content difference ($\Delta\text{Pco}_2/\text{C(a-cv)}\text{O}_2$) and to determine the smallest detectable changes in individual patients.

A total of 192 patients with arterial and central venous catheters were included prospectively. Two subsequent arterial and central venous blood samples were collected immediately one after the other and analyzed using the same point-of-care BG analyzer. The samples were analyzed for arterial and venous BG parameters, ΔPco_2 , and $\Delta\text{Pco}_2/\text{C(a-cv)}\text{O}_2$ ratio. Repeatability was expressed as the smallest detectable difference (SDD) and the least significant change (LSC). A change in value of these parameters exceeding the SDD or the LSC should be regarded as real.

The SDDs for arterial carbon dioxide tension, arterial oxygen saturation, central venous oxygen saturation (ScvO_2), and ΔPco_2 were small: ± 2.06 mm Hg, $\pm 1.23\%$, 2.92% , and ± 1.98 mm Hg, respectively, whereas the SDDs for arterial oxygen tension (PaO_2) and $\Delta\text{Pco}_2/\text{C(a-cv)}\text{O}_2$ were high: ± 9.09 mm Hg and ± 0.57 mm Hg/mL, respectively. The LSCs (%) for these variables were 5.06, 1.27, 4.44, 32.4, 9.51, and 38.5, respectively.

The repeatability of all these variables was good except for PaO_2 and $\Delta\text{Pco}_2/\text{C(a-cv)}\text{O}_2$ ratio for which we observed an important inherent variability. Expressed as SDD, a ScvO_2 change value of at least $\pm 3\%$ should be considered as true. The clinician must be aware that an apparent change in these variables in an individual patient might represent only an inherent variation.

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Abbreviations: ΔPco_2 = central venous-to-arterial carbon dioxide tension difference, $\Delta\text{Pco}_2/\text{C(a-cv)}\text{O}_2$ = ratio of ΔPco_2 over the central arteriovenous oxygen content difference, BG = blood gas, CV_w = within-subject coefficient of variation, FiO_2 = fraction-inspired oxygen, ICU = intensive care unit, LSC = least significant change, PaCO_2 = arterial carbon dioxide tension, PaO_2 = arterial oxygen tension, PcvCO_2 = central venous carbon dioxide tension, PcvO_2 = central venous oxygen tension, SaO_2 = arterial oxygen saturation, ScvO_2 = central venous oxygen saturation, SDD = smallest detectable difference, SD_{diff} = standard deviation of the difference.

INTRODUCTION

Serial blood gas (BG) analyses are needed to assess oxygenation and ventilation, monitor progress, and evaluate the effect of therapeutic intervention. For any given individual, when BG measurements are repeated over time, some degree of variation will be detected. Variation may result from any combination of within-subject variability and deterioration or amelioration of the patient's condition. The repeatability of BG parameters (the degree to which repeated measurements are similar in the absence of any clinical change) depends on the first components. Knowing the repeatability of the measure by determining the magnitude of the intraindividual component of variation is necessary in order to detect a true change in the clinical condition of a given patient and enable appropriate decision-making. Thus, repeatability is of paramount importance. Previously, it has been shown that the spontaneous variability of arterial BG values was substantial in stable critically ill patients.¹⁻³ However, clinicians may consider the current evidence as based on too small or potentially outdated studies.

The monitoring of central venous oxygen saturation (ScvO_2) is recommended in the management of severe sepsis.^{4,5} However, to the best of our knowledge, there are no data on the repeatability of ScvO_2 in intensive care unit (ICU) patients. This is crucial to consider in order to determine whether changes in ScvO_2 during resuscitation can be considered as real or only due to the within-subject variability. Recently, there has been a growing interest in the use of central venous-to-arterial carbon dioxide tension difference (ΔPco_2) as a tool to evaluate the adequacy of cardiac output to global metabolic demand in critically ill patients.⁶⁻¹⁰ Furthermore, the ratio of ΔPco_2 over the central arteriovenous oxygen content difference ($\Delta\text{Pco}_2/\text{C[a-cv]O}_2$) has been found to predict an increase in oxygen consumption in fluid responders.¹¹ Data on the repeatability of the calculated parameters are also lacking. Therefore, we sought to determine the repeatability and the smallest detectable difference (SDD) of BG parameters, ΔPco_2 , and $\Delta\text{Pco}_2/\text{C(a-cv)}\text{O}_2$ ratio in ICU patients.

