Spot Check Analysis of Gas Exchange: Invasive versus Noninvasive Methods

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Key Words

Blood gas analysis · Respiratory failure · Transcutaneous blood gas measurement

Abstract

Background: Correct measurement of PO₂ and PCO₂ is essential to establish appropriate therapy such as long-term oxygen therapy (LTOT) in patients suffering from respiratory failure. **Objectives:** We aimed to compare common invasive and noninvasive methods for assessing blood gas components for spot check analysis. **Methods:** Arterial (P_aO₂, P_aCO₂) and capillary blood gas (P_{CBG}O₂, P_{CBG}CO₂) measurements were taken consecutively in a randomized order and were compared with noninvasive measurements obtained from the transcutaneous monitoring of PO₂ and PCO₂ (P_tO₂, P_tCO₂, sensor-temperature 44°C). Capillary samples were taken from both arterialized earlobes, where samples of right earlobes were defined as a reference value. Pain assessment of all measurements was evaluated by each subject using the 100-mm visual analogue scale. **Results:** 83 patients and 17 healthy subjects were included. The mean difference between P_aO₂ and P_tO₂ was 11.9 ± 15.0 mm Hg, with lower limits of agreement (LLA) of –17.4 mm Hg (95% confidence interval (CI) –22.5 to –12.3 mm Hg), and upper limits of agreement (ULA) of 41.1 mm Hg (95% CI 36.0–46.2 mm Hg). The

comparison of P_aO₂ with P_{CBG}O₂ showed a mean difference of 5.6 ± 7.2 mm Hg (LLA –11.0; ULA 19.6 mm Hg). The mean difference between P_aCO₂ and P_tCO₂ was 1.1 ± 4.9 mm Hg (LLA –8.6; ULA 10.8 mm Hg) and that between P_aCO₂ and P_{CBG}CO₂ was 0.7 ± 2.0 mm Hg (LLA –3.3; ULA 4.8 mm Hg). The analysis of capillary blood gases (36.2 ± 22.3 mm) was rated as more painful than the analysis of arterial blood gases (26.1 ± 20.6 mm), while transcutaneous measurement was rated as the least painful method (1.9 ± 7.4 mm; all p < 0.0001). **Conclusions:** The comparison of different methods for blood gas measurements showed substantial differences between capillary and arterial PO₂ and between transcutaneous and arterial PO₂. Therefore, arterial PO₂ analysis is the essential method evaluating indication for LTOT. Nevertheless, comparative analysis further indicated capillary PCO₂ as an adequate surrogate for arterial PCO₂.

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Introduction

The assessment of arterial blood gases is essential for the diagnosis of hypoxemic and hypercapnic respiratory failure. The most accurate means of analyzing arterial blood gases (ABG) is via puncture of an arterial vessel, which serves as the gold standard technique [1, 2]. Anal-

ysis of capillary blood gases (CBG) obtained from arterialized earlobes or the fingertips is an alternative method that aims to reduce both the invasiveness of the procedure as well as the cost [3]. The accuracy of measuring the partial pressure of blood gases obtained from CBG has been extensively compared to gold standard ABG analyses of the partial pressure of arterial carbon dioxide ($P_a\text{CO}_2$) and of oxygen ($P_a\text{O}_2$). Overall, the correlation between ABG and CBG measurements are reportedly high [2, 3], but in the case of $P_a\text{O}_2$, the limits of agreement (LOA) between the two methods are unacceptably wide [4].

A recently published meta-analysis of 29 studies demonstrated that $P_a\text{CO}_2$ and pH values were adequately reflected when CBG was compared to ABG, but the accuracy of $P_a\text{O}_2$ was reportedly dependent on absolute $P_a\text{O}_2$ values, with sufficient method comparison only evident at $P_a\text{O}_2$ values <123 mm Hg [1]. As a consequence, the American Association for Respiratory Care guidelines indicated CBG as an appropriate replacement for ABG when assessing $P_a\text{CO}_2$. It was, however, deemed inadequate for the measurement of $P_a\text{O}_2$ [5]. In contrast, some national guidelines support the use of CBG as a diagnostic tool for the implementation of long-term oxygen therapy (LTOT) [6].

