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Converting venous acid–base and oxygen status to arterial in patients with lung disease

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ABSTRACT: The aim of the present study was to evaluate a method for calculating arterial values of pH, carbon dioxide tension (P_{CO_2}) and oxygen tension (P_{O_2}) from peripheral venous values.

In total, 40 patients were studied. Arterial and peripheral venous blood were sampled at a department of respiratory diseases. Arterial values were calculated from venous, and measured and calculated values of arterial pH, P_{CO_2} and P_{O_2} were compared.

Measured and calculated values of pH and P_{CO_2} correlated well, with the difference between them having a very small bias and standard deviation (pH -0.001±0.013, P_{CO_2} -0.09±0.28 kPa) within those considered acceptable for laboratory equipment and clinical practice. All but four patients had peripheral oxygen saturation (S_{p,O_2}) ⩽96%, and for these measured and calculated P_{O_2} correlated well, with a difference such that the bias and standard deviation suggested that calculated P_{O_2} may be clinically useful (P_{O_2} 0.11±0.53 kPa).

The present study evaluates a method for calculating arterial pH, carbon dioxide tension and oxygen tension from venous blood. It has been shown that arterial pH and carbon dioxide tension can be calculated precisely, and that oxygen tension can be calculated with reasonable precision in the vast majority of patients. This method might be useful in reducing the need for painful arterial punctures.

KEYWORDS: Acid–base chemistry, blood gas analysis, oxygen saturation

Arterial blood gas analysis is an important tool in assessing patient status. For patients residing in intensive care units (ICUs) with indwelling arterial catheters, the sampling of arterial blood is routine. In other departments blood is sampled *via* an arterial puncture with an increased risk of pain and haematoma [1–3].

Recently, studies have shown that values of acid–base status measured in peripheral venous blood correlate well with those measured in arterial blood, at least for values of pH, bicarbonate and carbon dioxide tension (P_{CO_2}) [4–6]. Large numbers of peripheral venous samples are taken easily and safely in medical departments, therefore implying a role for peripheral venous blood in the monitoring of acid–base status. In addition, a method has been recently proposed that enables calculation of values of arterial acid–base and oxygenation status (*i.e.* pH, P_{CO_2} and oxygen tension (P_{O_2})) from measurements performed in the peripheral venous blood [7]. This method has been shown to have good accuracy and precision when calculating arterial pH (bias±2SD: 0.002±0.027) or arterial P_{CO_2} (bias±2SD: -0.04±0.52 kPa) [8]. For calculation of P_{O_2}, precision was dependent on the oxygenation level, such that for peripheral oxygen saturation (S_{p,O_2}) values >96% the method was not considered useful for calculating P_{O_2}, and for S_{p,O_2} ⩽96% the accuracy and precision of calculated P_{O_2} was 0.21±1.85 kPa (bias±2SD) [8].

The previous evaluation of this method was in patients admitted to the wards of either ICUs or a department of pulmonary medicine, and these patients were studied under experimental conditions [8]. These experimental conditions differ from routine clinical practice in medical departments in several important respects. The majority of ICU patients have arterial catheters and are relatively immobile, making blood sampling simpler and less prone to error. Medical patients present as both admitted and outpatients, with admitted patients tending to have a poorer condition than outpatients, potentially giving larger arterial–venous differences in blood gas

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TABLE 1 Age and arterial blood measurements

Age yrs	68 (35–93)
pH	7.418 (7.237–7.508)
P_{CO_2} kPa	6.26 (3.92–11.2)
P_{O_2} kPa	8.97 (6.11–15.70)

Data are presented as median (range). P_{CO_2}: carbon dioxide tension; P_{O_2}: oxygen tension.

values and hence a greater signal-to-noise ratio for application of the conversion method. In experimental conditions, peripheral venous blood sampling was performed using a needle attached directly to a syringe, rather than the butterfly sampling needle and tube often used to sample venous blood in medical departments. In addition, the vast majority of patients included in the previous study, *i.e.* ICU patients, required supplementary oxygen as part of their clinical management [8], meaning that for the majority of patients S_{p,O_2} was >96%.

