

Agreement Between Transcutaneous Monitoring and Arterial Blood Gases During COPD Exacerbation

Kasper M Sørensen, Rebecca V Leicht, Christian J Carlsson, Mikkel Elvekjaer, Celeste Porsbjerg, Eske K Aasvang, and Christian S Meyhoff

BACKGROUND: Transcutaneous measurements of CO₂ and O₂ (P_{tcCO₂}, P_{tcO₂}) are noninvasive and allow for continuous monitoring in adults with exacerbation of COPD, but substantial accuracy issues may exist. We investigated agreement between results of arterial blood gas analysis and transcutaneous measurements of CO₂ and O₂ in patients with COPD. **METHODS:** Adult subjects were monitored after acute admission to a respiratory intermediate care unit or ICU due to exacerbation of COPD and with ongoing noninvasive ventilation or immediately following extubation. Monitored variables were continuous transcutaneous measurement and simultaneous routine arterial blood gas analysis. Agreement between measurements was assessed by calculating bias with 95% limits of agreement for single-point estimates of P_{tcCO₂} versus P_{aCO₂} and versus P_{aO₂}, and for changes in transcutaneous measurements between 2 time points (Δ P_{tcCO₂} and Δ P_{tcO₂}). We considered limits of agreement within ± 7.5 mm Hg to be acceptable. **RESULTS:** A total of 57 transcutaneous measurements were made in 20 subjects for comparison with concurrent arterial blood gas analysis at 36 time points. The bias (limits of agreement) for P_{tcCO₂} and P_{tcO₂} was 2.5 mm Hg (–10.6 to 15.6 mm Hg) and 11.2 mm Hg (–28.2 to 50.6 mm Hg), respectively. The bias for Δ P_{tcCO₂} and Δ P_{tcO₂} was 2.3 mm Hg (–3.8 to 8.3 mm Hg) and –5.3 mm Hg (–37.5 to 27 mm Hg), respectively. **CONCLUSIONS:** P_{tcCO₂} and P_{tcO₂} did not accurately reflect results from arterial blood gas analyses in this study of mostly hypercapnic subjects. Agreement between changes in CO₂ during the monitoring period was acceptable, however, and transcutaneous monitoring may be used for continuous monitoring of P_{CO₂} in conjunction with arterial blood gas analysis for reference. *Key words:* transcutaneous blood gas monitoring; noninvasive ventilation; COPD; hypercapnia; respiratory insufficiency; intensive care. [Respir Care 2021;66(10):1560–1566. © 2021 Daedalus Enterprises]

Introduction

Arterial blood gas analyses (ABGs) are frequently performed in patients with exacerbation of COPD. Noninvasive transcutaneous monitoring of CO₂ and O₂ partial pressure (P_{tcO₂} and P_{tcCO₂}) hold promising potential in terms of

reducing the need for arterial punctures and thereby reducing the risks and discomfort related to this procedure.¹ Moreover, transcutaneous monitoring allows for continuous measurement as an indicator of blood gas status and may be particularly useful in clinical settings where frequent assessments of oxygenation and ventilation are needed, including during

Mr Sørensen, Drs Leicht, Carlsson, Elvekjaer, and Meyhoff are affiliated with the Department of Anaesthesia and Intensive Care, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark. Mr Sørensen, Drs Leicht, Carlsson, Elvekjaer, Porsbjerg, and Meyhoff are affiliated with the Copenhagen Center for Translational Research, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark. Dr Porsbjerg is affiliated with the Department of Respiratory Medicine, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Copenhagen, Denmark. Dr Aasvang is affiliated with the Department of Anesthesiology, Centre for

Cancer and Organ Diseases, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark. Drs Aasvang, Meyhoff, and Porsbjerg are affiliated with the Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark.

Mr Sørensen and Dr Leicht are co-first authors.

Drs Aasvang and Meyhoff are joint senior authors.

