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REPORTS OF ORIGINAL INVESTIGATIONS

Agreement between venous and arterial blood gas analysis of acid-base status in critical care and ward patients: a retrospective cohort study

Concordance de l'équilibre acido-basique dans les analyses des gaz du sang artériel et veineux chez des patients hospitalisés aux soins intensifs ou à l'étage : une étude de cohorte rétrospective

Claudio M. Martin, MSc, MD, FRCPC, CCPE · Fran Priestap, MSc

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Abstract

Purpose *To determine whether the use of venous blood gases can be a suitable alternative to arterial sampling to evaluate acid-base status.*

Methods *The database of the clinical laboratory in a large academic hospital was searched for records of venous blood gas analysis and an arterial sample taken within ten minutes from the same patient. Bland-Altman analyses of pH, pCO_2, and lactate were performed for samples obtained from patients separately from within and outside the intensive care unit (ICU).*

Results *In 2,296 paired arterial-venous samples from 351 ICU patients, the bias was 0.044, −6.2 mmHg, and −0.07 mEq·L^{-1} for pH, pCO_2, and lactate, respectively. The range of agreement centred on this bias (upper minus lower level of agreement) was 0.134, 16.7 mmHg, and 1.35 mEq·L^{-1} for pH, pCO_2, and lactate, respectively. Intraclass correlation coefficients (ICCs) were 0.79, 0.76, and 0.99 for pH, pCO_2, and lactate, respectively, indicating excellent agreement. Multiple samples obtained from the same patient had a median standard deviation of 0.02, 2.77 mmHg, and 0.18 mEq·L^{-1} for pH, pCO_2, and lactate, respectively. Similar agreement was observed in samples from patients outside the ICU, although the ICC was only 0.53 for pCO_2.*

Conclusions *Venous gases are suitable for initial evaluation of acid-base status in critically ill patients. Based on clinical evaluation, an arterial sample may then be considered for confirmation, and thereafter, venous blood gases could be sufficient for monitoring response to treatment.*

Résumé

Objectif *Établir si l'utilisation des gaz du sang veineux peut remplacer de façon adéquate un prélèvement de sang artériel pour l'évaluation de l'équilibre acido-basique.*

Méthodes *Utilisant la banque de données du laboratoire clinique d'un grand hôpital universitaire, une recherche des analyses des gaz du sang veineux et d'un prélèvement de sang artériel effectués chez le même patient à moins de dix minutes d'intervalle a été effectuée. Des analyses de Bland-Altman du pH, de la pCO_2 et des lactates ont été obtenues pour des échantillons prélevés sur des patients dans et hors de l'unité de soins intensifs (USI).*

Résultats *Sur 2296 paires d'échantillons artériels et veineux provenant de 351 patients en USI, les biais étaient respectivement de 0,044, -6,2 mmHg et -0,07 mEq·L^{-1} pour, respectivement, le pH, la pCO_2 et les lactates. La plage de concordance centrée sur ces biais (niveau de concordance supérieur moins niveau de concordance inférieur) était de 0,134, 16,7 mmHg et 1,35 mEq·L^{-1} pour, respectivement, le pH, la pCO_2 et les lactates. Les coefficients de corrélation intracatégorie (ICC) étaient de 0,79, 0,76 et 0,99 pour, respectivement, le pH, la pCO_2 et les lactates, indiquant une excellente corrélation. Les multiples échantillons provenant d'un même patient présentaient un écart-type médian de 0,02, 2,77 mmHg et 0,18 mEq·L^{-1}*

C. M. Martin, MSc, MD, FRCPC, CCPE (✉) · F. Priestap, MSc
Schulich School of Dentistry and Medicine, Victoria Hospital, London Health Sciences Centre, Western University, 800 Commissioners Rd E, London, ON N6A 5W9, Canada
e-mail: cmartin1@uwo.ca

C. M. Martin, MSc, MD, FRCPC, CCPE
Critical Care Western, Department of Medicine, Schulich School of Dentistry and Medicine, Western University, London, ON, Canada

pour, respectivement, le pH, la pCO_2, et les lactates. Une concordance semblable a été constatée chez les patients hors de l'USI, bien que dans ce cas l'ICC n'ait été que de 0,53 pour la pCO_2.