Nevertheless, ABG and CBG are both still invasive and painful procedures. In addition, both techniques depend on the availability of a blood gas analyzer and are not able to provide continuous measurements in current clinical settings [7, 8]. Methods for noninvasive and continuous measurements were developed decades ago, the most important being transcutaneous measurements of PO_2 ($P_{\text{tc}}\text{O}_2$) and PCO_2 ($P_{\text{tc}}\text{CO}_2$) using skin electrodes [9]. The introduction of pulse oximetry in the 1980s, however, reduced the interest in these techniques, since the assessment of arterial oxygen saturation ($S_p\text{O}_2$) allows a continuous, adequate and noninvasive means of reflecting oxygenation. More recently, several studies have identified the clinical value of $P_{\text{tc}}\text{CO}_2$ monitoring [10–12]; this technique has been shown to adequately reflect $P_a\text{CO}_2$ following ongoing methodological refinements. However, only a few studies have evaluated $P_{\text{tc}}\text{O}_2$ monitoring. A high LOA between $P_{\text{tc}}\text{O}_2$ and $P_a\text{O}_2$ has been reported, which can possibly be attributed to the fact that the diffusion capacity of O_2 is inferior to that of CO_2 , a highly important factor for skin electrode measurements [13–15]. On the other hand, some studies which at least found sufficient correlations between $P_{\text{tc}}\text{O}_2$ and $P_a\text{O}_2$ [16–18]; these particular studies did not apply the method comparison of Bland and Altman [19].

Given that these 3 methods for blood gas assessment (ABG, CBG and transcutaneous measurement) have never

been directly compared using the most recently developed techniques, this study compared both CBG and transcutaneous measurements with the gold standard ABG, and evaluated their accuracy in measuring both PO_2 and PCO_2 .

Methods

The study protocol was approved by the institutional review board for human studies at Albert-Ludwigs University, Freiburg, Germany, and was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects. The study was registered by the German Clinical Trials Register under DRKS00000688.

Subjects

Adult patients with different respiratory disorders in a stable state of their disease were recruited during consultation for gas exchange evaluation at the Department of Pneumology, University Hospital, Freiburg, Germany. Subjects with peripheral artery occlusive disease, therapeutic anticoagulation, an inherited or acquired clotting disorder or blood flow disorders of the hand were excluded. Healthy volunteers were included as controls to enable a broad-spectrum assessment of blood gas values.

Study Design and Measurements

Demographic data (age, height, weight, sex, disease and handedness) were initially collected from each subject. All subjects were situated in a lying position with the upper body raised to a 45° angle. After baseline calibration of the device, a transcutaneous skin sensor for $P_{\text{tc}}\text{O}_2$ and $P_{\text{tc}}\text{CO}_2$ assessment (Tina TCM4; Radiometer Medical ApS, Brønshøj, Denmark) was placed on the right side of the chest in the mediusubclavicular position, with a preset sensor temperature of 44°C, as previously recommended [12, 18, 20]. After a stabilization time of 20 min [14, 21, 22], $P_{\text{tc}}\text{O}_2$ and $P_{\text{tc}}\text{CO}_2$ were continuously recorded. In addition, $S_p\text{O}_2$ was simultaneously assessed (DINAMAP PRO 300 V2, GE Healthcare). Next, a vasodilatory substance (20 mg ointment carrying 2.5 mg of 3% capsaicin, 0.5 g benzylnicotinate and 20 mg vaseline) was applied to both earlobes for 10 min. Sufficient collateral perfusion of the hand was then ascertained by performing the Allen test. Consecutive ABG and CBG measurements of capillary blood taken from both the right and left earlobes were performed in a randomized order: ABG/right earlobe CBG/left earlobe CBG versus ABG/left earlobe CBG/right earlobe CBG versus left earlobe CBG/ABG/right earlobe CBG. $P_{\text{tc}}\text{O}_2$ and $P_{\text{tc}}\text{CO}_2$, $S_p\text{O}_2$ were documented once at the time point of CBG extraction from the right earlobe. A schematic flow-chart of the study design is shown in figure 1.