MATERIALS AND METHODS

This prospective and observational study was conducted in a single, mixed medical, and surgical adult ICU with 15 beds. The study was approved by the local institutional ethics committee (comité d'éthique du centre hospitalier du Dr Shaffner de Lens). Informed consent was obtained from the next of kin of each patient.

Patients

Patients were included if they met all of the following criteria: age >18 years, catheter inserted either in a radial or femoral artery, and central line with the tip confirmed by x-ray to be in the superior vena cava near or at the right atrium. Exclusion criteria were pregnancy and unstable condition, the latter being defined by >10% variation in heart rate, mean arterial pressure, and the need for clinical intervention within 30-minute period before sampling.

Procedure

Arterial and venous BGs were sampled twice immediately one after the other to assess the repeatability of these variables. Arterial and venous BG samples were obtained from the arterial and central venous cannula, respectively, using a preheparinized 3-mL BG syringe (RAPIDLyte; Siemens Healthcare Diagnostic Inc, Deerfield, IL USA). Immediately before sampling, the intra-arterial and intravenous catheters were flushed using the standard flush solution of 0.9% sodium chloride without heparin. To reduce dilution effects, a 10-mL sample of blood was withdrawn (from each arterial and venous system) into the syringe and discarded prior to drawing the 3-mL test samples. The tap in between the sampling port and administration set tubing was turned 45° while changing syringes to ensure that the solution from the proximal tubing could not enter the deadspace. Air bubbles were expressed and the syringes were cupped and analyzed immediately, without temperature correction, using the GEM Premier 3000 (Instrumentation Laboratory Co, Paris, France). Maintenance, calibration, and quality control are performed on a regular basis by the central hospital laboratory. The analytical performance of this analyzer is described in the supplementary digital content (<http://links.lww.com/MD/A161>). The deadspace was 1.1 mL for the arterial system and 1.9 mL for the venous system.

No medical or nursing interventions were allowed while sampling was being performed.

Data Collection

Demographic data, ICU admission diagnosis, and the Simplified Acute Physiology Score were obtained on the day of enrollment. Mean arterial pressure, the ventilation (mechanical or spontaneous), and the use of vasopressor drugs were also registered.

Arterial BGs (P_{aO_2} , arterial carbon dioxide tension [P_{aCO_2}], and arterial oxygen saturation [S_{aO_2}]) and central venous BGs (central venous oxygen tension [P_{cvO_2}], central venous carbon dioxide tension [P_{cvCO_2}], and $ScvO_2$) were measured using the GEM Premier 3000 (Instrumentation Laboratory Co). The ΔP_{CO_2} was calculated as the difference between P_{cvCO_2} and P_{aCO_2} . The arterial blood hemoglobin concentration (Hb) was also measured on a GEM Premier 3000. This analyzer measures hematocrit using a technology called conductivity and then calculates Hb ($Hb = 0.31 \times \text{hematocrit}$). The first and second measurements of arterial Hb

concentrations were used to determine the oxygen content (arterial and venous) of each sample, respectively. The arterial oxygen content was calculated as $CaO_2 \text{ (mL)} = 1.34 \times S_{aO_2} \times Hb \text{ (g/dL)} + 0.003 \times P_{aO_2} \text{ (mm Hg)}$. The central venous oxygen content was calculated as $CcvO_2 \text{ (mL)} = 1.34 \times ScvO_2 \times Hb \text{ (g/dL)} + 0.003 \times P_{cvO_2} \text{ (mm Hg)}$. The $C(a-cv)O_2$ was calculated as $C(a-cv)O_2 \text{ (mL)} = CaO_2 - CcvO_2$.

