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ORIGINAL RESEARCH

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# Concordance and limits between transcutaneous and arterial carbon dioxide pressure in emergency department patients with acute respiratory failure: a single-center prospective observational study

Xavier Bobbia<sup>1†</sup>, Pierre-Géraud Claret<sup>1\*†</sup>, Ludovic Palmier<sup>1</sup>, Michaël Robert<sup>1</sup>, Romain Genre Grandpierre<sup>1</sup>, Claire Roger<sup>1</sup>, Patrick Ray<sup>2</sup>, Mustapha Sebbane<sup>1</sup>, Laurent Muller<sup>1</sup> and Jean-Emmanuel de La Coussaye<sup>1</sup>

## Abstract

**Introduction:** Transcutaneous CO<sub>2</sub> (PtCO<sub>2</sub>) is a continuous and non-invasive measure recommended by scientific societies in the management of respiratory distress. The objective of this study is to evaluate the correlation between PtCO<sub>2</sub> and blood pressure of CO<sub>2</sub> (PaCO<sub>2</sub>) by blood gas analysis in emergency patients with dyspnoea and to determine the factors that interfere in this correlation.

**Methods:** From January to June 2014, all patients admitted to resuscitation room of the emergency department targeted for arterial blood gases were included prospectively. A sensor measuring the PtCO<sub>2</sub> was attached to the ear lobe of the patient before the gas analysis. Anamnesis, clinical and laboratory parameters were identified.

**Results:** 90 patients with dyspnoea were included (with 104 pairs of measurements), the median age was 79 years [69-85]. The correlation between PtCO<sub>2</sub> and PaCO<sub>2</sub> was R<sup>2</sup> = 0.83 (p < 0.001) but became lower for values of PaCO<sub>2</sub> > 60 mm Hg. The mean bias (±SD) between the two methods of measurement (Bland-Altman analysis) was -1.4 mm Hg (±7.7) with limits of agreement of -16.4 to 13.7 mm Hg. In univariate analysis, PaO<sub>2</sub> interfered in this correlation. After multivariate analysis, the temperature (OR = 3.01, 95% CI = 1.16-7.09) and the PaO<sub>2</sub> (OR = 1.22, 95% CI = 1.02-1.47) were found to be significant.

**Conclusions:** In patients admitted in emergency unit for acute respiratory failure, there is a significant correlation between PaCO<sub>2</sub> and PtCO<sub>2</sub>, mainly for values below 60 mm Hg. The two limiting factors of use are hyperthermia and users training.

**Keywords:** Emergency service, Blood gas monitoring, Transcutaneous, Carbon dioxide, Partial pressure

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## Introduction

In patients with respiratory failure admitted to resuscitation room (RR), the monitoring of arterial blood gases is crucial for diagnosis and therapeutic guidance [1]. The gold standard remains the analysis of arterial blood gases. This implies an arterial puncture that it is invasive, time consuming and giving only punctual results [2,3]. In addition, pending the results of blood gas analysis does not allow for real-time adaptation of oxygen therapy and/or mechanical ventilation. Oxygen saturation by pulse oxymetry ( $SpO_2$ ) is widely used as a surrogate of arterial oxygen saturation ( $SaO_2$ ) [4]. In mechanically ventilated patients, end tidal  $CO_2$  ( $EtCO_2$ ) allows an indirect reliable continuous assessment of arterial  $PCO_2$ . In non-ventilated patients, assessment of  $EtCO_2$  is more complex, less accurate and often impossible. The transcutaneous monitoring of the carbon dioxide ( $PtCO_2$ ) could represent a good alternative for immediate and continuous assessment of  $PCO_2$  in RR, especially in non-ventilated patients. The transcutaneous continuous monitoring of the carbon dioxide has been recently recommended [5,6]. In the specific setting of RR,  $PtCO_2$  has been poorly studied. Numerous studies in infants [7,8] and adults [9-11] have found a good correlation between  $PaCO_2$  and  $PtCO_2$ . The main objective of this study was to investigate the relationship between measures of  $PtCO_2$  and  $PaCO_2$  in resuscitation room patients admitted. The secondary objective was to determine the factors that may disrupt the link between these two parameters.