Puncture of the right arterial radial artery with a cannula (Sterican® No. 18, 26G, B. Braun Melsungen AG, Melsungen, Germany) and a 2-ml blood gas monovette (Blutgas-Monovette®, SARSTEDT AG, Nümbrecht, Germany) was performed on the subject's fully extended wrist. Earlobe puncture was performed via a blood lancet (Solofix®, B. Braun Melsungen AG) and capillary tube (COBAS® capillary tube, Roche Diagnostics GmbH, Mannheim, Germany). Blood gas analysis was undertaken with a blood gas analyzer (COBAS b221, Roche Diagnostics GmbH) within a maximal time frame of 2 min after taking blood samples.

Fig. 1. Study protocol. CBG_l = Left-earlobe CBG; CBG_r = right-earlobe CBG; TCM = transcutaneous measurement.

Finally, the sensation of pain intensity of each method was evaluated by the subject via a 100-mm visual analogue scale (VAS: 0 = no pain, 50 = acceptable pain, 100 = maximal pain).

Statistics

Our primary aim was to compare both P_{tc}O₂ and capillary P_aO₂ measurements with the gold standard P_aO₂ measurement of ABG. This was performed by calculating the 95% lower limit of agreement (LLA) and the 95% upper limit of agreement (ULA), both with 95% confidence intervals (CI) for the differences between methods, in accordance with the statistical method described by Bland and Altman [19]. The methods for PO₂ measurement were considered to be in agreement when both limits were in the range of ± 15 mm Hg from zero. Agreement between the methods was established when the lower CI limit of the LLA was above -15 mm Hg and the upper CI limit of the ULA was below 15 mm Hg.

For sample size calculation, a standard deviation (SD) of 6 mm Hg was assumed according to previous findings [1, 17]. Assuming there is perfect agreement between methods, this results in an expected LLA of -11.8 mm Hg and an expected ULA of 11.8 mm Hg. Based on these assumptions, in order to show an agreement between both methods and the gold standard technique at (1) an al-

pha significance level of 0.0125 and (2) a power of 80%, inclusion of 100 subjects was necessary. Similar comparisons were also performed for PCO₂. Finally, comparisons for arterial oxygen saturation and pH were performed as appropriate.

Pain ratings recorded by all 3 methods on the 100-mm VAS were compared with the paired Wilcoxon test.

Results

From September 2010 to February 2011, a total of 83 patients and 17 healthy volunteers were included in the study. Demographic data are shown in table 1. Patients suffered from the following respiratory disorders: COPD (n = 15), lung fibrosis (n = 23), lung cancer (n = 13), sleep apnea syndrome (n = 15), bronchial asthma (n = 2), pneumonia (n = 5), cystic fibrosis (n = 3), sarcoidosis (n = 2), pulmonary arterial hypertension (n = 4) and amyotrophic lateral sclerosis (n = 1).

Table 1. Demographic data

n = 100	Mean	SD	Min.	Max.
Sex (male/female), n	65/35			
Age, years	55.5	16.0	20.0	83.0
Weight, kg	77.7	20.5	39.0	174.0
Height, m	1.7	0.1	1.5	1.9
BMI, kg/m ²	26.5	6.8	14.9	54.8
Hb, g/dl	13.1	1.7	9.4	18.9
O ₂ , l/min	1.4	1.8	0.0	7.0
O ₂ supplementation (yes/no)	36/64			
Handedness (right/left), n	95/5			

BMI = Body mass index; Hb = hemoglobin; O₂ = flow rate of supplemental oxygen.

