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Combined Use of Transcutaneous and End-Tidal Measures of Carbon Dioxide to Predict PCO_2 during General Anaesthesia in Adults

Yongming Cai*, Faling Yi, Man Luo, DeYu Tang, and Xianfa Cai

Department of Computer Science, South China Normal University, China

Abstract

Background: The aim of the present study was to integrate $PtcCO_2$ and $PetCO_2$ models to improve the accuracy and precision of PCO_2 measurements.

Methods: 26 ASA physical status I-III postoperative patients recovering from general anesthesia after surgery were selected for investigation. The carbon dioxide partial pressure (PCO_2) levels were determined six times during the anesthesia of each patient by using arterial blood gas analysis ($PaCO_2$), end-tidal ($PetCO_2$) and transcutaneous (PtcCO2) measurements. This study tested the hypothesis that combining $PetCO_2$ and $PtcCO_2$ measurements by a regression function, namely Pet_tcCO_2, will improve PCO_2 measurements during sedation. The Bland-Altman method was used for the statistical analysis, and a $p<0.05$ was considered statistically significant.

Results: A total of 156 data sets (i.e., $PaCO_2$, $PetCO_2$, and $PtcCO_2$) were obtained from 26 patients (63 ± 17 years old; 18 males, 8 females). The mean $PaCO_2$ was 44.3 ± 3.88 mm Hg. The mean $PetCO_2$ was 38.9 ± 4.01 mm Hg. The mean $PtcCO_2$ level was 46.1 ± 3.95 mm Hg. The average $PtcCO_2$-$PaCO_2$ difference was 3.8 ± 1.85 mm Hg. The average $PetCO_2$-$PaCO_2$ difference was -3.9 ± 1.95 mm Hg. When the value of Pet_tcCO_2 were combined, the fit equation was $Pet\_tcCO_2=7.24+0.36 \times PetCO_2+0.46 \times PtcCO_2$, R2= .66, $p<0.001$. The average Pet_tcCO_2-$PaCO_2$ difference was 2.1 ± 1.25 mm Hg.

Conclusions: The combined use of transcutaneous and end-tidal methods could help improve the accuracy and precision of PCO_2 measurements. Pet_tcCO_2 approach of combining $PetCO_2$ and $PtcCO_2$ techniques could be a new technology for PCO_2 measurement in spontaneously breathing patients have no serious lung disease.

Keywords: Arterial blood gas analysis; Anaesthesia; Noninvasive monitoring; End-tidal PCO_2; Transcutaneous PCO_2

Introduction

The early detection of hypoventilation in patients helps to prevent hypoxemia. Monitoring the partial pressure of carbon dioxide (PCO_2) is an essential means of assessing alveolar ventilation in patients during anesthesia, procedural sedation and emergency care [1-6]. Although the arterial blood gas(ABG) measurement of PCO_2 ($PaCO_2$) is regarded as the gold standard technique for PCO_2 assessments [7-9], it is an invasive and painful method that requires arterial blood gas analysis. Importantly, $PaCO_2$ also disrupts patient sleep patterns if performed at night.

In general, two different techniques for continuous non-invasive PCO_2 monitoring have been introduced into clinical practice, namely, end-tidal partial pressure of carbon dioxide ($PetCO_2$) and transcutaneous partial pressure of carbon dioxide ($PtcCO_2$) measurements [8,9]. These monitoring systems are noninvasive and display real-time data. $PetCO_2$ and respiratory waveforms from a capnograph can provide vital information about CO_2 retention and respiratory depression and can serve as an apnea monitor in spontaneously breathing patients [3,4,10]. $PtcCO_2$ sensors are not only widely used in neonatology and in critically ill infants but also used in adult patients during noninvasive mechanical ventilation, the transportation of critically ill adults, bronchoscopy etc [7,11,12].

However, according to the early studies, neither $PetCO_2$ nor $PtcCO_2$ monitoring has provided accurate estimates of $PaCO_2$ [13-15]. $PtcCO_2$ overestimates $PaCO_2$ and $PetCO_2$ significantly underestimates $PaCO_2$. Both the $PtcCO_2$ and $PetCO_2$ provide just an approximate estimation of $PaCO_2$. Clinical use of these monitors cannot be proposed under actual conditions but will be advantageous after correction of the limiting errors.