The purpose of the present study was to evaluate the method for conversion of peripheral venous values of acid–base and oxygenation status to arterial values in patients presenting at the department of pulmonary medicine, using sampling technology and blood samples routinely collected as part of clinical care.

MATERIALS AND METHODS

Patients

Arterial and peripheral venous blood was sampled from 40 patients (22 admitted and 18 outpatients) at the Dept of Respiratory Diseases at Aalborg Hospital (Aalborg, Denmark) of median age 68 yrs (range 35–93 yrs) and of whom 22 were females. Patients were all previously diagnosed with chronic lung disease resulting in hypercapnia and/or hypoxia, and were either acutely admitted or visiting the Dept of Respiratory Diseases for their biannual clinical assessment. The arterial acid–base and oxygenation status of the patients is summarised in table 1.

Data acquisition

All patients had arterial blood sampled as a routine part of clinical care. These samples were drawn *via* an arterial puncture into a syringe suitable for blood gas analysis (PICO70; Radiometer AS, Brønshoj, Denmark) and processed immediately to obtain values of arterial acid–base, oxygen, metabolism and electrolyte status (ABL 800; Radiometer AS).

All patients had venous blood sampled as a routine part of clinical care. A butterfly needle (Multifly; Sarsted AG & Co., Nübrecht, Germany), was inserted into a vein at the elbow. This butterfly included a 20-cm long and 0.8-mm diameter tube connected to a sealed sample adaptor. Blood was sampled into a standard venous blood collection tube (S-Monovette; Sarsted AG & Co.) using the vacuum principle, and into a