Statistical Analysis

The measurement error was calculated using the Bland–Altman method¹² and the within-subject coefficient of variation (CV_w). According to Bland and Altman, most disagreements between measurements are expected to fall between limits called “limits of agreement” defined as $d \pm 1.96$ standard deviation of the difference (SD_{diff}), where d is the mean difference between the pairs of measurements.¹² In this case, where there are 2 observations for each subject, the SD_{diff} estimates the within-subject variability of the measurements ($SD_{diff} = \sqrt{2 \times \text{within-subject SD}}$). Precision expressed according to the Bland–Altman method¹² gives an absolute and metric estimate of random measurement error, also called the SDD. Thus, a test is considered to be capable of detecting a difference, in absolute units, of at least the magnitude of the limits of agreement ($\pm 1.96 SD_{diff}$). The within-subject SD that was used to determine the 95% range for an individual “true” value is as follows: 95% range = within-subject SD $\times 1.96$.¹³ This will indicate that the “true” value for 95% of the subjects lies within this range, above, and below the actual value of the taken measurement. This indicates, how much reliance, say for diagnosis, can be placed on that reading.

A rank correlation coefficient for the mean versus differences plot, called Kendall correlation coefficient, was used to assess whether the differences were related to the size of the measurement.

The CV_w is the SD corrected for the mean of paired measurements. CV_w was calculated as $CV_w\% = \sqrt{\{[\sum(a-b)^2/2n]\}/[(Ma+Mb)/2]} \times 100$, where a and b are the first and second measurements, Ma and Mb are the mean values for the 2 groups, and n is the number of paired observations.¹⁴ The least significant change (LSC) is the minimum change that needs to be measured by a laboratory analyzer in order to recognize a real change of measurement.¹⁵ The LSC (%) was calculated using the following equation: $LSC = CV_w \times 1.96 \times \sqrt{2}$.

A sample size of 192 subjects is required to give good precision for estimating repeatability from 2 measurements with the width of the 95% confidence interval of the within-subject SD no wider than $\pm 10\%$.^{16,17} Statistical analyses were performed using SPSS (SPSS for windows release 17.0, Chicago, IL). $P < 0.05$ was considered statistically significant.

RESULTS

During the study period (December 2012 to January 2014), 488 patients were admitted to our ICU. Among them, 296 patients were not included because of absence of a central line in the superior vena cava ($n = 156$), absence of an arterial catheter ($n = 117$), and 23 patients were in unstable condition. Thus, 192 patients were included in this study, and their characteristics are shown in Table 1.

Table 2 summarizes the results of the various methods of calculating the variability in arterial and venous BG analyses. The variability in P_{aO_2} was particularly high because of the high 95% range (≈ 6 mm Hg) and the wide limits of agreement

(SDD \approx 9 mm Hg) found (Figure 1), reflecting a poor repeatability between measurements, although the CV_w was low for this variable (<5%). Additional results on the variability of Pao₂ in patients with Sao₂ < 94% and patients ventilated with high positive end-expiratory pressure (PEEP > 10 cmH₂O) and a high fraction inspired oxygen (FiO₂ > 50%) are provided in Tables S1 and S2, respectively (supplementary content, <http://links.lww.com/MD/A162>, <http://links.lww.com/MD/A163>). The repeatability of the other variables was, nevertheless, very good (Table 2).