Conclusions *Les gaz veineux sont adéquats pour l'évaluation initiale de l'équilibre acido-basique chez des patients dans un état critique. En se basant, sur l'évaluation clinique, un échantillon artériel peut alors être envisagé pour confirmation et, ensuite, les gaz du sang veineux pourraient être suffisants pour surveiller la réponse au traitement.*

Blood gas analysis is a vital component in the evaluation of acid-base status in critically ill patients with cardiac or pulmonary compromise.[1] Although arterial blood gas analysis is the gold standard, the procedure requires skill and can be painful, and although rare, it can result in pseudoaneurysms, vascular occlusion, and other complications.[2] Capillary blood gas analysis is an alternative that has excellent agreement with arterial samples.[3] It requires minimal skill but can be more time consuming, since arterialization of capillary blood requires adequate warming of the tissue.

Venous blood sampling can be obtained from indwelling central venous catheters or by peripheral venipuncture with minimal additional risk or discomfort to the patient. Venous blood gases have also been studied as an option for acid-base assessment, but mostly in the emergency room setting for patients with chronic lung disease and diabetic ketoacidosis.[4,5] Fewer studies have been reported in critically ill patients, particularly those being evaluated on general wards. These studies have used both central and peripheral venous sampling.[6-10] Current guidelines from the American Association for Respiratory Care recommend against using venous blood gases, although other statements in this publication suggest otherwise in specific circumstances.[1] Furthermore, although the authors state that they used the Grading of Recommendations Assessment, Development and Evaluation system,[11] appropriate methodologic details are not provided.

To determine whether venous gases can be a suitable alternative to arterial sampling for evaluating acid-base status, we extracted data from our hospital laboratory information system and examined the agreement between arterial and venous samples for patients separately in the intensive care unit and on the general wards.

Methods

We performed this retrospective study at the London Health Sciences Centre, a large teaching hospital with two sites (University and Victoria Hospitals) in London, Canada. This analysis of laboratory data was undertaken as a quality assurance project; thus, review by our University of Western Ontario Research Ethics Board was not required.

We obtained all blood gas data from the hospital laboratory information system for the time periods of the study. We created one data set for pH, pCO_2, or lactate results obtained from patients in the intensive care unit (ICU) (26 beds with medical, surgical, and trauma patients) at the Victoria Hospital site from May 1 to October 31,

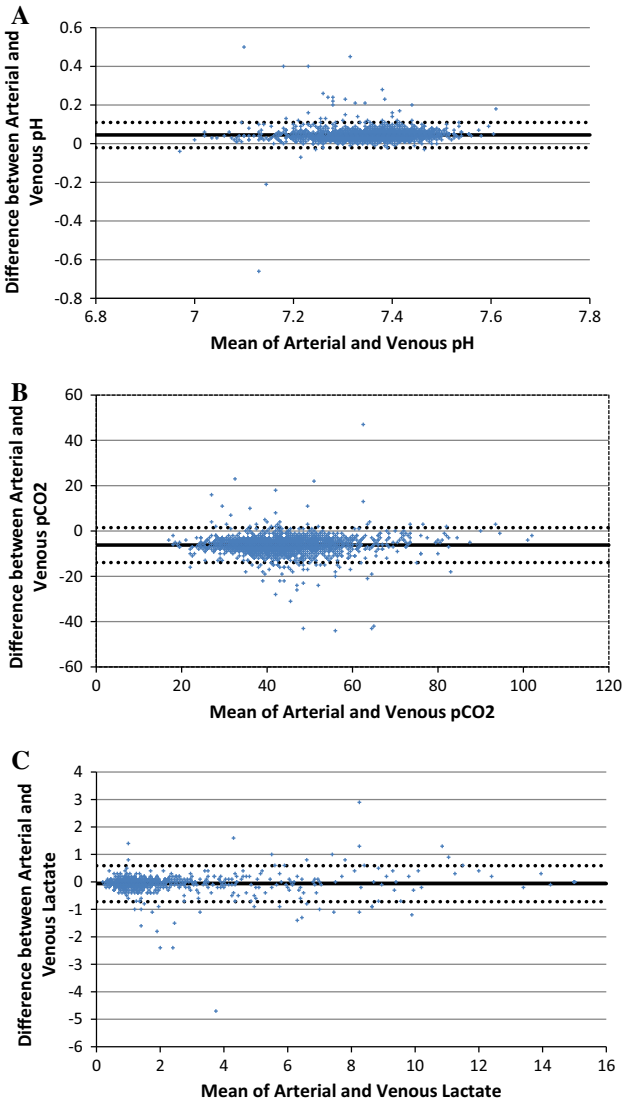

Fig. 1 Agreement between arterial and venous samples for pH (*panel A*), pCO_2 (*panel B*), and lactate (*panel C*) from patients in the intensive care unit. Each symbol is one pair of measurements. The solid line is the mean difference (bias) between pairs. The dashed lines represent the upper and lower limits of agreement (LoA). See Table 1 for sample size, standard error of the bias, and 95% confidence intervals for the LoA, which are too small to show on the figure