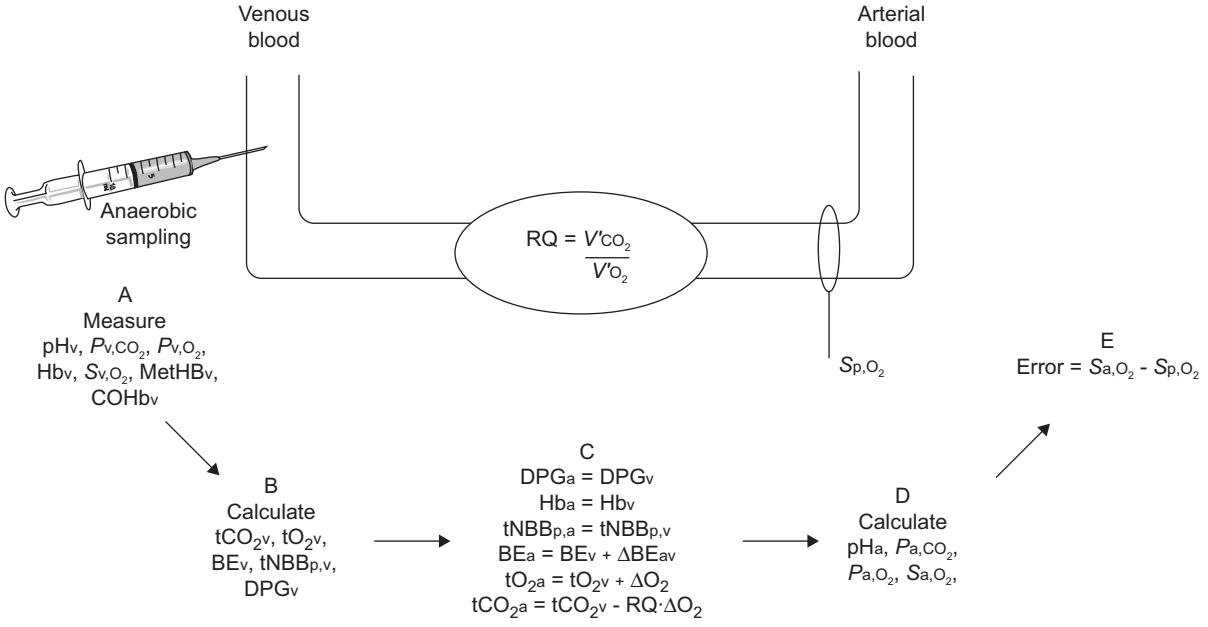

FIGURE 1. Calculation of arterial blood acid–base status from venous blood and arterial oxygen saturation measured using a pulse oximeter (S_{p,O_2}). A–E represent the mathematical steps included in the method. RQ: respiratory quotient; V'_{CO_2}: carbon dioxide production; V'_{O_2}: oxygen consumption; pHv: venous pH; P_{v,CO_2}: venous carbon dioxide tension; P_{v,O_2}: venous oxygen tension; Hbv: venous haemoglobin concentation; S_{v,O_2}: venous oxygen saturation; MetHbv: venous methaemoglobin concentration; COHbv: venous carboxyhaemoglobin concentration; tCO_2v: total venous carbon dioxide concentration; tO_2v: total venous oxygen concentration; BEv: venous base excess; $tNBB_{p,v}$: total venous plasma nonbicarbonate buffer concentration; DPGv: venous 2,3-diphosphoglycerate concentration; DPGa: arterial 2,3-diphosphoglycerate concentration; Hba: arterial haemoglobin concentration; $tNBB_{p,a}$: total arterial plasma nonbicarbonate buffer concentration; BEa: arterial base excess; ΔBEav: change in base excess from arterial to venous blood; tO_2a: total arterial oxygen concentration; ΔO_2: concentration of oxygen added; tCO_2a: total arterial carbon dioxide concentration; RQ·ΔO_2: concentration of carbon dioxide removed (ΔCO_2); pHa: arterial pH; P_{a,CO_2}: arterial carbon dioxide tension; P_{a,O_2}: arterial oxygen tension; S_{a,O_2}: arterial oxygen saturation. Reproduced from [7] with permission from the publisher.

syringe suitable for blood gas analysis (PICO50; Radiometer AS), fitted with an adaptor (Membran adaptor; Sarsted AG & Co.) to enable sampling from the butterfly's sample adaptor. Blood was analysed immediately for values of acid–base, oxygenation, metabolism and electrolyte status. Venous and arterial blood samples were taken within a 10-min period as part of normal clinical practice. In addition, the measurement of S_{p,O_2} was obtained from a pulse oximeter (Nonin Onyx 9500; Nonin Medical, Minneapolis, MN, USA) placed on an index finger. The data from two patients were excluded, due to sample error and the pulse oximeter running out of battery during blood sampling.