Figures 2 and 3 show the Bland–Altman diagrams for Δ Pco₂, and Δ Pco₂/C(a-cv)O₂ ratio, respectively. Results for repeatability of calculated variables are presented in Table 3. Although the variability of Δ Pco₂ expressed as the CV_w and LSC was high, the 95% range, and also the limits of agreement (SDD) for this calculated variable were small (Figure 2). Indeed, the 95% range for Δ Pco₂ was 1.4 mm Hg, that is, for a patient whose Δ Pco₂ was measured as 6 mm Hg, the patient's "true" value lies between 4.6 mm Hg (\approx 5) and 7.4 mm Hg (\approx 7). This suggests that the repeatability of Δ Pco₂ was good. However, the 95% range for the Δ Pco₂/C(a-cv)O₂ ratio was 0.4 mm Hg/mL. Thus, if a patient has a Δ Pco₂/C(a-cv)O₂ of 1.4 mm Hg/mL, the Δ Pco₂/C(a-cv)O₂ could be as low as 1 mm Hg/mL or as high as 1.8 mm Hg/mL. This indicates that the inherent variability of this ratio was important. There were no correlations between SD_{diff} and the averages of the first and second measurements for all measured and calculated variables (see Table S3, supplementary content, <http://links.lww.com/MD/A164>). Additional results on the repeatability of the measured and calculated variables in patients with septic shock are shown in Table S4 (supplementary content, <http://links.lww.com/MD/A165>).

DISCUSSION

The most important findings of our study are as follows: the repeatability of Sao₂, ScvO₂, Pco₂, and pH was very good, whereas the inherent natural variability of Pao₂ and Pao₂/FiO₂ was considerable; Δ Pco₂ was found to be repeatable, whereas the repeatability of Δ Pco₂/C(a-cv)O₂ was poorer.

TABLE 1. Characteristics of the Patients (n = 192)

Age, y	62 \pm 13
Sex, (men/women)	113/79
SAPS II	61 \pm 21
ICU mortality, n (%)	73 (38)
Mechanical ventilation, n (%)	168 (88)
Septic shock, n (%)	61 (32)
MAP, mm Hg	87 \pm 17
FiO ₂	0.44 \pm 0.20
Reasons for admission in ICU, n (%)	
Pneumonia	71 (37)
Peritonitis	46 (24)
Cardiac arrest	25 (13)
Pancreatitis	19 (10)
Cardiac failure	14 (7)
Stroke	11 (6)
Others	6 (3)

Values are expressed as mean \pm SD and count (%). FiO₂ = fraction-inspired oxygen, ICU = intensive care unit, MAP = mean arterial pressure, SAPS = simplified acute physiology, SAPS II = Simplified Acute Physiology Score.

All BG analytes assayed on point-of-care testing analyzers are measured with uncertainty due to random variation. Laboratory analytes are subject to 3 main sources of variations: preanalytical, analytical, and biological. Therefore, the results of these analytes change with time and the numbers we obtain are not constant. Preanalytical, analytical, and biological variations are included in the within-subject variation, which results from random fluctuation around an individual homeostatic set point.^{18,19} The magnitude of this variability must be known by the physicians to correctly interpret the results. The repeatability is the degree to which repeated measurements of the same parameter are similar when carried out under the same conditions of measurements.²⁰ In this study, we chose to evaluate the repeatability by taking 2 blood samples immediately one after the other in stable patients to avoid a real modification in the patient's condition. Furthermore, preanalytical and analytical factors were the only 2 sources of variation that we could act on to minimize the within-subject variation and studied the repeatability of each variable reliably. In our study, we used the same preheparinized BG syringe with the same volume and preparation conditions for the 2 blood samples. Also, blood discard volumes of >3 times the dead-space of catheters were withdrawn to avoid the risk of diluting the samples with flush solution.²¹ Also, special care was taken to dislodge any air bubbles by gently tapping the sides of the samplers. Moreover, the 2 different samples were analyzed immediately after being taken. Therefore, taking all these precautions, we believe that the preanalytical errors were minimized in this study. Similarly, analytical errors were lessened as BG analyzer was calibrated several times a day. Furthermore, GEM Premier 3000 (Instrumentation Laboratory Co) has an active automated performance quality control program termed Intelligent Quality Management, which continually controls the entire process of sample analysis, enables instantaneous error detection, and performs corrective actions for error elimination.