Table 1 Comparison of pH, pCO_2, and lactate from arterial and venous samples from patients in the ICU

Parameter	Bias (SE)	Lower limits of agreement (95% CI)	Upper Limits of agreement (95% CI)	Overall range of agreement	ICC (95% CI)
pH	0.045	−0.018	0.109	0.134	0.79
	(0.001)	(−0.022 to −0.015)	(0.106 to 0.112)		(0.78 to 0.81)
pCO_2 (mmHg)	−6.2	−14.1	1.6	16.7	0.76
	(0.16)	(−14.59 to −13.69)	(1.17 to 2.07)		(0.75 to 0.78)
Lactate ($mmol \cdot L^{-1}$)	−0.07	−0.69	0.56	1.35	0.99
	(0.015)	(−0.74 to −0.65)	(0.52 to 0.61)		(0.99 to 0.99)

Venous samples were obtained within 10 min of the arterial sample. The bias and limits of agreement (LoA) were calculated using the Bland-Altman method[12] and Zou's method to account for multiple samples from the same patient.[13] The overall range of agreement is the upper 95% confidence interval (CI) for the upper LoA minus the lower 95% CI for the lower LoA. There were 2,296 samples from 351 patients for pH and pCO_2 measurement and 945 samples from 261 patients for lactate measurement. ICC = intraclass correlation coefficient; ICU = intensive care unit; SE = standard error

2010. We created a second data set for samples obtained from outside the ICUs at both sites, excluding the pediatric critical care unit and the newborn and neonatal wards. The Critical Care Outreach Team (CCOT) at each site supports all adult inpatient areas, including intermediate care units for trauma, vascular surgery, thoracic surgery, coronary care, and transplant. The data available from the laboratory system specified the type of sample, i.e., arterial, venous, or capillary, but provided no other details regarding the indication or patient condition. The ICU has standard protocols for paired samples of arterial and venous blood gases used to monitor oxygen delivery and extraction. Indications for samples on the wards were not recorded and rely on individual physician practice, which may have included the CCOT.

The sample size was chosen based on convenience, although we wanted a minimum of 100 paired samples. In order to achieve this, we added the period from May 1 to October 31, 2009 to the second (non-ICU) data set. Any result that was reported as "less than" or "greater than" was set to the value that followed (e.g., pH <6.80 was set to 6.80). Only one sample (pH) required this censoring.

Statistical analysis

Venous samples were paired with arterial or capillary samples if the time stamps in the database were within ten minutes of each other. Descriptive statistics, including the mean difference between pairs (bias) and intraclass correlation coefficient (ICC)—most appropriate for repeated measurements on the same patient—were calculated. Bland-Altman plots[12] were created. To account for multiple pairs of measurements from the same patient, we used a SAS® macro for the method of variance estimates recovery (MOVER) to calculate 95% confidence intervals (CIs) around the lower and upper limits of agreement.[13] Since the blood gas values might change over time between measurements from the same patient, we used the varying true value (case 1) method. Bubble plots from the MOVER macro and probability plots of the residuals were examined to ensure that the assumptions underlying the analysis were not violated. We plotted the mean differences against the number of samples and the time interval to examine for possible bias. In those ICU cases (patients) where there were two or more arterial-venous pairs, measures of central tendency and distribution around the difference in result were reviewed.

All analyses were performed using SAS v9.4 (SAS Institute, Inc., Cary, NC, USA), including the %INTRACC macro for the ICC (http://support.sas.com/kb/25/031.html#ref).

Results

We identified 2,441 paired samples from ICU patients. The mean (standard deviation [SD]) time between samples was 3.8 (1.6) min. Of these pairs, 2,296 were arterial–venous combinations from 351 patients; 945 samples from 261 patients had lactate results. The number of sample pairs ranged from 1–63 per patient. Bland–Altman plots of the pH, pCO_2, and lactate results were created from the arterial-venous pairs (Fig. 1). Results for bias, agreement limits, and correlation are summarized in Table 1. We found only 15 venous-capillary samples, which we do not report due to the small sample size.