## Patients and methods

### Setting and study population

This single-center prospective observational study was conducted from January to June 2014 at the emergency department (ED) of Nîmes University Hospital. According to the French Law (Law 88-1138 relative to Biomedical Research of 20 December 1988 modified on 9 August 2004), this non-interventional study did not require approval by an ethics committee nor informed signed consent from patients. It was reviewed and approved by our Institutional Review Board (number: 13/06-02). Moreover, the present study was declared to and approved by the national commission for data processing and civil liberties. All patients provided written informed consent. All adult patients oriented in the RR and with an arterial blood gas during laboratory tests were likely to be included in the study. Exclusion criteria were the realization of venous blood gases and non-compliance of the study protocol (incorrect installation of the sensor or signal abnormality of the monitor or backup).

The  $PtCO_2$  measurement was performed by a Stow-Severinghaus sensor (tc Sensor 92 by Radiometer™, Copenhagen, Denmark). The sensor was placed on the earlobe heating skin to a temperature of 44°C resulting in

a dilatation of capillary bed that allows a 20 times faster diffusion of gases ( $CO_2$  and  $O_2$ ) from the skin to the sensor [12]. On the sensor, carbon dioxide reacts with water to form carbonic acid which dissociates into  $H^+$  and  $HCO_3^-$  thereby changing pH values. These pH changes are translated into  $PtCO_2$  value through the Henderson-Hasselbalch formula [13].

Before the study, medical and paramedical staff were trained in the operation and maintenance of the monitor  $PtCO_2$  type TCM TOSCA monitor (Radiometer™, Copenhagen, Denmark). Patients in whom RR admission was required were included. The  $PtCO_2$  sensor was attached to the ear lobe of the patient allowing continuous measurement of  $PtCO_2$ . Arterial blood gases and the usual additional assessments were performed at the same time. The medical team was blinded for the value of  $PtCO_2$ .

Medical patient data were collected and computerized after initial collection on paper case report form (CRF). Blood pressure, heart rate and respiratory rate, blood oxygen saturation, Glasgow coma scale, temperature, time for completion of the arterial blood gases, catecholamines use, NIV or tracheal intubation were recorded by the attending physician. Epidemiological characteristics of patients such as admission modalities, length of hospital stay and biological data were collected on the CRF.  $PtCO_2$  values were automatically saved every ten seconds by the monitor  $PtCO_2$ . The primary outcome variable was concordance between the simultaneous  $PaCO_2$  and  $PtCO_2$  values. Sample size calculation was based on the anticipated variation in the differences between the measurements and the required precision. Using previous study [14] for an estimate of the variation between the differences, a sample size of 50 patients gives a precision of  $\pm 0.19$  kPa in the limits of agreement. The secondary outcome was to determine the factors that interfere in this correlation.

### Statistical analysis

Patient characteristics are described using qualitative variables (using frequencies and percentages) and quantitative variables (using means and standard deviation or median with interquartile depending on type of distribution). The concordance between  $PtCO_2$  and  $PaCO_2$  was evaluated by linear regression (correlation coefficients) and Bland-Altman analysis, which determined bias, precision, and agreement of  $PtCO_2$  and  $PaCO_2$ , taking the automated analysis in the laboratory as the reference. The Pearson correlation coefficient was used to demonstrate the presence or absence of a relationship between  $PtCO_2$  and  $PaCO_2$ . Relationships between measurement differences ( $|PaCO_2 - PtCO_2|$ ) and patient characteristics were investigated by regression analysis. Variables related to the difference between  $PtCO_2$  and  $PaCO_2$  in the univariable analysis (defined by  $p < 0.10$ , forward selection)

were further analysed in a multivariable model (analysis of covariance). We introduced in this model PaCO<sub>2</sub> but did not introduce pH and PtCO<sub>2</sub> to avoid a collinear bias. Overall model fit was assessed using the Hosmer-Lemeshow test. All statistical tests were 2-sided. A P value less than 0.05 was considered significant for all analyses.

Analyses were performed with the use of R 3.0.2 (R Core Team 2013, R: A language and environment for statistical computing, R Foundation for Statistical Computing, Vienna, Austria). The authors had full access to and take full responsibility for the integrity of the data.

## Results

Between January 2014 and June 2014, 102 patients were screened. Only 90 patients were analyzed with 104 PtCO<sub>2</sub> values (Figure 1). Table 1 shows the characteristics of the 104 measurements. After linear regression analysis of 104 couples, there was a significant correlation between PaCO<sub>2</sub> and PtCO<sub>2</sub> with  $R^2 = 0.83$  ( $P < 0.001$ ) (Figure 2). The linear regression equation between the two variables was  $\text{PaCO}_2 = 0.81 \times + 10.86 \text{ PtCO}_2$ . The Bland-Altman (12) is shown in Figure 3. The mean bias was -1.4 mm Hg ( $\pm 7.7$ ) and limits of agreement (bias  $\pm 1.96$  SD) between the two techniques were -16.4 mm Hg and 13.7 mm Hg. The Pearson's correlation coefficient was 0.94 (95% CI = 0.87-0.94,  $P < 0.001$ ).