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noninvasive ventilation (NIV).² As approximately 12% of patients hospitalized with exacerbation of COPD require NIV, the scope of clinical use is substantial.^{3,4} Furthermore, arterial blood sample procedures are potentially painful.⁵ In 1 study, up to 50% of subjects reported pain > 5 on a scale of 10 in numeric ranked pain, and with > 1 puncture on average required to obtain a blood sample,⁶ a noninvasive technique to reduce the puncture frequency is obviously directly beneficial. Although rare, each puncture carries with it the risk of infection, and not so rarely a hematoma develops.⁷

The sensor for transcutaneous monitoring was invented over 50 years ago.⁸ It heats the skin to increase blood flow and arterialize the blood while increasing permeability for diffusion of blood gases.⁹ According to the American Association for Respiratory Care clinical practice guideline,¹⁰ the technology is currently applicable in various settings, including sleep investigations, during mechanical ventilation, and in evaluation of tissue perfusion, but a recent systematic review found substantial differences between P_{aCO_2} and P_{tcCO_2} measurements depending on sensor placement site and temperature and the clinical indication for use.¹¹ Some studies suggest that the accuracy of P_{tcCO_2} may decrease at higher levels of P_{aCO_2} , but these reports are conflicting.¹²⁻¹⁴ The trending ability of transcutaneous monitoring may be useful in clinical practice, but further studies of this application are needed.¹¹

The aim of this study was to assess agreement between single-point estimates of ABGs and transcutaneous measurements in patients with exacerbation of COPD during NIV treatment or immediately after extubation. We

QUICK LOOK

Current knowledge

Transcutaneous monitoring of P_{CO_2} and P_{O_2} has been used in neonates for years, but agreement between arterial values and transcutaneous values has not been as good in adults. Recent studies have reported contrasting results regarding agreement in adult subjects and some studies exhibited larger discrepancies when subjects were hypercapnic.

What this paper contributes to our knowledge

Transcutaneous measurements of CO_2 and O_2 did not accurately reflect arterial values in subjects with moderate to severe exacerbation of COPD. Agreement between changes in CO_2 was acceptable.

hypothesized that 95% limits of agreement (LoA) between the 2 methods for both P_{CO_2} and P_{O_2} would be within ± 7.5 mm Hg. We also aimed to evaluate agreement between the 2 methods' ability to reflect changes in the blood gases, hypothesizing that 95% LoA were within ± 7.5 mm Hg. We further compared agreement with ABGs at 2 different placements sites of the sensor, hypothesizing that there would be acceptable agreement at both sites.

Methods

This study was conducted at Bispebjerg Hospital from April to December 2019. An application to the regional ethics committee (H-19015292) was waived, and the study was approved by the hospital board of directors as a quality improvement study.

We included adult subjects (≥ 18 y old) who were either hospitalized acutely at a respiratory intermediate care unit or ICU for treatment of exacerbation of COPD with NIV or had recently been extubated after mechanical ventilation. Patients were excluded if inclusion was not possible within 24 h of initiation of NIV or within 2 h after extubation. Patients were also excluded if there were no arterial blood gas analyses scheduled in the 3 h following inclusion or if they had severe dermatological problems or known allergic reactions to the equipment.

We used the TCM5 Flex monitor connected to sensor 84 (Radiometer Medical, Brønshøj, Denmark). The sensor consists of a Stow-Severinghaus-type P_{tcCO_2} electrode combined with a Clark-type P_{tcO_2} electrode. The sensor was automatically calibrated prior to every session, and the sensor membrane was changed as recommended by the manufacturer.

Transcutaneous sensors were placed simultaneously on both the anterior aspect of the subjects' right upper arm and

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Correspondence: Christian S Meyhoff MD PhD, Bispebjerg Bakke 23, 2400 Copenhagen, NV, Denmark. E-mail: christian.sylvest.meyhoff@regionh.dk.