Table 2. Comparison of PO₂ evaluation methods

n	Measurement 1			Measurement 2			Difference		LOA (95% CI)	
	variable	mean	SD	variable	mean	SD	mean	SD	lower	upper
100	P _a O ₂	80.4	17.7	P _{tc} O ₂	68.5	21.4	11.9	15.0	-17.4 (-22.5 to -12.3)	41.1 (36.0–46.2)
100	P _a O ₂	80.4	17.7	P _{CBGr} O ₂	74.8	13.9	5.6	7.2	-8.5 (-11.0 to -6.1)	19.6 (17.2–22.0)
100	P _{CBGr} O ₂	74.8	13.9	P _{tc} O ₂	68.5	21.4	6.3	15.8	-24.7 (-30.1 to -19.3)	37.3 (32.0–42.7)
100	P _{CBGr} O ₂	74.8	13.9	P _{CBGl} O ₂	75.6	14.7	-0.8	5.2	-11.1 (-12.9 to -9.3)	9.4 (7.7–11.2)

P_{CBGl}O₂ = Left-earlobe capillary partial pressure of oxygen; P_{CBGr}O₂ = right-earlobe capillary partial pressure of oxygen.

Gold Standard PaO₂ versus Transcutaneous PO₂ and Capillary PO₂

The mean difference between gold standard P_aO₂ and P_{tc}O₂ was 11.9 ± 15.0 mm Hg. The LLA was -17.4 mm Hg (95% CI -22.5 to -12.3 mm Hg), and the ULA was 41.1 mm Hg (95% CI 36.0–46.2 mm Hg; table 2; fig. 2). The mean difference between gold standard P_aO₂ and right-earlobe capillary PO₂ was 5.6 ± 7.2 mm Hg, with an LLA of -8.5 mm Hg (95% CI -11.0 to -6.1 mm Hg), and ULA of 19.6 mm Hg (95% CI 17.2–22.0 mm Hg; table 2; fig. 3). Consequently, acceptable agreements with the gold standard ABG could not be shown with transcutaneous or capillary PO₂ values.

Gold Standard PaCO₂ versus Transcutaneous PCO₂ and Capillary PCO₂

Comparisons between PCO₂ measurements are shown in table 3 and in figures 4 and 5. The mean difference between gold standard P_aCO₂ and P_{tc}CO₂ was 1.1 ± 4.9 mm Hg. The LLA was -8.6 mm Hg (95% CI -10.2 to -6.9 mm

Hg), and the ULA was 10.8 mm Hg (95% CI 9.1–12.5 mm Hg; table 3; fig. 4). The mean difference between gold standard P_aCO₂ and right-capillary PCO₂ was 0.7 ± 2.1 mm Hg, with an LLA of -3.3 mm Hg (95% CI -4.0 to -2.6 mm Hg) and ULA of 4.8 mm Hg (95% CI 4.1–5.5 mm Hg; table 3; fig. 5).

Gold Standard Arterial Oxygen Saturation and pH Measurements versus Transcutaneous and Capillary Measurements

Method comparisons of SO₂ and pH measurements are shown in tables 4 and 5.

Comparison of Capillary Measurements from Both Earlobes

Comparison of capillary measurements of all parameters between the right and the left earlobe are shown in tables 2–5. The mean difference in PO₂ between the right and left earlobe was -0.8 ± 5.2 mm Hg, with an LLA of -11.1 mm Hg (95% CI -12.9 to -9.3 mm Hg), and ULA of 9.4 mm Hg (95% CI 7.7–11.2 mm Hg), while the mean

Table 3. Comparison of PCO₂ evaluation methods

n	Measurement 1			Measurement 2			Difference		LOA (95% CI)	
	variable	mean	SD	variable	mean	SD	mean	SD	lower	upper
100	P _a CO ₂	42.0	6.9	P _{tc} CO ₂	40.9	5.8	1.1	4.9	-8.6 (-10.3 to -6.9)	10.8 (9.1–12.5)
100	P _a CO ₂	42.0	6.9	P _{CBGr} CO ₂	41.3	6.9	0.7	2.1	-3.3 (-4.0 to -2.6)	4.8 (4.1–5.5)
100	P _{CBGr} CO ₂	41.3	6.9	P _{tc} CO ₂	40.9	5.8	0.4	4.8	-9.1 (-10.7 to -7.5)	9.8 (8.2–11.5)
100	P _{CBGr} CO ₂	41.3	6.9	P _{CBGl} CO ₂	41.0	6.8	0.3	2.0	-3.7 (-4.4 to -3.0)	4.2 (3.5–4.9)

P_{CBGl}O₂ = Left-earlobe capillary partial pressure of carbon dioxide; P_{CBGr}O₂ = right-earlobe capillary partial pressure of carbon dioxide.