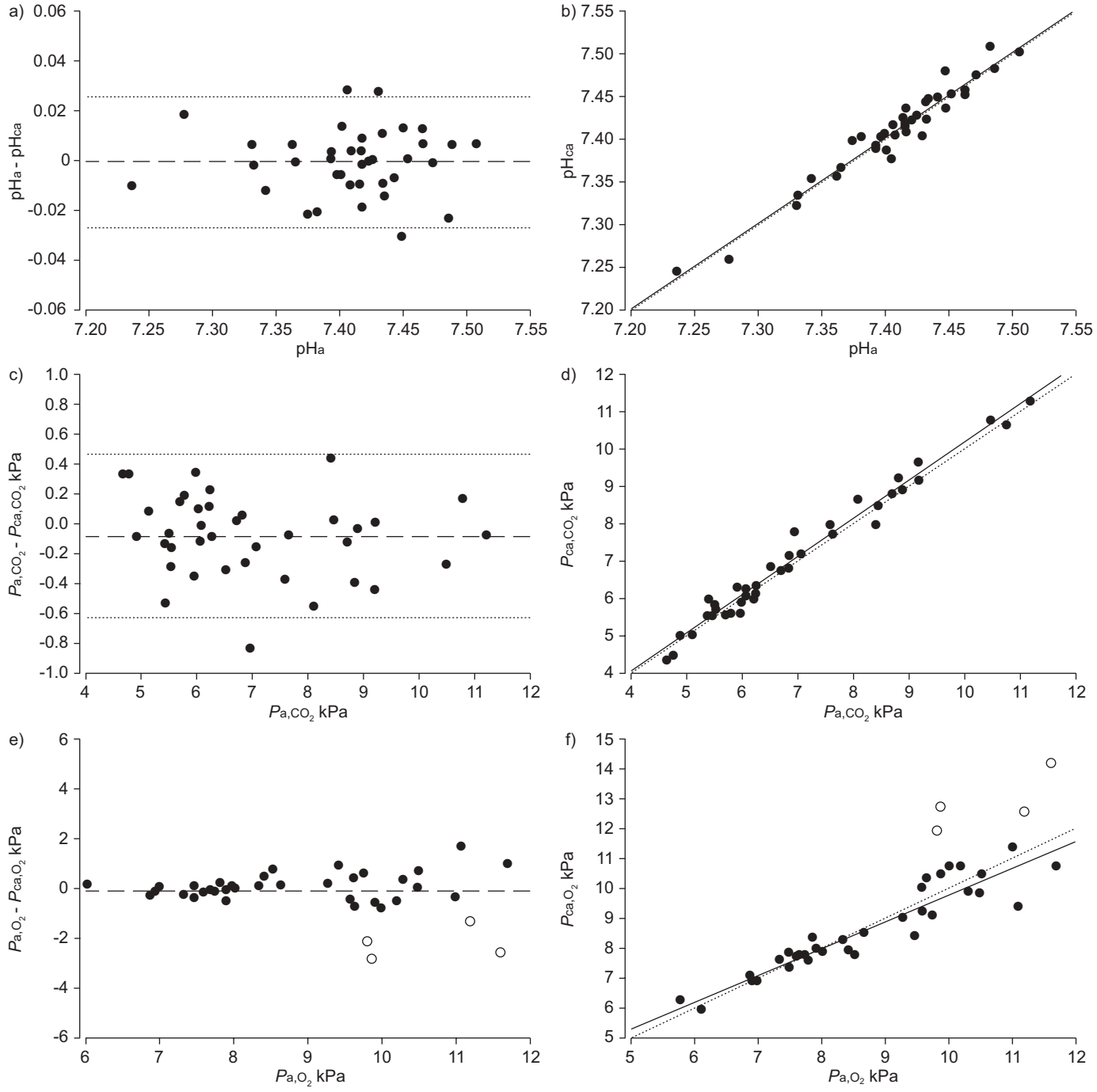

FIGURE 2. a, c and e) Bland–Altman and b, d and f) scatter plots comparing measured arterial (a) and calculated arterial (ca)values of a and b) pH (pH_a and pH_{ca}, respectively) c and d) carbon dioxide tension (P_{a,CO_2} and P_{ca,CO_2}, respectively) and e and f) oxygen tension (P_{a,O_2} and P_{ca,O_2}, respectively). a, c and e) Bias (mean difference; – – – –) and 95% limits of agreement (±2SD; ·····) are shown. b, d and f) Linear regression lines between measured and calculated values (——) and associated lines of identity (·····) are shown. e and f) Data with peripheral oxygen saturation ⩾97% (○) were not included in calculation of the bias or regression line for oxygen tension. Correlation coefficients (r^2) and regression equations were as follows. b) r^2=0.95, $pH_{ca}=(1.00\times pH_a)+0.02$; d) r^2=0.98, $P_{ca,CO_2}=(1.03\times P_{a,CO_2})-0.09$; f) r^2=0.86, $P_{ca,O_2}=(0.89\times P_{a,O_2})+0.84$.

Blood sampling was performed in the present study as for routine clinical practice and, following contact with the local ethics committee, the investigators were informed that application for ethical approval was not required.