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over the major pectoral muscle immediately after inclusion. The skin was inspected for suitability and then cleansed with 83% ethanol and allowed to dry before placement of an adhesive fixation ring. Two drops of contact gel were applied on the skin in the center of the fixation ring before positioning the sensor with light pressure for correct contact to skin surface. The sensor was automatically heated to 43.5°C, at which time monitoring began.

Stable values of P_{tCO_2} were reached after ~ 10 min and for P_{tO_2} after an additional 10 min, presumably signifying full arterialization of the capillary bed. The attending health care staff was blinded to the transcutaneous measurements.

Routine ABG samplings from the radial artery were performed as part of standard clinical practice by either clinical ward staff or the investigator. The number and timing of ABGs were at the discretion of the attending physician. The time when blood filled the syringe was noted by the investigator as the time of ABG. The ABG samples were analyzed using a Radiometer ABL90 analyzer (Radiometer Medical).

Each subject was monitored for 3 h. Transcutaneous measurements of P_{tCO_2} and P_{tO_2} were stored with a sampling frequency of 1 measurement per second, and the values corresponding to time of ABG were calculated as time of ABG plus 2 min, recommended due to response and lag time of the sensor and monitoring system.¹⁵ We recorded sampling time and the results of up to 2 ABGs and the corresponding transcutaneous measurements during the monitoring period. Demographic data, clinical characteristics, physiological vital signs, and results of ABG analyses were obtained from the electronic medical records.

The primary outcome was agreement between the CO_2 and O_2 partial pressures of corresponding ABG and transcutaneous measurements (ie, P_{aCO_2} vs P_{tCO_2} , and P_{aO_2} vs P_{tO_2}). For the primary analysis we pooled concurrent measurements from sensors placed on the upper arm and the chest (ie, up to 2 measurements from each site) and compared both readings to results from the corresponding ABG analysis. We also compared agreement with ABGs between sensor placements. The secondary outcome was agreement between changes in the CO_2 and O_2 partial pressures of corresponding ABG and transcutaneous measurements from first to second sampling (ie, ΔP_{aCO_2} vs ΔP_{tCO_2} and ΔP_{aO_2} vs ΔP_{tO_2}). For this analysis, we compared transcutaneous readings from the arm and chest separately to corresponding ABG analyses.

Demographic and clinical characteristics were summarized in frequency tables using counts and percentages for categorical variables and means and standard deviation for continuous variables. Agreement between ABGs and transcutaneous measurements were determined by calculating the mean difference between the 2 methods and corresponding 95% CI for the 95% LoA, adding a random-effects model to the analysis, to account for multiple

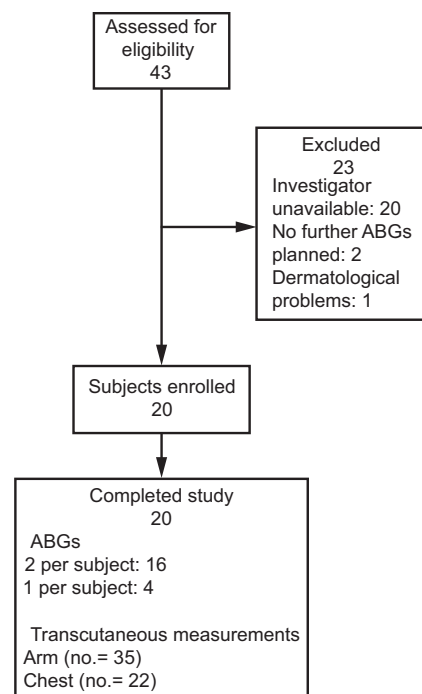


Fig. 1. Flow chart. ABG = arterial blood gas analysis.