Therefore, if $PetCO_2$ and $PtcCO_2$ monitoring are determined to be just as accurate as invasive, intermittent $PaCO_2$ measurements, this continuous and non-invasive technique could become the preferred means for monitoring spontaneously breathing patients. The aim of this study was to investigate combining use of the $PetCO_2$ and $PtcCO_2$ methods to offset their deviation with $PaCO_2$. The new model namely Pet_tcCO_2 would take advantage of both $PetCO_2$ and $PtcCO_2$ methods to reduce deviations and improve measurement accuracy. The accuracy (i.e., mean difference of the measurements) and precision (i.e., standard deviation (SD) of measurements) of Pet_tcCO_2, $PetCO_2$, and $PtcCO_2$ techniques in monitoring PCO_2 were evaluated.

Patients and Methods

This study was approved by the local ethics committee for human research and was performed in accordance with ethical standards outlined in the October 2008 Declaration of Helsinki. Patients were informed of the planned study procedures and were asked for their informed consent. 26 ASA physical status I-III postoperative patients who recovering from general anesthesia after surgery were selected

***Corresponding author:** Yongming Cai, Department of Computer Science, South China Normal University, Guangzhou, 510006, P.R.China, E-mail: 78572951@qq.com

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for this prospective clinical-experimental study. Patients with severe cardiovascular or respiratory diseases, such as coronary heart disease, congestive heart failure, or chronic obstructive pulmonary disease were excluded from this study.

A 16-gauge (16-G) IV catheter was placed into the median cubital vein for fluid transfusion, and a 20-G arterial catheter was inserted into the left radial artery under local anesthesia for ABG sampling. The catheters were flushed using a pressure bag with 500 mL of heparinized saline. Before anesthesia, patients' heart rate (HR) and arterial blood pressure were recorded as the preinduction values. Anesthesia was induced with propofol (4 μg/mL using the target concentration infusion), fentanyl (2 μg/kg), and atracurium (0.6 mg/kg).

After surgery, patients were kept in the postanesthesia care unit where routine monitoring consisted of electrocardiogram and noninvasive arterial blood pressure. Patients' lungs were ventilated with 100% oxygen (2 L/min), and their tidal volume and respiratory rate were adjusted to maintain the $PetCO_2$ within 35 to 45 mm Hg. Anesthesia was maintained with propofol (2 g/mL with target concentration infusion model), desflurane (6%), and fentanyl to keep the blood pressure and HR within 20% of the preinduction values. Additional analgesia was provided by IV paracetamol and morphine as required. The study period started with patients' breathing spontaneously and receiving oxygen (3L/m^{-1}) through a facemask.

$PetCO_2$ was calculated by a portable capnometer (Tidal Wave Sp, Model 715, Novametrix Medical System Inc.) from a facemask. The device had a 5-Hz internal sampling rate and identified the highest PCO_2 level during the last third of expiration by using a built-in proprietary algorithm.

To monitor $PtcCO_2$, a TINA TCM4 device (Radiometer Copenhagen, Brønshøj, Denmark) was used. The TCM4 device provides $PtcCO_2$ information continuously and noninvasively. Before the sensor being placed on patients' ear lobes, the electrode membrane and skin at the sensor site were cleaned with alcohol, and the electrode was calibrated. The working temperature of the electrode was kept between 41 and 42°C.

A stationary ABL625 blood gas analyzer (Radiometer Copenhagen Brønshøj, Denmark) was used to determine arterial CO_2. ABG samplings were intermittently obtained for every patient at six time points (i.e., 15, 30, 45, 60, 90, and 120 min). The measurement started after the transcutaneous sensor had been on the patients' ear lobes for 15 minutes and the patients' blood pressure, HR, tidal volume, and respiratory rate were constant to obtain the stable $PtcCO_2$ and $PetCO_2$. $PetCO_2$ and $PtcCO_2$ were simultaneously and continuously monitored, and values were recorded at 1-min intervals before each arterial blood sample was taken.

Previous studies [5-7] showed that $PetCO_2$ and $PtcCO_2$ correlate well with $PaCO_2$. Most time $PtcCO_2$ values are higher than $PaCO_2$ and $PetCO_2$ values are lower than $PaCO_2$. We supposed the new Pet_tcCO_2 method could combine $PetCO_2$ and $PtcCO_2$ techniques to offset the deviation. Thus, this study integrated $PetCO_2$ and $PtcCO_2$ methods into a single approach, namely Pet_tcCO_2, and its accuracy was compared with that of $PaCO_2$ techniques. Because $PetCO_2$ and $PtcCO_2$ are linear correlation with $PaCO_2$, the combined value Pet_PtcCO_2 could be also linear correlation with $PaCO_2$. $PaCO_2$ was the dependent variable, while $PetCO_2$ and $PtcCO_2$ values were considered arguments. Experimental data were used to calculate the coefficient of the linear model.