Venous to arterial conversion method

The following is a brief summarising description of the venous to arterial conversion method. Figure 1 illustrates the method for calculating arterial acid–base and oxygenation status from measurements in the venous blood and pulse oximetry, described in detail previously [7]. The method calculates arterial values using mathematical models [9] to simulate the transport of venous blood back through the tissues until simulated arterial oxygenation matches that measured by pulse oximetry. In this simulation, oxygen is added to and carbon dioxide removed from venous blood using a constant value of the respiratory quotient (RQ), selected in the present study to be 0.82 [7], and no strong acid is removed from the blood on its simulated passage from the veins to the arteries, *i.e.* change in base excess from arterial to venous blood (ΔBE_{av}) is 0 mmol·L^{-1}.

Calculated arterial values of pH, P_{CO_2} and P_{O_2} were compared with the simultaneously measured arterial values using Bland–Altman plots and scatter plots of measured *versus* calculated. Values of bias and standard deviation between measured and calculated arterial values are reported, along with values of correlation coefficients (r^2) and parameter values for regression lines.

RESULTS

Figure 2 compares measured arterial and calculated arterial values using the venous to arterial conversion method. As illustrated in the Bland–Altman plots of figure 2 and in table 2, calculated values of arterial pH and P_{CO_2} had very small bias and standard deviation, with these errors being within those considered acceptable for the performance of laboratory equipment (table 2) and well within the limits of error acceptable in clinical practice [11, 12]. Measured and calculated values of pH and P_{CO_2} correlated extremely well (r^2 for pH=0.95, r^2 for P_{CO_2}=0.98), with regression lines comparing well to the lines of identity. As illustrated in figure 2, the error in calculated P_{O_2} values was greater at higher levels of P_{O_2}. Table 2 reports values of standard deviation for P_{O_2} values corresponding to $S_{p,O_2} \leqslant 96\%$ (34 patients) and $S_{p,O_2} \leqslant 98\%$ (38 patients). These errors are outside those considered acceptable for the performance of laboratory equipment but may be useful in clinical practice. When data points with $S_{p,O_2} \geqslant 97\%$ were excluded (fig. 2), values of measured and calculated P_{O_2} correlated well (r^2=0.86).

Figure 3 illustrates the sensitivity of calculations of arterial pH, P_{CO_2} and P_{O_2} to error in S_{p,O_2}. Each of the plots represents simulation of one of these variables when a standard venous blood sample (pH 7.370, P_{CO_2} 6.1 kPa, P_{O_2} 5.5 kPa, oxygen saturation (S_{O_2}) 75%, haemoglobin concentration 9.3 mmol·L^{-1}, methaemoglobin concentration 0 mmol·L^{-1}, carboxyhaemoglobin concentration 0 mmol·L^{-1}) is used to calculate arterial values using an S_{p,O_2} value ranging from 80 to 96%. Errors in S_{p,O_2} of $\pm$4% gave rise to a small variation in calculated arterial pH with an SD of $\pm$0.0025 (fig. 3a), which was fairly constant over the range of S_{p,O_2} values and had a maximum of 0.005. A similar picture was seen in the error in calculation of arterial P_{CO_2} (fig. 3b). Errors in S_{p,O_2} of $\pm$4% gave rise to a small variation in calculated arterial P_{CO_2} with an SD of 0.06 kPa, which was again fairly constant over the range of S_{p,O_2} values and had a maximum SD of 0.12 kPa. The errors in calculation of arterial P_{O_2} are illustrated in figure 3c and d, figure 3d being a magnified version of figure 3c (see Discussion section).

DISCUSSION

Arterial blood gas analysis is an important tool in assessing patient status, but outside the ICU blood sampling is typically performed from an arterial puncture and is associated with pain and increased risk of haematoma.

The present study provides further evaluation of a method for calculating arterial acid–base and oxygenation status from measurements taken in peripheral venous blood [7]. Unlike a previous study [8], the present study has evaluated use of the method using routinely available blood samples in a patient group where arterial catheters are uncommon, *i.e.* patients presenting at a department of pulmonary medicine.

The current study has illustrated the potential for application of the method as part of the routine management of patients presenting at the department of pulmonary medicine.