observations per individual.¹⁶ We used the method of variance estimates recovery to calculate the 95% CI for LoA.¹⁷ Results were plotted using standard Bland-Altman plots. Limits of agreement within ± 7.5 mm Hg were considered clinically acceptable.¹⁸ We compared agreement with ABGs of transcutaneous sensors placed on the arm and chest, respectively, using mixed linear models with difference between ABG and transcutaneous measurement as the response variable and sensor placement as the explanatory variable, with subject identification number as a random effect to account for multiple observations per individual. We analyzed the effect of the absolute level of P_{aCO_2} and P_{aO_2} on agreement using mixed linear models with the absolute difference between ABGs and transcutaneous measurements as the response variable and P_{aO_2}/P_{aCO_2} as the explanatory variable, with subject identification number as a random effect and adjusting for heteroscedasticity across blood gas levels. All data analyses were conducted using the statistical software R 3.6.2 and the *rmcorr*, *lme4*, and *nlme* add-on packages (R Foundation for Statistical Computing, Vienna, Austria).¹⁹⁻²²

Results

Forty-three patients admitted with a confirmed diagnosis of exacerbation of COPD were screened, and 23 fulfilled an exclusion criterion (Fig. 1). The study included 20 subjects, of whom 16 subjects were monitored during NIV (median monitoring time: 2 h, 29 min) and 4 subjects were

Table 1. Subject Baseline Characteristics

Male, <i>n</i> (%)	10 (50.0)
Age, mean \pm SD, y	71.5 \pm 8.7
Body mass index, mean \pm SD, kg/m ²	26.4 \pm 7.7
COPD GOLD class, <i>n</i> (%)	
Grade 1	1 (5.0)
Grade 2	3 (15.0)
Grade 3	5 (25.0)
Grade 4	6 (3.0)
Unavailable data	5 (25.0)
mMRC dyspnea scale, <i>n</i> (%)	
Grade 1	1 (5.0)
Grade 2	3 (15.0)
Grade 3	2 (1.0)
Grade 4	10 (5.0)
Unavailable data	4 (2.0)
FEV ₁ /FVC	0.5 (0.5–0.6)
Unavailable data, <i>n</i>	6
FEV ₁ , % of expected	44 (36–49)
Unavailable data, <i>n</i>	3
Vital signs, median (IQR)	
Breathing frequency, breaths/min	23 (18–27)
Unavailable data, <i>n</i>	2
Heart rate, beats/min	101 (94–114)
Diastolic blood pressure, mm Hg	63 (53–75)
Systolic blood pressure, mm Hg	124 (102–150)
Mean arterial pressure, mm Hg	84 (68–96)
Temperature, °C	36.7 (36.2–37.1)
AVPU scale, <i>n</i> (%)	
A: Awake	17 (85.0)
V: Responds to verbal stimuli	2 (1.0)
P: Responds to pain stimuli	1 (5.0)
U: Unresponsive	0 (0)
Respiratory values for subjects with NIV, mean \pm SD	
Expiratory PAP, cm H ₂ O	6.1 \pm 1.2
Inspiratory PAP, cm H ₂ O	19.3 \pm 4.0
Tidal volume, mL	511 \pm 166
F _{IO₂}	0.49 \pm 0.22
Minute volume, L/min	10.6 \pm 5
Unavailable data, <i>n</i>	5
F _{IO₂} after extubation	0.29 \pm 0.1

Data are presented as *n* (%), mean \pm SD, or median (interquartile range). *N* = 20 subjects.
 GOLD = Global Initiative for Chronic Obstructive Lung Disease
 mMRC scale = modified Medical Research Council
 NIV = noninvasive ventilation
 PAP = positive airway pressure

monitored shortly after extubation (median monitoring time: 2 h, 53 min). Ten subjects were male, mean \pm SD age was 71.5 \pm 8.7 y, and mean \pm SD body mass index was 26.4 \pm 7.7 kg/m² (Table 1). Additional baseline characteristics of the subjects, such as respiratory values are presented in Table 1.