Statistical analysis was performed with Statistical Product and Service Solutions (SPSS) software version 18. Linear relationships alone (i.e., correlations and correlation coefficients) do not adequately demonstrate the consistency between two clinical measurement techniques [16-18]. Bland-Altman analysis [19] was applied to assess the mean bias and limits of agreement (LOA) (± 2 standard deviation of bias) of $PaCO_2$ and $PtcCO_2$, $PaCO_2$ and $PetCO_2$, $PaCO_2$ and Pet_tcCO_2. According to the quality criteria for blood gas analyzer devices, variation in the mean bias of $PtcCO_2$ and $PetCO_2$ and $PaCO_2$ of 3.5% and a variation of LOA of 12.5% could be accepted. A mean bias ≤ ± 2.5 mm Hg and LOA ≤ ± 5 mm Hg was defined as good agreement. Differences were considered statistically significant when $p<0.05$.

Mahalanobis distance [20] was used to compare the similarity of PCO_2 measurements by $PaCO_2$, $PtcCO_2$, $PetCO_2$ and Pet_tcCO_2. The smaller Mahalanobis distance of the two methods means the more similarity of the two methods.

The following equation is defined to calculate the deviation of the different methods.

$$D_{X,Y} = \sqrt{\sum_{i=1}^{6} (\frac{X_i - Y_i}{S_i})^2} = \sqrt{(X-Y)^t S^{-1} (X-Y)} \quad (1)$$

Note that X=$PaCO_2$ *and* $Y \in \{PetCO_2, PtcCO_2, Pet\_tcCO_2\}$. S is a covariance matrix. The variable i represents the time point of the measurements. And $D_{X,Y}$ represents the Mahalanobis distance between the measure method of X and Y.

Results

A total of 156 data sets (i.e., $PaCO_2$ (immediate response mobile analyzer (IRMA)), $PetCO_2$, and $PtcCO_2$) from 26 patients (18 males, 8 females) were obtained after receiving informed consent. Patients were 63 ± 17 years old (range, 31–81 years) and had body mass indices of 28.0 ± 7.9 kg.m^{-2}.

All data sets (n=156) were complete, and the different measurement techniques were performed without complications. Table 1 shows the results of $PaCO_2$, $PtcCO_2$, and $PetCO_2$ measurements at six time points: 15, 30, 45, 60, 90, 120 min.

In these samples, both $PtcCO_2$ and $PetCO_2$ were correlated with $PaCO_2$. As shown in Figure 1A and Figure 2A, the linear regression equations between $PtcCO_2$ and $PetCO_2$ and $PaCO_2$ were obtained ($PaCO_2$=0.63×$PtcCO_2$+12.89, r^2=0.53, $p<0.01$; $PaCO_2$=0.59×$PetCO_2$+19.35, r^2=0.45, $p<0.05$). In addition, $PtcCO_2$ was also correlated with $PaCO_2$ at each time point (r^2=0.59, 0.65, 0.51, 0.61, 0.66 and 0.54, respectively, $p<0.05$). And $PetCO_2$ was also correlated with $PaCO_2$ at each time point too (r^2=0.47, 0.44, 0.53, 0.65, 0.57 and 0.56, respectively, $p<0.05$).

	15 min (mm Hg)	30 min (mm Hg)	45 min (mm Hg)	60 min (mm Hg)	90 min (mm Hg)	120 min (mm Hg)	Total (mm Hg)
$PaCO_2$	40.5 ± 3.76	42.9 ± 4.72	45.8 ± 2.76	46.2 ± 3.44	43.5 ± 2.94	41.6 ± 1.99	44.3 ± 3.88
$PetCO_2$	36.3 ± 4.13	38.8 ± 3.94	39.2 ± 2.84	39.6 ± 3.91	37.9 ± 5.11	36.9 ± 4.23	38.9 ± 4.01
$PtcCO_2$	39.7 ± 3.62	44.1 ± 4.34	47.5 ± 5.37	47.8 ± 3.54	46.7 ± 2.35	45.1 ± 3.82	46.1 ± 3.95

Table 1: Comparison of PCO_2 values determined using the various methods.