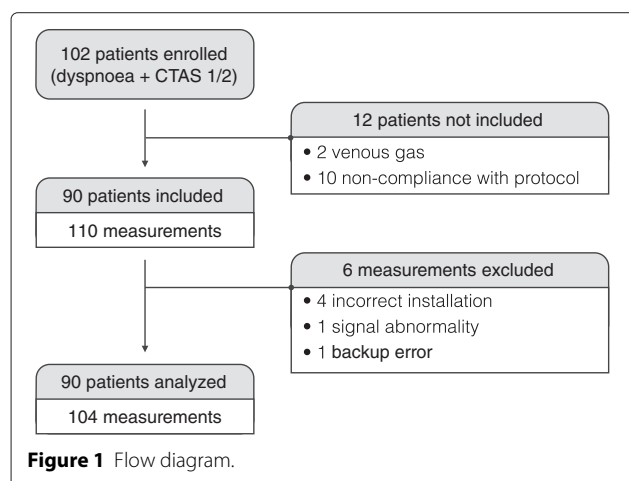
For group with PaCO<sub>2</sub> < 60 mmHg,  $R^2 = 0.70$  ( $P < 0.001$ ) and the mean bias was -3.5 mm Hg ( $\pm 5.0$ ). For group with PaCO<sub>2</sub> > 60 mmHg,  $R^2 = 0.57$  ( $P < 0.001$ ) and the mean bias was 4.1 mm Hg ( $\pm 10.2$ ).

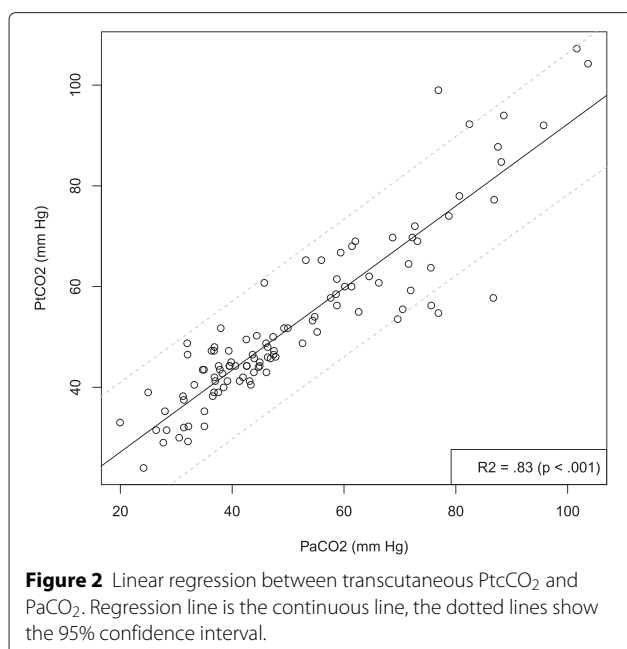
In univariate analysis, the only factor associated with a difference between PaCO<sub>2</sub> and PtCO<sub>2</sub> was PaO<sub>2</sub> (Table 2). In multivariate analysis with three explanatory variables (PaCO<sub>2</sub>, PaO<sub>2</sub>, temperature), we found the temperature and the PaO<sub>2</sub> to be significantly associated with a high