We recorded 57 transcutaneous measurements (35 and 22 from sensors on the upper arm and chest, respectively) for comparison with concurrent ABGs at 36 time points (16 subjects had 2 ABGs analyzed during the monitoring

Table 2. Summary of ABG and Transcutaneous Measurements of CO₂ and O₂

ABG measurements	
pH	7.3 (7.3–7.4)
BE, mEq/L	6.4 (1.9–9.0)
Lactate, mM	0.9 (0.7–1.2)
P _{CO₂} , mm Hg	54 (47–75)
P _{O₂} , mm Hg	63 (59–74)
Transcutaneous measurements	
P _{CO₂} , mm Hg	53 (44–71)
P _{O₂} , mm Hg	57 (49–65)

Data are presented as median (interquartile range). *n* = 36 ABGs; *n* = 57 transcutaneous measurements.

ABG = arterial blood gas

period, and 4 subjects had only 1 ABG analyzed) (Fig. 1). In 29 of 36 ABGs, P_{aCO₂} was elevated above 45 mm Hg, signifying hypercapnia. Mean \pm SD levels of transcutaneous and arterial blood gasses in the study population are presented in Table 2.

The mean difference (bias) between P_{aCO₂} and P_{tcCO₂} was 2.5 mm Hg with LoA of –10.6 to 15.6 mm Hg. The 95% CI for the lower LoA was –15.4 to –5.7 mm Hg; the 95% CI for the upper LoA was 10.8–17.1 mm Hg (Fig. 2). The mean difference between P_{aO₂} and P_{tcO₂} was 11.2 mm Hg with LoA of –28.2 to 50.6 mm Hg. The 95% CI for the lower LoA was –40.2 to –16.1 mm Hg; the 95% CI for the upper limit was 38.5–62.6 mm Hg (Table 3, Fig. 2).

The mean difference between agreement with ABGs of transcutaneous sensors placed on the upper arm and chest was 0.0 kPa (95% CI –0.01 to 0.08, *P* = .68) for CO₂ and 0.1 kPa (95% CI –0.4 to 0.6, *P* = .77) for O₂, as shown in Figure E1 (see the supplementary materials at <http://www.rcjournal.com>).

The O₂ measurements of 2 subjects (no. = 8) appeared to be outliers (Fig. 2B) and were removed for sensitivity analyses. After removing these measurements, the mean difference between P_{aO₂} and P_{tcO₂} was 1.1 kPa with LoA of –1.9 to 0.64 kPa.

Linear regression analysis of the relationship between the absolute difference between P_{aCO₂} and P_{tcCO₂} as a function of P_{aCO₂} showed a slope of 0.07 (95% CI –0.04 to 0.17, *P* = .22), whereas the corresponding slope for O₂ measurements was 0.48 (95% CI 0.21–0.76, *P* < .001).

Mean \pm SD time between 2 ABG measurements for the same subject was 95.1 \pm 33 min. Mean changes in transcutaneous blood gasses, measured with the sensor placed on the arm and chest, and changes in arterial blood gasses between the 2 measurement time points are shown in Table E1 (see the supplementary materials at <http://www.rcjournal.com>).