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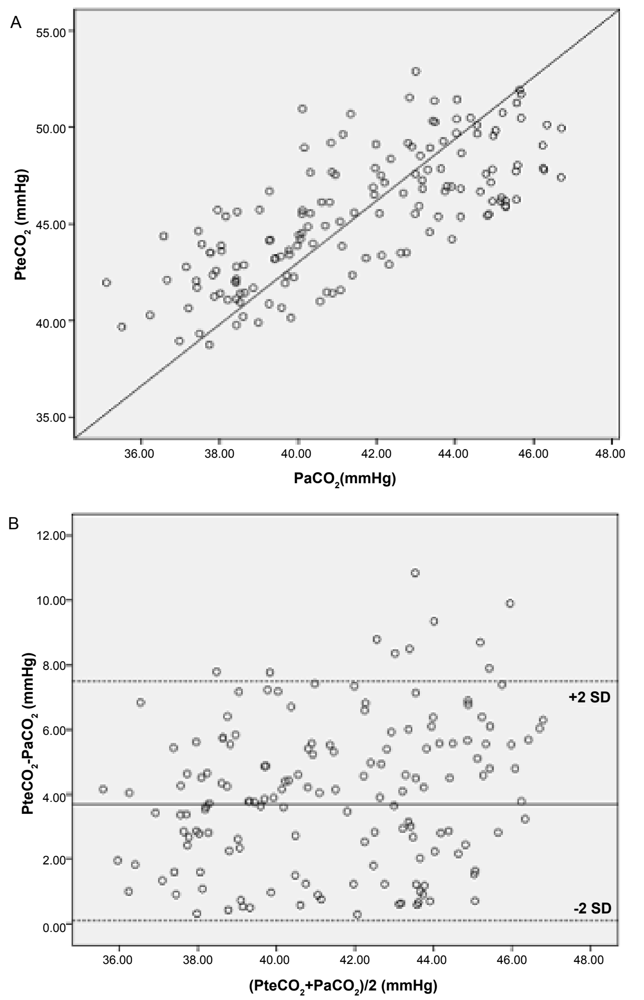

Figure 1: (A) Correlation between $PaCO_2$ and $PtcCO_2$ shows a coefficient r=0.73. Regression analysis: $PaCO_2$=0.63×$PtcCO_2$+ 12.89, r=0.73, p<0.01. (B) Bias and LOA between $PaCO_2$ and simultaneously measured PtcCO2 measurements. The solid line represents the mean of the differences (= bias) between $PaCO_2$ and $PtcCO_2$ (3.8±1.85 mmHg). The dashed lines are equivalent to 2SDs of the means (= LOA).

Using a Bland-Altman analysis to determine LOAs (i.e., mean ± 2SD), the three techniques showed different accuracies (Figures 1B and 2B). The bias and precision of transcutaneous measurements (3.8 ± 1.85 mm Hg, not significant (n.s.)) were comparable and revealed no significant differences. The bias and precision of end-tidal measurements (-3.9 ± 1.95 mm Hg, n.s.) were comparable and revealed no significant differences too. Results showed a linear relationship between $PetCO_2$ and $PaCO_2$, and the $PetCO_2$ method seemed to underestimate $PaCO_2$ values. The $PetCO_2$ technique resulted in 6 outliers with a negative bias. Therefore, this technique was below the given interval (mean ± 2 SD), which causes an underestimation of actual PCO_2 values determined by reference measurements. An analysis of the transcutaneous measurement revealed 10 outliers above the given interval with a positive bias. This finding suggests that the $PtcCO_2$ technique systematically overestimated PCO_2 levels.

The previous results showed that $PetCO_2$ and $PtcCO_2$ values were significantly correlated with the $PaCO_2$. SPSS was used to calculate multiple linear regression equation Parameters. The linear regression module was selected. $PetCO_2$ and $PtcCO_2$ acted as the independent variables, and $PaCO_2$.acted as the dependent variable. A best-fit formula (Pet_tcCO2=7.24+0.36×$PetCO_2$+0.46×$PtcCO_2$, R^2=0.66, p<0.01; Figure 3) and curve were obtained. Pet_tcCO_2 value was obtained from the formula. The difference between Pet_tcCO_2 and $PaCO_2$ was shown in Figure 4. The bias and precision of Pet_tcCO_2 measurement (2.1 ± 1.25 mm Hg, n.s.) were comparable and revealed no significant differences to $PaCO_2$.

In order to compare $PtcCO_2$ and $PetCO_2$ and Pet_tcCO_2 which had the smallest deviation to the $PaCO_2$, Mahalanobis distances from $PaCO_2$ to $PtcCO_2$ and $PetCO_2$ and Pet_tcCO_2 were calculated through the experiment data. The result was showed in Figure 4. The Mahalanobis distance between $PetCO_2$ and $PaCO_2$ was 83.4, $PtcCO_2$ and $PaCO_2$ being 51.3, Pet_tcCO_2 and $PaCO_2$ being 21.6, respectively. Pet_tcCO_2 was found to be more similar to $PetCO_2$ and $PtcCO_2$ methods.