In ward patients, there were only four patients with repeated sampling. We therefore limited our analysis to the first sample from these patients, resulting in 124 pH results, 115 pCO_2 results, and 105 lactate results from paired arterial and venous samples. The mean (SD) time between samples was 5.7 (2.4) min. Results (Fig. 2; Table 2) are

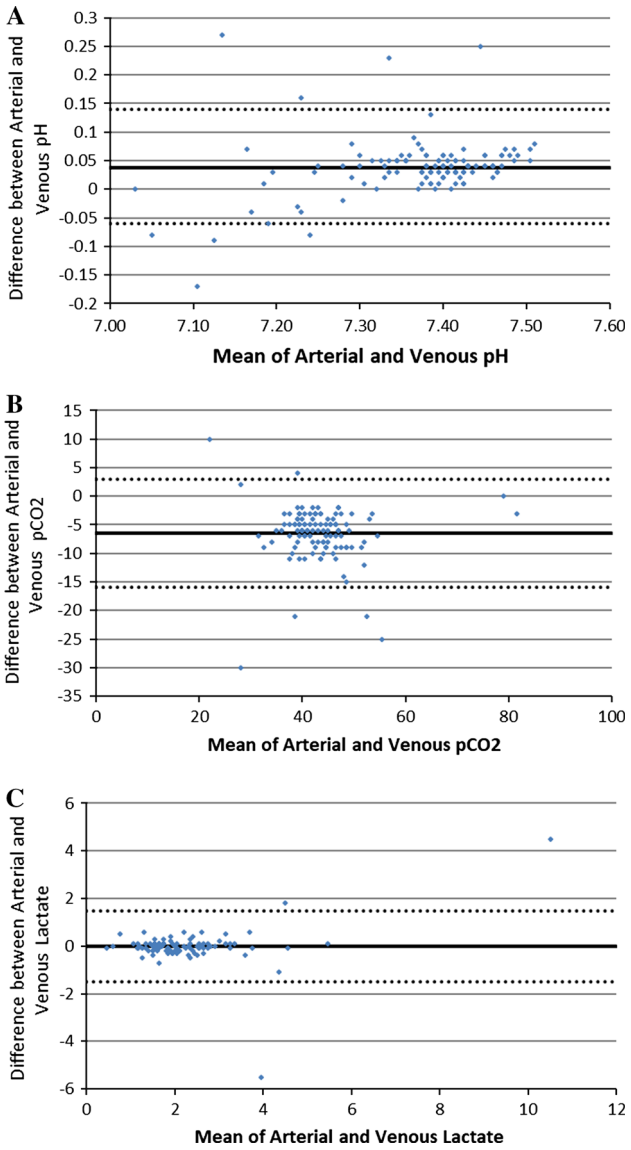

Fig. 2 Agreement between arterial and venous samples for pH (*panel A*), pCO_2 (*panel B*), and lactate (*panel C*) from patients outside the intensive care unit. Each symbol is one pair of measurements. See Table 2 for sample sizes. The solid line is the mean difference (bias) between pairs. The dashed lines represent the upper and lower limits of agreement (LoA)

similar to the ICU setting. We do not report on the 25 venous-capillary gas combinations from the ward patients due to the small sample size.

To explore reproducibility within individual patients, we reviewed the SDs for the arterial-venous differences for ICU patients who had more than one arterial-venous pair. There were 274 patients with a median (range) of 8 (2-63) arterial-venous pairs for pH and pCO_2. There were 168 patients with a median (range) of 4 (2-30) paired results for lactate. These results are provided in Table 3.

Table 2 Arterial and venous pH, pCO_2, and lactate obtained from patients outside the ICU

Parameter	Bias (SE)	Limits of agreement	Overall range of agreement	ICC (95% CI)
pH	0.038 (0.020)	−0.062 to 0.138	0.200	0.79 (0.72 to 0.85)
pCO_2 (mmHg)	−6.48 (0.21)	−15.9 to 2.97	18.9	0.53 (0.40 to 0.65)
Lactate ($mmol \cdot L^{-1}$)	−0.016 (0.085)	−1.51 to 1.48	2.99	0.81 (0.73 to 0.86)

Venous samples were obtained within 10 min of the arterial sample. The bias and limits of agreement (LoA) were calculated using the Bland-Altman method.[12] All sample pairs were from individual patients (124 patients with pH and pCO_2, 105 patients with lactate measurements). Overall range of agreement is the upper LoA minus the lower LoA. ICC is the intraclass correlation coefficient and is reported with 95% confidence interval (CI). ICU = intensive care unit; SE = standard error

We did not observe any relation between the time interval or number of samples and the differences in measured values between arterial and venous samples (data not shown). The probability plot was symmetrical but not normal due to outliers. We repeated the analysis excluding the outliers (pH and pCO_2, $n = 33$ outliers; lactate, $n = 64$ outliers), and the limits of agreement were narrower and still within the original CI (data not shown).