Fig. 2. Bland-Altman plot of P_aO₂/P_{tc}O₂.

Fig. 3. Bland-Altman plot of P_aO₂/P_{CBGr}O₂.

Table 4. Comparison of SO_2 evaluation methods

n	Measurement 1			Measurement 2			Difference		LOA (95% CI)	
	variable	mean	SD	variable	mean	SD	mean	SD	lower	upper
99	S_aO_2	96.0	1.7	S_pO_2	96.1	2.7	0.1	1.9	-3.7 (-4.3 to -3.0)	3.9 (3.2–4.5)
98	S_aO_2	96.0	1.7	$\text{S}_{\text{CBGr}}\text{O}_2$	95.3	1.9	0.6	1.1	-1.5 (-1.9 to -1.1)	2.8 (2.4–3.1)
99	$\text{S}_{\text{CBGr}}\text{O}_2$	95.3	1.9	S_pO_2	96.1	2.7	0.8	1.7	-2.7 (-3.3 to -2.1)	4.2 (3.6–4.8)
99	$\text{S}_{\text{CBGr}}\text{O}_2$	95.3	1.9	$\text{S}_{\text{CBGl}}\text{O}_2$	95.2	2.2	0.1	0.9	-1.7 (-2.0 to -1.4)	1.9 (1.6–2.2)

$\text{S}_{\text{CBGl}}\text{O}_2$ = Left-earlobe capillary oxygen saturation; $\text{S}_{\text{CBGr}}\text{O}_2$ = right-earlobe capillary oxygen saturation; S_aO_2 = gold standard arterial oxygen saturation; S_pO_2 = oxygen saturation from pulse oximetry.

Fig. 4. Bland-Altman plot of $\text{P}_a\text{CO}_2/\text{P}_{\text{tc}}\text{CO}_2$. **Fig. 5.** Bland-Altman plot of $\text{P}_a\text{CO}_2/\text{P}_{\text{CBGr}}\text{CO}_2$.

Table 5. Comparison of pH evaluation methods

n	Measurement 1			Measurement 2			Difference		LOA (95% CI)	
	variable	mean	SD	variable	mean	SD	mean	SD	lower	upper
100	pH _a	7.42	0.03	pH _{CBGr}	7.42	0.03	-0.01	0.02	-0.04 (-0.04 to -0.03)	0.03 (0.02-0.03)
100	pH _{CBGr}	7.42	0.03	pH _{CBGI}	7.43	0.03	0.0	0.02	-0.04 (-0.04 to -0.03)	0.03 (0.02-0.04)

pH_a = Gold standard arterial pH; pH_{CBGI} = left-earlobe capillary pH; pH_{CBGr} = right-earlobe capillary pH.

Table 6. Comparison of pain levels after ABG, CBG and transcutaneous blood gas measurement

n = 100	Mean	SD	Min.	Max.
Pain _a	26.1	20.6	0.0	80.0
Pain _{CBG}	36.2	22.3	0.0	100.0
Pain _{tc}	1.9	7.4	0.0	50.0

All group comparisons resulted in $p < 0.0001$.

Pain_a = Pain assessment on 100-mm VAS after gold standard ABG; Pain_{CBG} = pain assessment on 100-mm VAS after CBG; Pain_{tc} = pain assessment on 100-mm VAS after transcutaneous blood gas measurement.

difference in PCO₂ was 0.3 ± 2.0 mm Hg with an LLA of -3.7 mm Hg (95% CI -4.4 to -3.0 mm Hg) and ULA of 4.2 mm Hg (95% CI 3.5 – 4.9 mm Hg).