TABLE 2 Differences between measured and calculated values for arterial blood, compared with laboratory performance guidelines

	Arterial - calculated arterial values	Laboratory acceptable performance criteria[#]
Subjects n	38	
pH	-0.001±0.026	±0.04
P_{CO_2} kPa	-0.09±0.55	±0.67[+]
P_{O_2} kPa		
$S_{p,O_2} \leqslant 96\%$	0.11±1.05[¶]	±0.6[§]
$S_{p,O_2} \leqslant 98\%$	-0.13±1.79	±0.6[§]

Data are presented as bias±2SD, unless otherwise stated. P_{CO_2}: carbon dioxide tension; P_{O_2}: oxygen tension; S_{p,O_2}: peripheral oxygen saturation. [#]: acceptable range, assuming that these guidelines are comparable to a 95% confidence interval given by 2SD; [¶]: n=34; [+]: original value given as ±5 mmHg; [§]: original value given as ±3SD of measurement equipment error, where 1SD is assumed to be 0.2 kPa according to Radiometer AS (Brønshoj, Denmark) [10].

Calculation of arterial values could be performed with a similar precision to that for patients studied previously, despite the potential for increased error due to the logistics of blood sampling in routine clinical practice, and the use of butterfly-type needles and sample tubing. The accuracy and precision of calculated values of arterial pH and P_{CO_2} were almost identical to those reported previously [8], and the precision was within laboratory acceptable performance criteria [12]. For S_{p,O_2} values $\leqslant$96%, the method can calculate P_{O_2} with an average SD of 0.53 kPa, which may be useful in clinical practice. The current SD is lower than that seen previously [8], where SD was 0.93 kPa. This is due to the lower values of arterial oxygenation seen in the patients presenting in the current study, with about 50% of patients having S_{p,O_2} $\leqslant$92%. For S_{p,O_2} values >96% it has previously been argued that the calculation of P_{O_2} values becomes imprecise due to the flat shape of the oxygen dissociation curve at high levels of oxygenation. Only four of the current patients presented with S_{p,O_2} $\geqslant$97%, as illustrated in figure 2. The small number of patients with high levels of oxygen indicates that the method might be applicable for calculation of arterial pH, P_{CO_2} and P_{O_2} in the vast majority of patients visiting pulmonary medical departments.

To understand whether the results presented in the current study would be reflected in a broader population, it is necessary to consider the sensitivity of calculations to measurement error and to the assumptions contained in the method. The method does not include calculation for the effects of varying blood temperature. All blood samples are measured at 37°C and all calculations performed at this temperature. Any necessary corrections for temperature can be performed using existing algorithms present in commercial blood gas analysers.

It has previously been shown that calculations performed using the method are insensitive to errors in measurement of venous blood gases, being linear over a range of input conditions and of an order of magnitude similar to the direct measurement of arterial blood [7]. This analysis of variation in venous measurements implicitly includes any variation in parameters describing the shift of the oxygen dissociation curve, *e.g.* partial pressure of oxygen in the blood at S_{O_2} of 50%, or 2,3-diphosphoglycerate concentration. Similar analysis has also been performed for variation in the values of RQ and ΔBE_{av} [7]. Variation in ΔBE_{av} of 0.2 mmol·L^{-1} gives rise to errors in calculated pH, P_{CO_2} and P_{O_2} of 0.006, 0.08 kPa and 0.07 kPa, respectively. These errors are small, but it is clear