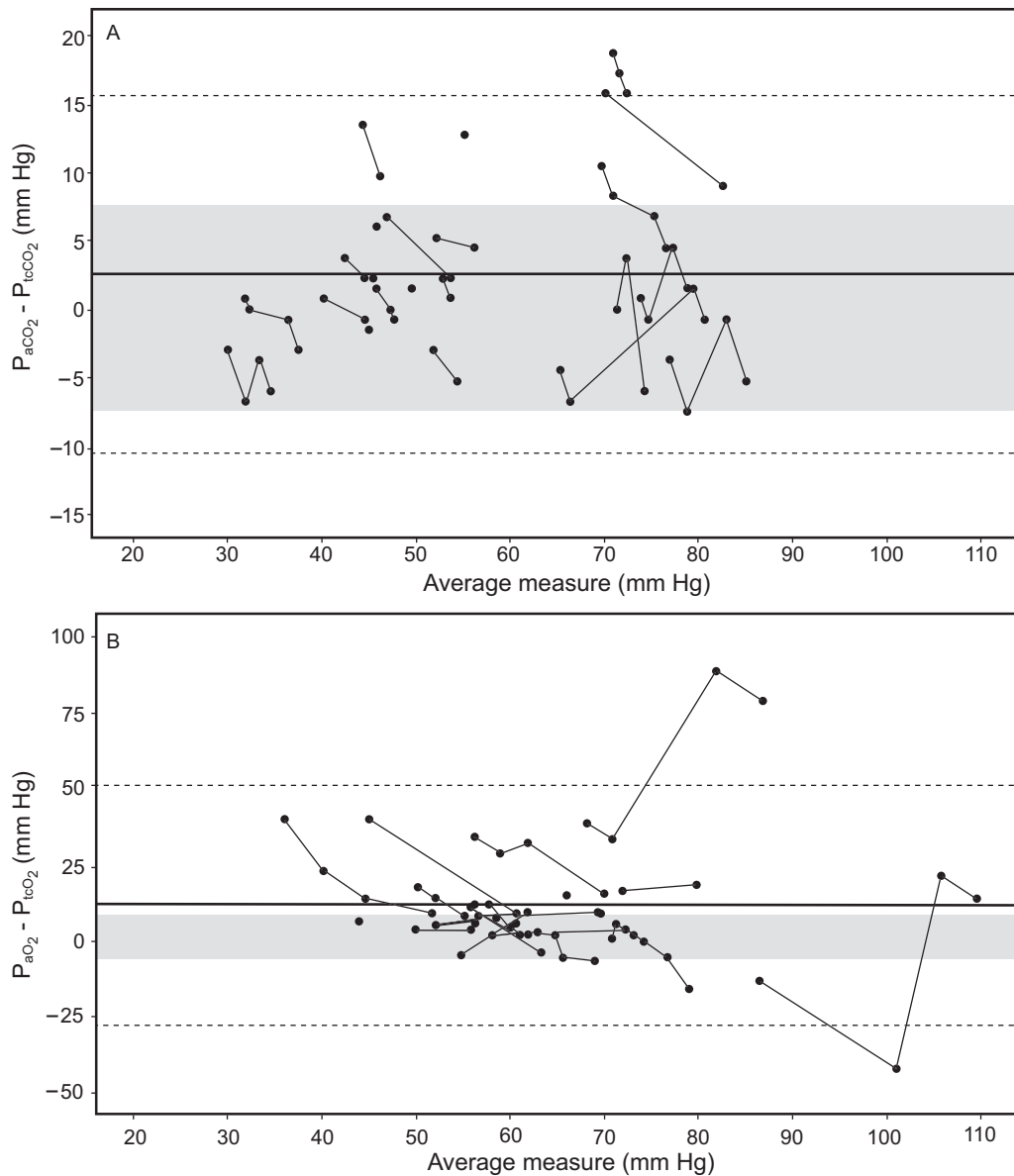


Fig. 2. Bland-Altman plots of agreement between arterial blood gas analysis and transcutaneous measurements of P_{CO_2} (A) and P_{O_2} (B). Solid lines show mean bias; dotted lines show upper and lower 95% limits of agreement. Measurements from the same subject are connected by lines. The shaded area shows the predefined clinically acceptable limits of agreement of ± 7.5 mm Hg. Average measures were calculated as (arterial pressure + transcutaneous pressure)/2.