**Table 1 Patient characteristics**

Male sex, no. (%)	51 (57)
Age, mean ( $\pm$ SD) - year	76 (15)
Past medical history, no. (%)	
Acute pulmonary edema	27 (29)
Chronic obstructive pulmonary disease	27 (29)
Ischemic heart disease	21 (23)
Home oxygen	16 (17)
Clinical data at admission, median (IQR)	
Heart rate - beats/min.	94 (80-110)
Systolic blood pressure - mm Hg	122 (106-144)
Diastolic blood pressure - mm Hg	69 (60-78)
Respiratory rate - breaths/min.	24 (19-28)
Glasgow coma scale	15 (14-15)
Temperature - °C	37.0 (36.2-37.6)
Laboratory values, median (IQR)	
PaCO <sub>2</sub> - mm Hg	46.2 (37.6-66.8)
PtCO <sub>2</sub> - mm Hg	47.2 (42.1-60.0)
PaO <sub>2</sub> - mm Hg	73.5 (63.0-89.0)
pH	7.37 (7.30-7.43)
HCO <sub>3</sub> - mEq/L	26.0 (22.8-29.7)
Base excess - mmol/L	1.9 (-1.9-5.8)
Lactate - mmol/L	1.3 (0.7-2.2)
Hemoglobin - g/dL	12.3 (10.9-13.8)
White blood cells - G/L	12.4 (7.9-15.5)
C-reactive protein	41 (8-122)
Glycemia - g/L	1.4 (1.2-1.7)
Brain natriuretic peptide - ng/L	1704 (579-6200)
Diagnosis, no. (%)	
Heart failure	25 (27)
COPD	14 (15)
Pneumonia	42 (46)
Pulmonary embolism	5 (5)
Outcome, no. (%)	
Noninvasive ventilation required	41 (45)
Intubation required	4 (4)
Admitted to hospital	61 (66)
Admitted to ICU	19 (21)
Discharged from ED	10 (11)
Death at the ED	2 (2)
Inpatient mortality	9 (10)

COPD: Chronic obstructive pulmonary disease; ED: Emergency department; ICU: Intensive care unit; IQR: Interquartile range; PaCO<sub>2</sub>: Partial pressure of carbon dioxide in the blood; PtCO<sub>2</sub>: Transcutaneous partial pressure of carbon dioxide in the blood; PaO<sub>2</sub>: Partial pressure of dioxygen in the blood.

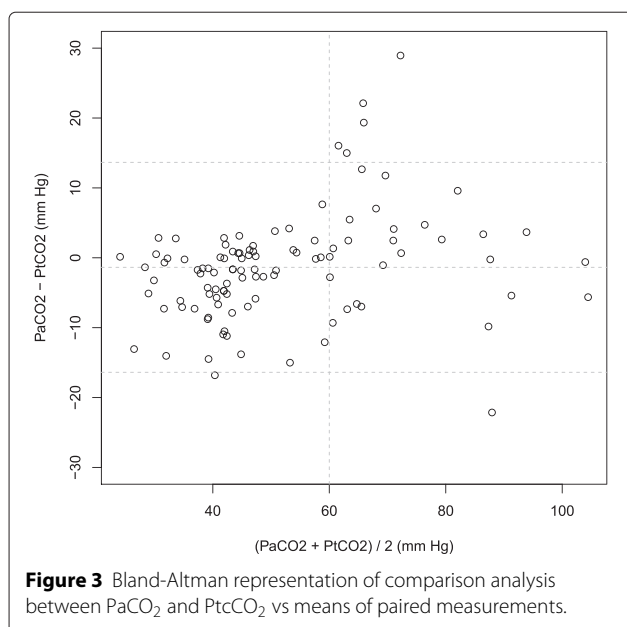




difference between  $PaCO_2$  and  $PtCO_2$  (Table 2). In this model, 11 observations were deleted because of missing data. This model has a nonsignificant Hosmer-Lemeshow chi-square goodness-of-fit statistic. The higher the temperature of the patient, the higher the difference between  $PaCO_2$  and  $PtCO_2$  was significant (Figure 4).

## Discussion

To our knowledge, this study is the largest cohort of  $PtCO_2$  measurements in ED. The mean bias was  $-1.4$