Repeatability measurements could be reported by multiple statistical methods. In this work, we used the Bland–Altman method and the CV_w. The CV_w is the ratio of within-subject SD to the mean value of the 2 measurements. Thus, the interpretation of the CV_w is as a percentage. However, this figure implies that there is a systematic error even in data sets in which no such bias exists (like our data) because the percentage value (eg, 11.7%) of the lowest measurement in the data set is much smaller than 11.7% of the highest measurement. In this study, we found no correlation between mean versus difference for all measured and calculated variables, which confirms the lack of any systematic bias (Table S2, <http://links.lww.com/MD/A163>). Therefore, the repeatability expressed in absolute units (SDD) was not related to the size of the measurements, and it is a preferable measure for use in daily practice as compared with the CV_w and the derived LSC.

The variability that we found in Pao₂ was substantial but lesser to that previously reported.^{1–3} Indeed, our results indicate that if a patient has a reported Pao₂ of 70 mm Hg, the Pao₂ could be as low as 64 mm Hg or as high as 76 mm Hg due only to inherent variability. Also, in an individual patient, a Pao₂ change can be considered significant only if the change between the measurements exceeds 9 mm Hg (Figure 1). The spontaneous variability expressed as mean CVs found in the previous studies ranged from 4.6% to 6.1% for Pao₂ and from 3% to 4.7% for Paco₂.^{1–3} Conversely, in our study, the repeatability was very good for Paco₂ (Table 2). Differences between our and those studies may stem from several factors. First, in the

TABLE 2. Mean Values and Repeatability of Arterial and Venous BG Variables

	First Sample	Second Sample	Mean Difference	95% CI Mean Difference	SD _{diff}	SDD (95% LOA)	CV _w , %	LSC, %	95% CI LSC
Pao ₂ , mm Hg	95.65 ± 33.32	95.65 ± 32.30	0	−0.66 to 0.65	4.64	±9.09	3.43	9.51	8.3 to 10.7
Sao ₂ , %	95.83 ± 3.38	95.79 ± 3.32	0.037	−0.054 to 0.13	0.63	±1.23	0.46	1.27	1.12 to 1.44
PcvO ₂ , mm Hg	37.44 ± 7.19	37.96 ± 7.47	−0.52	−0.69 to −0.35	1.18	±2.31	2.21	6.12	5.37 to 6.89
ScvO ₂ , %	65.47 ± 11.61	65.75 ± 11.55	−0.28	−0.49 to −0.06	1.49	±2.92	1.61	4.44	3.90 to 5.00
Paco ₂ , mm Hg	40.35 ± 10.03	40.76 ± 10.02	−0.41	−0.56 to −0.26	1.05	±2.06	1.83	5.06	4.45 to 5.71
PcvCO ₂ , mm Hg	46.81 ± 10.61	46.51 ± 10.22	0.30	0.11 to 0.48	1.26	±2.47	1.91	5.28	4.63 to 5.95
pHa	7.37 ± 0.11	7.37 ± 0.11	0	0.002 to 0.005	0.01	±0.02	0.10	0.28	0.24 to 0.30
pHcv	7.34 ± 0.10	7.34 ± 0.10	0	−0.002 to 0.001	0.01	±0.02	0.10	0.28	0.24 to 0.30
Hb, g/dl	10.6 ± 2.39	10.36 ± 2.38	0	−0.04 to 0.01	0.16	±0.31	1.07	2.96	2.55 to 3.29

Data are presented as mean ± SD. BG = blood gas, CI = confidence interval, CV_w = within-subject coefficient of variation, Hb = arterial hemoglobin concentration, LOA = limits of agreement, LSC = least significant change, mean difference = mean of the difference between the first and the second variables measurement, Paco₂ = arterial carbon dioxide tension, Pao₂ = arterial oxygen tension, PcvCO₂ = central venous carbon dioxide tension, PcvO₂ = central venous oxygen tension, pHa = arterial pH, pHcv = central venous pH, Sao₂ = arterial oxygen saturation, ScvO₂ = central venous oxygen saturation, SDD = smallest detectable difference, SD_{diff} = SD of the difference between the first and the second variable measurement.