Table 3. Bland-Altman Characteristics of Agreement Between ABG and Transcutaneous Measurements of CO_2 and O_2

Test	Bias (LoA), mm Hg
P_{CO_2}	2.5 (−1.5 to 15.6)
P_{O_2}	11.2 (−28.2 to 50.6)

LoA = 95% limits of agreement
ABG = arterial blood gas

Bland-Altman plots of paired changes in ABGs and transcutaneous measurements of CO_2 and O_2 are shown in Figure E3 (see the supplementary materials at <http://www.rcjournal.com>). The mean difference between ΔP_{aCO_2} and ΔP_{tcCO_2} measured on the upper arm was 2.2 mm Hg with LoA of −4 to 8.3 mm Hg. The 95% CI of the lower limit was −6.6 to −1.3 mm Hg, and the 95% CI of the upper limit was 5.6–10.9 mm Hg; the mean difference between ΔP_{aO_2} and ΔP_{tcCO_2} measured on the upper arm was −5.3 mm Hg with LoA of −37.9 to 27.4 mm Hg. The 95% CI of the lower limit was −52.1 to −23.6 mm Hg, and the 95% CI of

the upper limit was 13.1–41.6 mm Hg (Table E2; see the supplementary materials at <http://www.rcjournal.com>). The mean difference between ΔP_{aCO_2} and ΔP_{tcCO_2} measured on the chest was 1.9 mm Hg with LoA of –2.6 to 6.5 mm Hg. The 95% CI for the lower limit was –5.3 to 0.1 mm Hg, and the 95% CI for the upper limit was 3.8–9.1 mm Hg; the mean difference between ΔP_{aO_2} and ΔP_{tcO_2} measured on the chest was –10 mm Hg with LoA –59.9 to 39.9 mm Hg. The 95% CI of the lower limit was –89.4 to –30.3 mm Hg, and the 95% CI for the upper limit was 10.3–69.4 mm Hg.

After removing outliers for O_2 measurements ($n = 2$ from both upper arm and chest measurements), the mean difference between ΔP_{aO_2} and ΔP_{tcO_2} measured on the upper arm was 0.0 mm Hg with LoA of –15.8 to 16.5 mm Hg. The mean difference between ΔP_{aO_2} and ΔP_{tcO_2} measured on the chest was 1.5 mm Hg with LoA of –21.0 to 24.0 mm Hg.

Discussion

Transcutaneous measurements of CO_2 and O_2 underestimated ABG values by 2.5 and 11.2 mm Hg, respectively, in this observational study of subjects with an exacerbation of COPD. Limits of agreement were wide, and all exceeded the predefined clinically acceptable threshold of ± 7.5 mm Hg. Changes in CO_2 detected with transcutaneous measurements were within acceptable limits of agreement with ABGs, although the 95% CI around the limits of agreement were wide.

Previous reports on the accuracy of transcutaneous monitoring of blood gases have been conflicting. In a study of 40 elderly subjects admitted due to acute cardiac or pulmonary disorders, Janssens et al²³ reported that P_{tcCO_2} only underestimated P_{aCO_2} by 0.075 mm Hg with 95% LoA of –8.3 to 8.3 mm Hg, making it compatible with clinical use, while the reported bias for P_{tcO_2} was large and comparable to our findings. Similarly, in a study of 25 subjects with asthma or pneumonia, Perrin et al²⁴ reported a bias for P_{tcCO_2} of –0.075 mm Hg with 95% LoA of –3.8 to 3.8 mm Hg.

In contrast, several recent studies^{14,15,25} of hypercapnic subjects in acute respiratory distress have reported that P_{tcCO_2} could significantly underestimate P_{aCO_2} , which is also suggested by our findings. Some of these studies reported decreasing reliability of P_{tcCO_2} with increasing levels of hypercapnia.^{14,25} In our study, accuracy of P_{tcCO_2} appeared to be stable across the mainly hypercapnic range of P_{aCO_2} .

Removing outliers at the high range of P_{aO_2} improved agreement for O_2 measurements, but linear regression analysis adjusted for the apparent heterogeneity of variance suggests that P_{tcO_2} measurements are more erratic at higher levels of P_{aO_2} (eg, patients receiving oxygen supplementation). The reasons for the mentioned discrepancies are uncertain but may include differences in patient populations in terms of disease process and severity; make of

monitoring equipment; differences in staff training regarding device use; or unknown effects of clinical signs of respiratory failure such as altered skin perfusion, sweating, and fever.