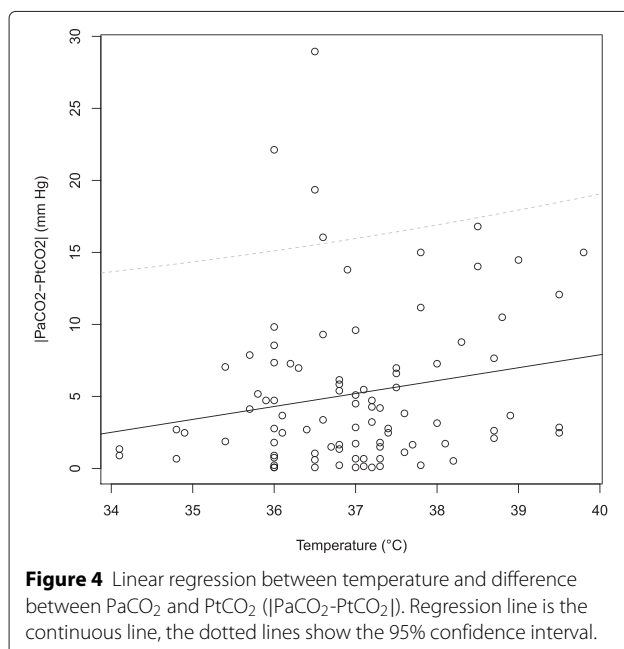
mm Hg ( $\pm 7.7$ ) and the limits of agreement (bias  $\pm 1.96$  SD) between the two techniques were  $-16.4$  mm Hg and  $13.7$  mm Hg. There was a significant correlation between  $PaCO_2$  and  $PtCO_2$  ( $R^2 = 0.83$ ,  $p < 0.001$ ). This value is comparable to what was shown in intensive care ( $R^2 = 0.86$ ,  $p < 0.01$ ) [9] while other studies have found better correlation ( $R^2$  coefficient between 0.91 and 0.99 [15-17]). First, this difference can be explained by the recruitment of our patients, performed only in RR with acute respiratory failure. Because a majority of our patients were non-intubated, our results highlight the feasibility and the potential interest of  $PtCO_2$  as  $EtCO_2$  cannot easily be monitored in non-intubated patients. Indeed, the extreme values of  $PaCO_2$  and high  $PaCO_2$  values were reported as possibly interfering in the correlation- $PtCO_2$   $PaCO_2$  [9,18-20]. Second, this difference may result from the use of the device by a large number of doctors. Calibration, sensor placement and latency to reach the plateau value of  $PtCO_2$  may differ from one doctor to another. This may lead to poorer reproducibility; some operators use the apparatus less frequently. However, this reflects our center daily practice and occurs when there is any change of material. Third, our population was more likely to have breathing disorders and therefore agitation and/or sweating leading to mobilization of the sensor which may disrupt the measurement. Our study found a value  $PtCO_2$  generally greater than the value of  $PaCO_2$  measured. Indeed, linear regression equation is  $PtCO_2 = 0.81 \times + 10.86 PaCO_2$ . This overestimation is in accordance with available literature [9,21,22]. This overestimation may have implications for patients requiring non-invasive ventilation and with no blood gas reference. Thus, the recommendations highlight the need to conduct a gas analysis to verify the correlation between the  $PaCO_2$  and  $PtCO_2$  [5]. This parameter is particularly important to consider given that the analysis of Bland-Altman reveals a poorer correlation values  $PtCO_2 > 60$  mm Hg. The value of the mean bias reported in our study corresponds to those found in the literature ( $-1.4$  to  $4.6$  mm Hg) [15,23,24]. This dispersion of the correlation for high values of  $PaCO_2$  was previously reported. The accuracy of  $PtCO_2$  seems to be restricted to patients with  $PaCO_2$  values of  $< 56$  mm Hg [25]. One explanation for this poor correlation with the clinical manifestations of hypercapnia (excessive sweating and vasodilatation) leading to a lower diffusion of carbon dioxide [25]. In our study, after multivariate analysis, only the temperature was associated with a poor correlation between  $PaCO_2$  and  $PtCO_2$  (HR = 1.15 [0.2-2.10],  $p = 0.018$ ). The notion that the temperature can influence the correlation had been raised by Rodriguez et al. [26]. The linear regression analysis reveals that the higher is the body temperature, the greater the difference between the  $PaCO_2$  and  $PtCO_2$  is important. This poor correlation can be explained by

**Table 2 Relationships between measurement differences ( $|\text{PaCO}_2\text{-PtCO}_2|$ ) and patient characteristics, univariate and multivariate analysis (ANCOVA)**

Variable	Univariate analysis		Multivariate analysis	
	OR [95% CI]	P-value	OR [95% CI]	P-value
Sex	1.61 [0.18-14.25]	0.66		
Past medical history				
Acute pulmonary edema	0.29 [0.03-2.96]	0.29		
COPD	0.60 [0.06-6.18]	0.67		
Ischemic heart disease	0.75 [0.06-8.91]	0.82		
Home oxygen	1.01 [0.06-16.77]	0.99		
Heart rate	0.98 [0.94-1.03]	0.40		
Systolic blood pressure	1.01 [0.97-1.05]	0.60		
Diastolic blood pressure	0.97 [0.91-1.03]	0.33		
Respiratory rate	1.01 [0.88-1.18]	0.85		
Temperature	2.45 [0.93-6.49]	0.07	3.01 [1.16-7.80]	0.03
$\text{PaCO}_2$	1.05 [1.00-1.12]	0.06	1.06 [1.00-1.12]	0.05
$\text{PtCO}_2$	1.06 [1.00-1.13]	0.06		
$\text{PaO}_2$	1.21 [1.01-1.45]	0.04	1.22 [1.02-1.47]	0.03
$\text{HCO}_3$	0.96 [0.80-1.15]	0.64		
Base excess	0.96 [0.82-1.12]	0.60		
Lactate	1.44 [0.43-4.79]	0.54		
Hemoglobin	1.20 [0.74-1.95]	0.45		
White blood cells	0.91 [0.74-1.12]	0.38		
C-reactive protein	1.00 [0.99-1.01]	0.72		
Glycemia	4.70 [0.62-35.58]	0.13		
Brain natriuretic peptide	1.00 [1.00-1.00]	0.82		