Pain Assessment of the Measurements

Analysis of the 100-mm pain VAS showed significant differences between methods: CBG (36 ± 22 mm) was rated to be more painful than that of ABG (26 ± 21 mm) and the transcutaneous measurement was rated as the least painful (2 ± 7 mm; all $p < 0.0001$) (table 6).

Discussion

To the best of our knowledge, this is the first study to evaluate 3 different techniques for blood gas analysis that aim to provide spot check measurements of gas exchange: arterial, capillary and transcutaneous blood gas analysis. Based on the method comparison protocol by Bland and Altman [19], this study revealed that, at the primary end point, substantial differences existed between capillary and gold standard P_aO₂ (ABG), as well as between transcutaneous PO₂ measurements and P_aO₂. This was concluded from the unacceptably high limits of agreement

based on prespecified criteria [1, 18]. For PCO₂, the limits of agreement were within a more acceptable range, even though the criteria for PCO₂ were not prespecified in this trial.

Gold Standard P_aO₂ versus Transcutaneous PO₂

One of the major goals of our investigation was to evaluate a noninvasive blood gas measuring tool such as transcutaneous assessment of PO₂. In contrast to P_{tc}CO₂, little data exist regarding the relative accuracy of transcutaneous vs. arterial PO₂ measurements [20]. In line with our findings, P_{tc}O₂ measurements have previously been shown to be inaccurate [14, 16, 23]. Weaver [16] compared gold standard P_aO₂ to P_{tc}O₂ in healthy subjects who breathed in either room air or oxygen, and found a mean difference of 60 mm Hg, with an LLA of -110 and ULA of 220 mm Hg. Similarly, in a study by Janssens et al. [14] including patients >75 years, the mean difference between P_{tc}O₂ and P_aO₂ was reported to be 15 ± 20 mm Hg, with an LLA of -25 mm Hg and ULA of 55 mm Hg. To date, most optimal values for the mean difference and LOA between gold standard P_aO₂ and P_{tc}O₂ have been reported by Cuvelier et al. [24], who studied patients undergoing long-term mechanical ventilation; here, the mean difference for P_aO₂ <115 mm Hg was 7 ± 9 mm Hg, with an LLA of -10 mm Hg and ULA of 24 mm Hg. All of the aforementioned studies used the same transcutaneous monitor with a sensor temperature between 43 and 44°C. Our results show a mean difference between P_{tc}O₂ and P_aO₂ of 12 ± 15 mm Hg, where the LLA and ULA were -17 and 41 mm Hg, respectively. This confirms the abovementioned previous findings and limitations, indicating that P_{tc}O₂ assessment – even with the latest technology – cannot be recommended as a substitute for arterial or capillary PO₂ measurement.

Gold Standard P_aO₂ versus Capillary PO₂

Previous studies comparing gold standard and capillary P_aO₂ have yielded conflicting results [1]. For example, the mean difference of 2 ± 6 mm Hg (an LLA of -9

mm Hg and ULA of 14 mm Hg) reported in the meta-analysis was considerably smaller than what we observed, i.e. 6 ± 7 mm Hg (an LLA of -9 mm Hg and ULA of 20 mm Hg) [1]. Capillary PO_2 often underestimates the gold standard P_aO_2 because of the insufficient arterialization of blood, leading to a venous admixture. This also explains why the accuracy of capillary P_aO_2 and gold standard P_aO_2 is better with lower PO_2 values, because the arteriovenous PO_2 difference is smaller [25]. The definition of clinically acceptable results of method comparison was one difficulty of the study. We defined a clinically acceptable agreement limit for method comparison if the LOA were in the range of ± 15 mm Hg from zero [1, 18]. However, as national and international guidelines recommend a P_aO_2 of 55–60 mm Hg for the initiation of LTOT, small differences in these values due to methodological differences can have important clinical consequences [5, 6, 26]. Eaton et al. [27] reported that 16% of 100 COPD patients would be treated inappropriately with LTOT based on the capillary PO_2 . This strongly corroborates our findings as well as the American Association for Respiratory Care guidelines [5], since alternative methods of gold standard P_aO_2 assessment show clear limitations for capillary and transcutaneous assessment. Furthermore, the results of this study highlight the fact that assessment of alternative methods to gold standard P_aO_2 is essential for evaluating whether there is an indication for LTOT. Importantly, this is in contrast to the German guidelines of LTOT, where CBG is reported to be a valuable tool but might lead to inappropriate therapeutic decisions, as pointed out above [6].