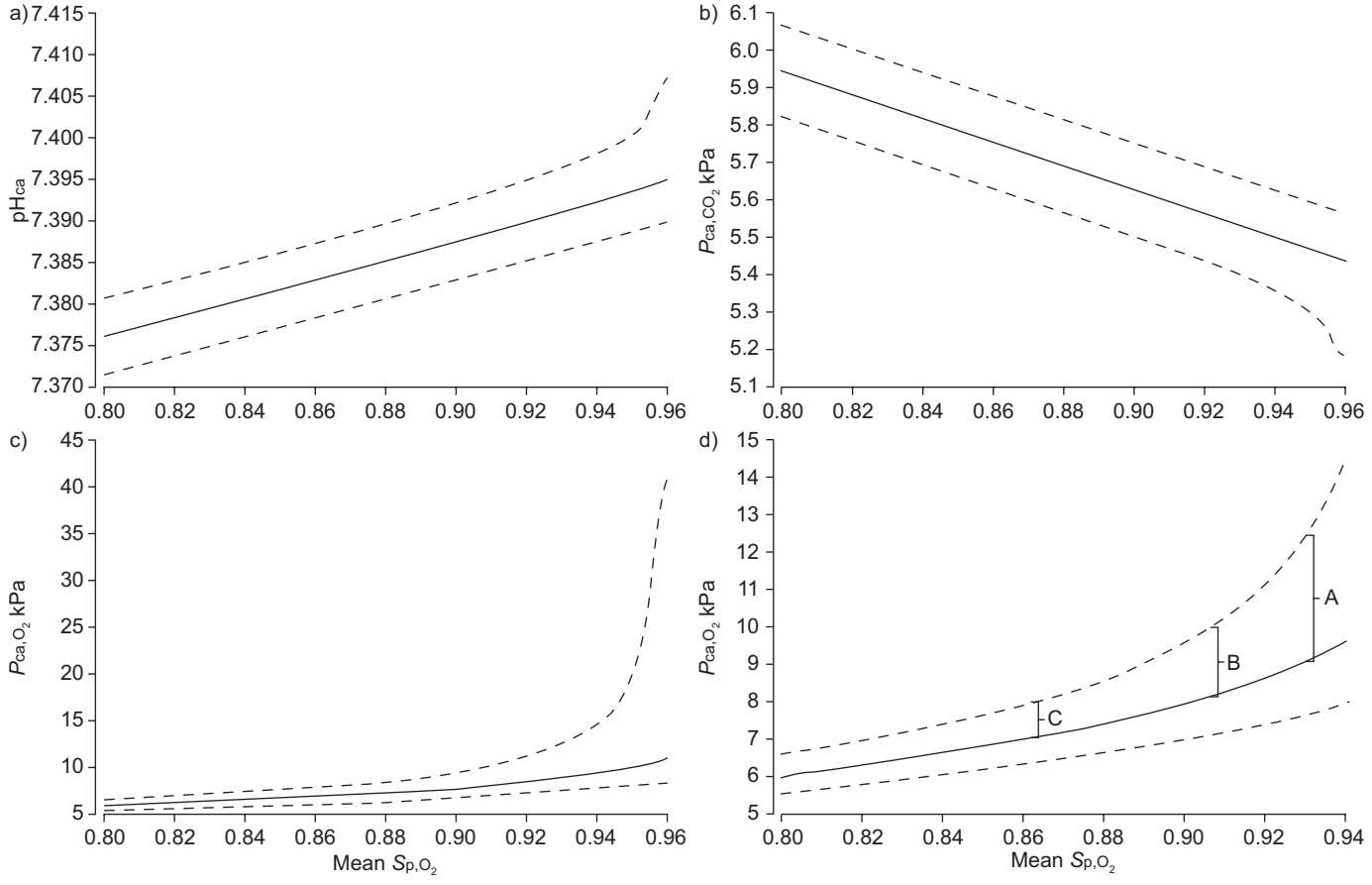

FIGURE 3. Simulations performed using the current study method, to illustrate the sensitivity of calculated values of arterial a) pH (pH_{ca}), b) carbon dioxide tension (P_{ca,CO_2}) and c and d) oxygen tension (P_{ca,O_2}) to variation in peripheral oxygen saturation (S_{p,O_2}), over a range of values of S_{p,O_2} (80–96%). d) Magnification of c). Plots are drawn for calculation of pH_{ca}, P_{ca,CO_2} and P_{ca,O_2} for mean S_{p,O_2} (——) and mean S_{p,O_2} ±4% (– – –), which is consistent with two times the reported SD for measurement of S_{p,O_2} [13, 14]. A, B and C are points discussed in the main text.

that errors in ΔBE_{av} amouting to several millimoles would be significant. The results presented in the current study and previously [8] are inconsistent with large changes in base excess across the peripheral sampling site even during sepsis. It is possible, however, that some caution is warranted in situations of acute changes in peripheral perfusion or acid–base status, such as hypovolaemic shock. Previous analysis of the sensitivity to variation in RQ has shown that the literature has reported a value of RQ variation equal to 0.08 [15], which gives rise to small errors in calculated values of pH, P_{CO_2} and P_{O_2} equal to 0.005, 0.10 kPa and 0.06 kPa.