Discussion

Blood gas analysis is an important test for the evaluation of acid-base status in unstable or critically ill patients. When compliance with a clinical practice guideline is evaluated, there is evidence of inappropriate use in patients, including both unnecessary testing in some patients but lack of testing in others.[14] This non-concordance may be due in part to difficulties in obtaining arterial blood samples, which is the gold standard for this test. Using a large laboratory database, we have shown good agreement between arterial and venous samples for pH, pCO_2, and lactate for patients on general wards and in the intensive care unit. More specifically, repeated samples from the same patient have excellent agreement, indicating that venous blood gases can be used to evaluate and monitor acid-base status in a wide variety of patients.

Venous sampling for blood gas analysis may be preferred when compared with arterial samples. While there is no direct evidence, the probable benefits of venous samples are less patient discomfort and fewer

Table 3 Reproducibility of arterial-venous differences for multiple samples obtained from the same patient in the ICU

Parameter	Number of patients	Mean standard deviation	Median SD [IQR]
pH	274	0.020	0.01 [0.01 - 0.02]
pCO_2 (mmHg)	274	2.77	2.12 [1.41 - 3.24]
Lactate ($mEq{\cdot}L^{-1}$)	168	0.18	0.10 [0.06 - 0.16]

The standard deviation (SD) for the arterial-venous differences for patients who had more than one measurement pair provides further information about the agreement between the arterial and venous samples from the same patient. ICU = intensive care unit; IQR = interquartile range

complications such as arterial injury, thrombosis, embolization, hematomas, aneurysm formation, and reflex sympathetic dystrophy. Less risk of needlestick injury to healthcare workers is also expected, particularly if an existing central venous catheter is used.

In contrast, the potential risk associated with venous sampling is inaccurate patient assessment. Nevertheless, our results in both ICU and non-ICU patients indicate that pH assessment from venous samples is sufficiently accurate and reproducible for clinical decision-making. The level of agreement using Bland-Altman analysis has to be interpreted within the clinical context.[15] There is a very small and expected positive bias of 0.038-0.045 pH units and a range of agreement of 0.2-0.134 for samples from non-ICU and ICU patients, respectively. Repeated measurements from the same patient show good reproducibility, with a mean SD of 0.02. We consider the agreement between venous and arterial pCO_2 as moderate, with some potential for differences that are clinically important. The ICCs indicate excellent agreement, except for pCO_2 obtained outside the ICU which suggests moderate agreement between the arterial and venous samples. We propose that a venous gas may be sufficient for the initial acid-base assessment of a patient. Based on the results and clinical circumstances, an arterial gas may then be considered. Venous samples would then be appropriate for monitoring the response to treatment.

Our results are consistent with previously published studies that were performed on smaller sample sizes and selected types of patients.[6-10] Treger also performed an anecdotal review, concluding that some, but not all, studies showed good agreement. These authors similarly noted limitations of these studies, such as specific patient group samples, analysis of only one or some parameters rather than all commonly used parameters, and examination of only one arterial blood gas and venous blood gas sample per patient.[9] Kelly *et al.* reported a systematic review limited to adult patients in the emergency department setting. They found a weighted mean difference and level of agreement for pH and pCO_2 that were similar to our study.[4]

Strengths of our study include the large number of unselected samples from both ICU and non-ICU locations within an academic hospital, a wide range of pH and pCO_2 values, and the ability to evaluate repeated samples within the same patient. Limitations are the retrospective analysis and lack of details regarding the patient demographics, diagnoses, anatomic site for the venous samples, and use of different blood gas analyzers. Our choice of ten minutes between the two samples was arbitrary, and patient conditions may have changed during that time. Nevertheless, these limitations also suggest that our results can be applied widely and that attention to such details would likely produce even better agreement between venous and arterial samples for analysis of acid-base status.

In conclusion, we suggest that venous pH has sufficient agreement to be interchangeable with arterial values, although the clinical circumstances need to be considered. In some cases, an arterial sample may be warranted for confirmation, and venous samples can then be used to monitor the response to treatment. Agreement between venous and arterial pCO_2 is not as strong so more caution is required when interpreting these results.

Conflicts of interest None declared.

Editorial responsibility This submission was handled by Dr. Hilary P. Grocott, Editor-in-Chief, *Canadian Journal of Anesthesia.*

Author contributions *Claudio M. Martin* conceived the study, was involved in all aspects of the design, analysis, and interpretation of results, and wrote the initial draft. *Fran Priestap* acquired and managed the data, developed and conducted the data analysis, performed the literature search, and reviewed and revised the manuscript.

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