ANCOVA: Analysis of covariance; COPD: Chronic obstructive pulmonary disease; CI: Confidence interval;  $\text{PaCO}_2$ : Partial pressure of carbon dioxide in the blood;  $\text{PtCO}_2$ : Transcutaneous partial pressure of carbon dioxide in the blood;  $\text{PaO}_2$ : Partial pressure of dioxygen in the blood.

the fact that the higher the patient's temperature, the greater the difference between the temperature sensor ( $44^\circ\text{C}$ ) is low, resulting in small changes in local perfusion and thus altering the local production of  $\text{CO}_2$ . This hypothesis follows directly from the operating principle of



the sensor [5]. It could also be hypothesized that a high body temperature promotes sweating and vasodilatation making far more difficult sensor measurement. Finally, a low blood pressure can also be a cause a poor correlation [27]. This hypothesis cannot be confirmed by the present data, has few patients has shock criteria. Similarly, the assumption that the pH may explain poor correlation [20] is not confirmed in our study in the multivariate analysis.

#### Limitations

First, our study has few patients with hemodynamic instability requiring the establishment of intravenous fluids or vasopressor support. It is therefore difficult to conclude to any contribution from the low-speed on the correlation between  $\text{PaCO}_2$  and  $\text{PtCO}_2$ . Several studies have shown that the correlation between the  $\text{PtCO}_2$   $\text{PaCO}_2$  and is not affected by the use of catecholamine but by dermal vasoconstriction secondary to a state of shock [9,22,26]. Secondly, body mass index (BMI) has not been measured over the study. Several studies reported conflicting conclusions regarding the influence of the thickness of the skin, indirectly estimated by BMI, on the diffusion of  $\text{CO}_2$  to the skin and therefore the values of  $\text{PcCO}_2$  [9,22,24,25]. Third, the majority of patients had received only blood gases during the treatment, not for obtaining intra-individual

correlations between different values  $PtCO_2$  and  $PaCO_2$ . This analysis was important to be able to easily predict  $PaCO_2$  values from continuous measurement of  $PtCO_2$  in patients requiring several hours of surveillance [26,28].

## Conclusions

In patients admitted in emergency unit for acute respiratory failure, there is a significant correlation between  $PaCO_2$  and  $PtCO_2$ , mainly for values below 60 mm Hg. The two limiting factors of use are hyperthermia and users training.

## Key messages

- In patients admitted in emergency unit for acute respiratory failure, there is a significant correlation between  $PaCO_2$  and  $PtCO_2$ .
- This correlation is comparable to what was shown in intensive care.
- The two limiting factors of use are hyperthermia and users training.

## Abbreviations

ANCOVA: Analysis of covariance; BMI: Body mass index; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; CRF: Case report form; ED: Emergency department;  $EtCO_2$ : End tidal  $CO_2$ ; ICU: Intensive care unit; IQR: Interquartile range; OR: Odds ratio; RR: Resuscitation room;  $PaCO_2$ : Partial pressure of carbon dioxide in the blood;  $PtCO_2$ : Transcutaneous partial pressure of carbon dioxide in the blood;  $PaO_2$ : Partial pressure of dioxygen in the blood;  $SaO_2$ : Arterial oxygen saturation;  $SpO_2$ : Oxygen saturation by pulse oxymetry.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

XB, PGC, LP and MR conceived the study and wrote the manuscript. JELC was the director of this research project and participated to the writing of this manuscript. LP and MR performed the exams. PGC was the responsible of the statistical analysis. XB, PGC, LP, MR, RGG, CR, PR, MS, LM and JELC have been involved in drafting the manuscript or revising it critically for important intellectual content. XB, PGC, LP, MR, RGG, CR, PR, MS, LM and JELC have given final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final manuscript.

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