The largest source of measurement error is due to the pulse oximetry measurement of S_{p,O_2} (fig. 3). Errors in S_{p,O_2} of $\pm 4\%$ gave rise to a small variation in calculated arterial pH that was fairly constant over the range of S_{p,O_2}. A similar picture was seen in the error in calculation of arterial P_{CO_2}. The errors in calculation of arterial P_{O_2} are a little more complex to interpret than for pH and P_{CO_2}, but some important conclusions can be drawn, as follows. From a clinical perspective, a pulse oximeter that reads too low, as represented by the bottom dashed line on figure 3c, results in an underestimate of arterial P_{O_2} and potentially more aggressive treatment of the patient with supplementary oxygen, fluids or other intervention. These interventions carry their own risk, but the risk of hypoxaemia associated with a pulse oximeter that reads too high is not present. For a pulse oximeter that overestimates oxygen saturation, the maximal error exists when the true value is 96% and the pulse oximeter reads 100%. As shown on figure 3c, the error at this level is large but clinically unimportant, as both the true and overestimated P_{O_2} levels are normal or above. In neither case would the patient require oxygen therapy.

The effects of error in S_{p,O_2} on the important clinical assessment, *i.e.* whether the patient has a low arterial P_{O_2}, can be seen in figure 3d. If three situations where a pulse oximeter overestimated S_{p,O_2} are considered, labelled A, B, and C on figure 3d, conclusions can be drawn as follows. From the difference in calculated and ''true'' arterial P_{O_2} indicated by label A on figure 3d, it can be seen that if the calculated P_{O_2} is $\geqslant$12.5 kPa, then the true value is $>$9 kPa. From the point labelled B, it can be seen that if the calculated P_{O_2} is $\geqslant$10 kPa, then the true value is $>$8 kPa. From the point labelled C, it can be seen that if the calculated P_{O_2} is $\geqslant$8 kPa, then the true value is $>$7 kPa. This analysis shows that errors in S_{p,O_2} are unimportant to the calculation of arterial pH and P_{CO_2}. It also shows the potential of calculated values of P_{O_2} to identify patients in need of supplementary oxygen, or where an arterial sample might be most beneficial. The improving precision of calculated values of P_{O_2} at lower oxygenation shows that the error in S_{p,O_2} is least important in the most critical clinical situations. This is seen in both this sensitivity analysis, and from the results of the current study (fig. 2), where the errors in calculated P_{O_2} illustrated in the Bland–Altman plot were reduced with lower oxygen levels.

The venous–arterial calculation method assumes that the peripheral venous sampling site is from a limb with a clearly recognisable pulse and a normal capillary response, such that the anaerobic metabolism at the tissue site is negligible. The present study used routinely available blood samples and, thus, no attempt was made to ensure that this was the case, above that of normal clinical practice. It is, therefore, interesting that the results are in line with previous, experimentally controlled conditions.

The present study has evaluated a method for calculating arterial values of pH, carbon dioxide tension and oxygen tension from measurements in peripheral venous blood and a pulse oximeter, for patients presenting at a department of pulmonary medicine. It has been shown that values of arterial pH and carbon dioxide tension can be calculated precisely from peripheral venous blood and that values of arterial oxygen tension can be calculated with precision that may be clinically useful, at least when peripheral oxygen saturation $\leqslant$96%. The current study has shown the potential for use of the method in departments of pulmonary medicine, where it might replace routinely taken arterial samples, eliminating the need for painful arterial punctures.

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