previous studies,^{1–3} the variability of arterial BGs was evaluated over a time period of about 1 hour. The occurrence of minor alterations in the patient’s condition (microatelectasis, mismatch between pulmonary ventilation and perfusion, changes in respiratory rate and oxygen consumption), even in apparently stable patients, cannot completely be excluded during this time. Thus, these changes could have contributed to the increased variability of Pao₂ and Paco₂ measurements reported in those studies. Second, our study included a greater number of patients with various types of pathologies; therefore, it was more representative of ICU patients than the previous studies,^{1–3} among which the largest sample size was only of 29 patients. We cannot explain why we found an important within-subject variability for Pao₂. However, our study was designed to evaluate the magnitude of the variability of BG parameters and was not designed to determine the causes of the variability. Moreover, we found that the variability in Pao₂ was not

reflected in the variability of Sao₂ (Table 2). The sigmoidal shape of the oxygen–hemoglobin dissociation curve can explain the very low variability in Sao₂. Indeed, at the Pao₂ values seen in our study, the dissociation curve is relatively flat, which means that Sao₂ does not change significantly, even with large variations in the Pao₂. Furthermore, even in patients with Sao₂ values no longer on the flat portion of the oxyhemoglobin curve (Sao₂ < 94%), the variability of Sao₂ remained low, (SDD ≈ 2%) whereas the variability of Pao₂ was still significant (SDD ≈ 7 mm Hg) (Table S1, <http://links.lww.com/MD/A162>). The same results were found in patients ventilated with high PEEP and high FiO₂ (Table S2, <http://links.lww.com/MD/A163>). Thus, in clinical practice, it is probably better to rely on Sao₂ values rather than Pao₂ when assessing the oxygenation status of patients. However, Sao₂ that is provided by GEM Premier 3000 (Instrumentation Laboratory Co) is a calculated

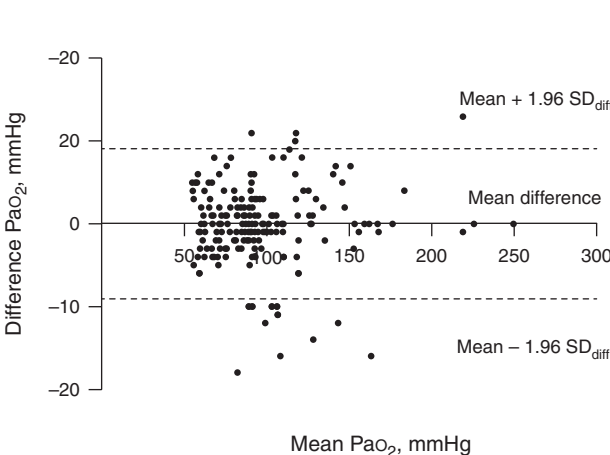


FIGURE 1. Bland–Altman plot of the difference against the mean of the 2 Pao₂ measurements. Pao₂ = arterial oxygen tension.

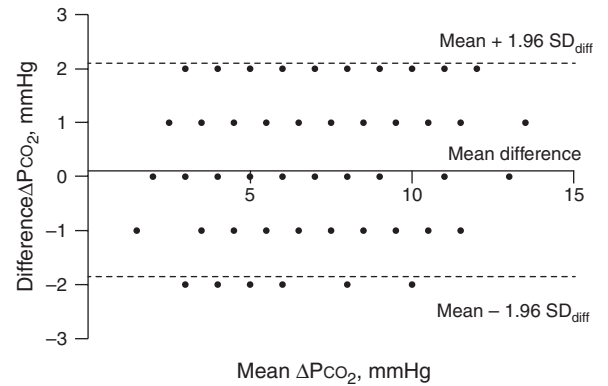


FIGURE 2. Bland–Altman plot of the difference against the mean of the 2 ΔPco₂. The dots are less than the number of patients included (192) because many of these patients had the same difference values. ΔPco₂ = central venous-to-arterial carbon dioxide tension differences.