A major strength of this study is the close monitoring of subjects hospitalized with exacerbation of COPD, the majority being in a hypercapnic state, allowing for evaluation of the accuracy of transcutaneous monitoring of blood gases in a highly relevant clinical setting. The study also included repeated measurements per subject, increasing statistical power and allowing for analysis of agreement in detection of changes in blood gases over time, which may be equally important in clinical practice.

Some limitations must be noted. First, ABGs were only drawn upon clinical indication, and we only recorded 1 measurement for a subset of subjects. We accounted for this unbalanced data structure in the statistical analyses. Second, a variety of areas for sensor placement is suggested by the manufacturer. In a large meta-analysis of 73 studies, including 7,021 paired measurements of transcutaneous and arterial P_{CO_2} , Conway et al¹¹ concluded that sensors should preferentially be applied to the earlobe and that users should consider setting the temperature of the sensor higher than 42°C when monitoring at other sites. For this study, the upper arm and the area over the major pectoralis muscle were chosen to avoid entanglement with the NIV mask and a sensor temperature of 43.5°C was used. Some transcutaneous measurements from the chest were not recorded due to technical issues at this sensor placement, and a relatively larger part of the total number of transcutaneous measurements (ie, 35 vs 22) were derived from the sensors placed on the upper arm. Moreover, the smaller number of transcutaneous measurements at the chest may have hampered our ability to analyze agreement with ABG analysis in detection of changes in blood gases for this sensor placement. However, we did not find any difference in agreement with ABGs between the 2 sensor placements, and we believe that both pooled observations and observations from separate sensor placements accurately reflect the performance of the transcutaneous measurements. Third, the time lag from initiation of monitoring with the TCM5 Flex until reliable values of blood gases were obtained (ie, 10 min for P_{tcCO_2} and 20 min for P_{tcO_2}) was a challenge in cases where sensor replacement was indicated, either because of unintended disconnection or periodic repositioning. Furthermore, on 2 occasions the system performed a mandatory stabilization immediately after startup without any previous warning. This process takes from 40 min to 8 h, according to the user guide provided by the manufacturer, and resulted in 2 subjects only being monitored with sensors on the upper arm in this study. More importantly, such delays may severely hamper use of the system for monitoring critically ill patients in a clinical setting.

In this study, there was a clinically acceptable agreement between changes in ABG values and transcutaneous measurements ΔP_{tCO_2} , as previously observed,¹⁵ but not for ΔP_{tO_2} . This is clinically relevant because changes to P_{CO_2} serve as an important marker of treatment response in patients with exacerbation of COPD including during NIV. Transcutaneous measurements allow for continuous monitoring of changes in P_{CO_2} and may reduce the need for repeated arterial punctures, thus improving patient comfort.⁶ However, the wide LoA ranges for single-point estimates reported in this study, which allow for substantial underestimation (ie, up to > 15 mm Hg) of absolute values of P_{aCO_2} , present a safety concern, as noted by Kelly and Klim.²⁵ A recent review proposed negating this problem by drawing a reference ABG at the start of transcutaneous monitoring to detect a possible gap between P_{tCO_2} and P_{aCO_2} and then calibrating equipment accordingly.²⁶

In this study, transcutaneous monitoring of P_{tO_2} was in poor agreement with P_{aO_2} in terms of both point estimates and changes. S_{pO_2} is a pseudo-marker for P_{aO_2} , so oxygenation status can already be continuously monitored using pulse oximetry.²⁷ Hence the need for continuous monitoring of P_{tO_2} may be limited, while monitoring of P_{tCO_2} provides additional valuable information to clinicians in an ICU setting as well as in general medical wards.

Conclusions

Transcutaneous measurements of CO_2 and O_2 did not accurately reflect arterial values in subjects with moderate to severe exacerbation of COPD. Agreement between changes in CO_2 was acceptable, and transcutaneous monitoring may be used for continuous monitoring of P_{CO_2} in conjunction with ABG analysis for reference.

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