SO₂ Analysis of Invasive and Noninvasive Techniques

Interestingly, the comparison of noninvasive and invasive SO_2 assessments showed more favorable results regarding LOA for method comparison, which is in contrast to the aforementioned limitations of $P_{tc}O_2/P_aO_2$ and $P_{CBG}O_2/P_aO_2$ method comparison. Therefore, SO_2 assessment is at least more favorable than $P_{tc}O_2$ as a noninvasive means of analyzing oxygenation in the blood. Furthermore, SO_2 assessment could show benefits compared to invasive $P_{CBG}O_2$ analysis, but this is speculative as it was not the aim of this study.

Gold Standard P_aCO_2 versus Transcutaneous PCO_2 and Capillary PCO_2

Method comparison according to Bland and Altman [19] revealed a clinically acceptable [1, 28] agreement limit for capillary and gold standard P_aCO_2 , as reported in the meta-analysis by Zavorsky et al. [1]. Furthermore,

in line with a number of recently published studies, our data support the clinical value of $P_{tc}CO_2$ monitoring, which provides an accurate tool for the continuous, non-invasive monitoring of PCO_2 [11, 14, 29, 30].

Comparison of Capillary Measurements from Both Earlobes

This is the first study to compare CBG from both earlobes. In line with the findings presented above, the wide-ranging LOA between the earlobes indicate the difficulty of CBG in arterialization and the achievement of a reliable PO_2 assessment. Despite the fact that this comparison was not the primary focus of our trial, these findings are important, since this diagnostic error might lead to inappropriate therapeutic consequences. Therefore, important clinical decisions should generally not be based on single measurements.

Pain Assessment

ABG was reported by our subjects to be less painful than CBG. In contrast, 2 previous studies reported ABG to be associated with a higher level of discomfort than earlobe sampling [8, 27] and only 1 study, by Fajac et al. [7], showed no difference between these 2 methods. In line with their study, we used a very thin needle (26-gauge), which might have been the reason for ABG being less painful [7]. In contrast, the other 2 studies that indicated more discomfort used 22- or 23-gauge needles [8, 27]. We evaluated pain after each measurement, including 2 CBG procedures on each earlobe. Despite advising the patient that only 2 CBG measurement on each earlobe had to be assessed for pain, one could speculate that pain evaluation of CBG was biased due to the double sampling.

Limitations

A limitation of this study is that only one spot check measurement was performed during steady state. Therefore, these results cannot be directly transferred to dynamic circumstances such as daily activity, LTOT therapy or mechanical ventilation. Furthermore, we did not include venous blood gas analyses, which are often used in the emergency room in several countries for the initial assessment of gas exchange. However, since venous blood gas analyses were previously reported to be inappropriate using the approach we have described [5], the focus remained on the analysis of oxygenation via PO_2 next to PCO_2 .

A major methodological strength of this study was that statistical variability in the calculated LOA was taken into

account. Whereas previous studies reported only the calculated limits, we also presented the 95% CIs for LLA and ULA, thereby showing the statistical precision of these calculations, as proposed by Bland and Altman [19]. Furthermore, a formal, statistically based, sample-size calculation was performed during study planning, which led to results with adequate precision.

Conclusions

The comparison of different methods for blood gas measurements showed substantial differences between capillary and arterial PO_2 as well as between transcutaneous and arterial PO_2 . Arterial PO_2 analysis is therefore the essential method to evaluate indications for LTOT. Nevertheless, comparative analysis further indicated that capillary PCO_2 is an adequate surrogate for arterial PCO_2 .

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Conflict of Interest

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