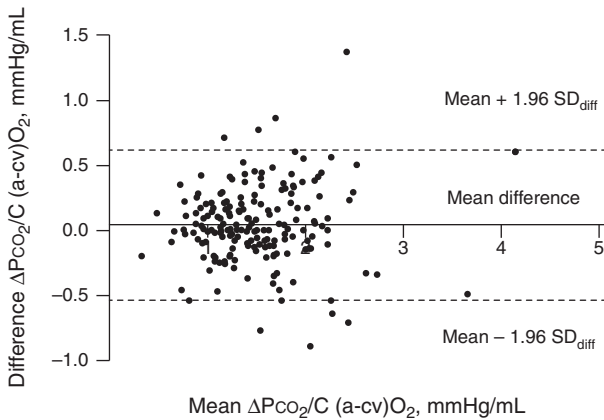


FIGURE 3. Bland–Altman plot of the difference against the mean of the 2 ΔPco_2 over the central arteriovenous oxygen content difference ($\Delta\text{Pco}_2/\text{C(a-cv)O}_2$) ratio. ΔPco_2 = central venous-to-arterial carbon dioxide tension differences, $\Delta\text{Pco}_2/\text{C(a-cv)O}_2$ = ratio of ΔPco_2 over the central arteriovenous oxygen content difference.

and not a measured parameter. Thus, our results regarding Sao_2 might not be applicable to other devices that directly measure Sao_2 (co-oximeter). These devices, based on spectrophotometric principles, utilize numerous wavelengths of light to measure the concentrations of oxy-hemoglobin saturation directly. Thus, the within-subject variability of a measured Sao_2 will depend on the intraindividual variability of parameters that influence the oxy-hemoglobin dissociation curve such as pH, temperature, and 2,3 DPG. In our study, the within-subject variability of pH was minuscule as shown in Table 2. Furthermore, there is no reason to believe that the temperature of the patient has changed over the sampling period. It is for these reasons that we do not think that the within-subject variability of measured Sao_2 would be greater than the calculated Sao_2 . However, further studies are needed to validate this hypothesis.

It is of interest to note that the repeatability of ScvO_2 was found to be good and was most likely due to the low variability in PcvO_2 (Table 2). Indeed, the 95% range for an individual true value of ScvO_2 was small ($\pm 2\%$). For a patient whose ScvO_2 was measured as 70%, the “true” value lies between 68% and 72%. Therefore, the reliance that we can place on reading a value of ScvO_2 is good. This finding is of clinical importance

since implementation of ScvO_2 as a resuscitation goal was associated with decreased mortality in septic shock patients.^{4,22}

To our knowledge, this is the first study investigating the spontaneous variability of ScvO_2 , ΔPco_2 , and $\Delta\text{Pco}_2/\text{C(a-cv)O}_2$ ratio in critically ill patients. We found a good repeatability of ΔPco_2 related to the small within-subject variability of the parameters on which it depends. It is well known that when a reported result is derived from >1 actual measurement through their addition, subtraction, multiplication, or division, the uncertainty of the final result can be calculated by summing the uncertainty components of the contributing measurements.¹⁸ Therefore, the more variables in the formula, the more uncertainty exists in the result. This may explain why the inherent variability of $\Delta\text{Pco}_2/\text{C(a-cv)O}_2$ ratio was found to be significant (Table 3), even though the within-subject variability of the parameters on which it depends were small. Monnet et al¹¹ suggested that considering the $\Delta\text{Pco}_2/\text{C(a-cv)O}_2$ ratio as a surrogate of the respiratory quotient, this ratio could be used as a marker of global anaerobic metabolism in critically ill patients. They found that a $\Delta\text{Pco}_2/\text{C(a-cv)O}_2$ ratio at baseline ≥ 1.8 mm Hg/mL predicted with high sensitivity and specificity an increase of oxygen consumption in patients whose oxygen delivery increased after fluid administration. However, according to our results, this threshold value could be as low as 1.4 mm Hg/mL or as high as 2.2 mm Hg/mL (Table 3). This ratio is not trustworthy and therefore probably not reliable for use at the bedside.

How significant is an observed change between 2 successive measurements? This must be a common problem in the clinical interpretation of BG monitoring. Changes in results are often interpreted against empirical criteria. For example, the difference may be considered significant when the test result has doubled or tripled. Changes in results are caused by within-subject variation as well as by deterioration or improvement of the patient’s condition. The magnitude of the “critical difference” between results—that is, a change that must occur before significance can be claimed—may be calculated as the SDD or LSC. This means that in an individual patient, in 95% of cases, a ΔPco_2 change value >2 mm Hg or 32.4% is a true ΔPco_2 change and is not due to natural variation.

Our study has several limitations. First, it is a single-center study. Our findings might not apply to other populations. However, our ICU admits a variety of medical and surgical patients, and our population is likely to be representative of other general ICU populations. Second, our results depend on

TABLE 3. Mean Values and Repeatability of Calculated Variables

	First Sample	Second Sample	Mean Difference	95% CI Mean Difference	SD _{diff}	SDD (95% LOA)	CV _w , %	LSC, %	95% CI LSC
ΔPco_2 , mm Hg	6.19 \pm 2.35	5.99 \pm 2.35	0.12	−0.02 to 0.26	1.01	\pm 1.98	11.7	32.4	28.5 to 36.5
CaO_2 , mL	13.88 \pm 3.13	13.88 \pm 3.12	0.00	−0.01 to 0.03	0.14	\pm 0.27	0.71	1.96	1.69 to 2.19
CcvO_2 , mL	9.47 \pm 2.87	9.51 \pm 2.87	−0.04	−0.07 to 0.00	0.22	\pm 0.43	1.64	4.53	3.96 to 5.10
$\Delta\text{Pco}_2/\text{C(a-cv)O}_2$, mm Hg/mL	1.49 \pm 0.56	1.45 \pm 0.54	0.04	0.00 to 0.08	0.29	\pm 0.57	13.9	38.5	34.0 to 43.6
$\text{PaO}_2/\text{FiO}_2$, mm Hg	241.8 \pm 101.2	241.3 \pm 99.4	0.55	−0.97 to 2.01	10.58	\pm 20.73	3.1	8.6	7.51 to 9.65

Data are presented as mean \pm SD. C(a-cv)O_2 = difference between arterial and central venous oxygen content, CaO_2 = arterial oxygen content, CcvO_2 = central venous oxygen content, CI = confidence interval, CV_w = within-subject coefficient of variation, FiO_2 = fraction-inspired oxygen, LOA = limits of agreement, LSC = least significant change, mean difference = mean of the difference between the first and the second variable measurement, PaO_2 = arterial oxygen pressure, ΔPco_2 = central venous-to-arterial carbon dioxide tension difference, $\Delta\text{Pco}_2/\text{C(a-cv)O}_2$ = ratio of ΔPco_2 over the central arteriovenous oxygen content difference, SDD = smallest detectable difference, SD_{diff} = SD of the difference between the first and the second variable measurement.

the point-of-care BG analyzer used (GEM Premier 3000; Instrumentation Laboratory Co) and might not be applicable to other devices. Nevertheless, the analytical performance of this device is considered well comparable with most established central laboratory BG analyzers.^{23,24} Interestingly, the SD_{diff} of duplicate analyses of whole blood samples obtained from the operating rooms, the ICU, or the emergency department showed no differences between the GEM Premier 3000 and reference central laboratory instruments.²⁵ The GEM Premier 3000 is also the device that is used in our central laboratory hospital for BG analysis. Furthermore, this analyzer is used by hundreds of hospitals in Western countries, making our findings highly relevant to medical practice in many institutions. According to the manufacturer, over 12,000 point-of-care machines just like ours are currently in use all over the world. Therefore, we believe that the principles established by our observations are likely to be generalizable.

CONCLUSION

The short-term repeatability of BGs was good except for Pao_2 even in stable ICU patients not undergoing therapeutic intervention. Significant spontaneous variation in the $\Delta Pco_2/C(a-cv)O_2$ ratio occurred over short-time intervals, whereas the repeatability of ΔPco_2 was good. The clinician should take into account this inherent variability as well as the clinical spectrum of a patient and make informed clinical decisions based on them.

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