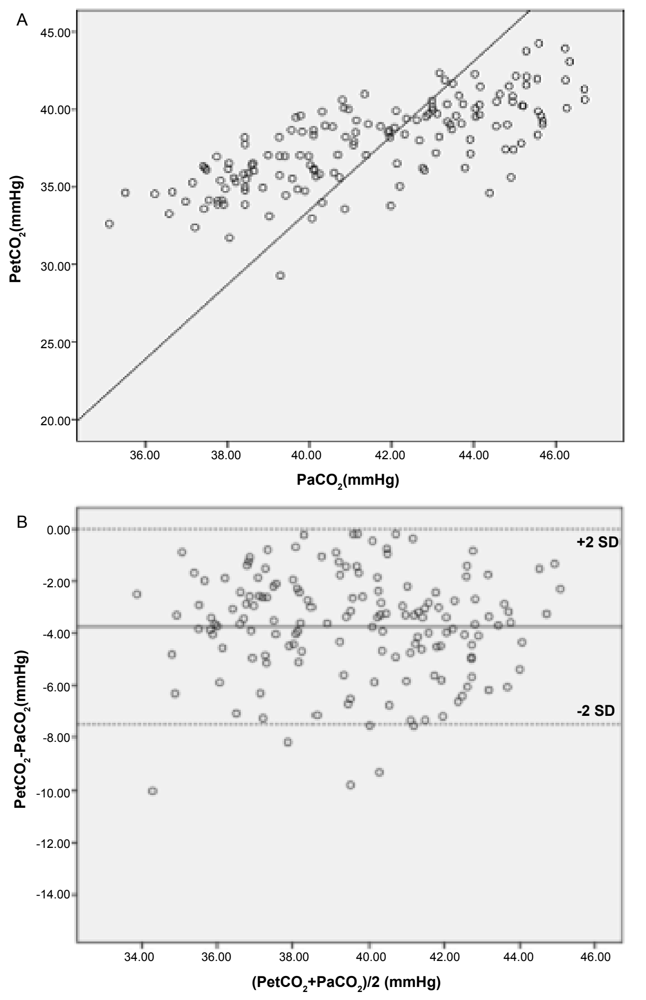

Figure 2: (A) Correlation between $PaCO_2$ and $PetCO_2$ shows a coefficient R^2=0.84. Regression analysis: $PaCO_2$ =0.51 × $PetCO_2$+19.35. (B) Bias and LOA between $PaCO_2$ and simultaneously measured $PetCO_2$ measurements. The solid line represents the mean of the differences (= bias) between $PaCO_2$ and $PetCO_2$ (–3.9 mmHg). The dashed lines are equivalent to 2SDs of the means (= LOA).

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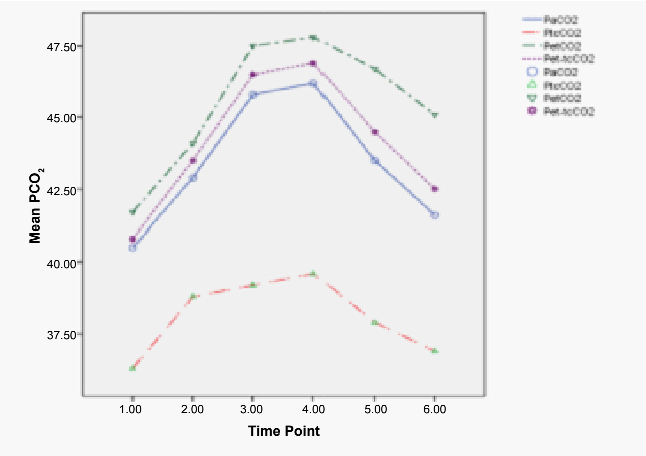

Figure 3: Pet_tcCO_2 matched curve of PtcCO_2 and PetCO_2 was added to Average course of PaCO_2 and PtcCO_2 and PetCO_2 measurements during sedation. Arterial samples were drawn at six time points: 15, 30, 45, 60, 90, 120 min after the start of data recording; PtcCO_2 and PetCO_2 were measured continuously.

Discussion

The purpose of this study was to combine the use of PetCO_2 and PtcCO_2 to improve the acquisition and reliability of PCO_2 measurements of spontaneously-breathing patients after general anesthesia. Some of the earlier studies have confused the role of capnography or transcutaneous in predicting PaCO_2. Russel et al. [21] found significant correlation between capnography and arterial blood gas measurements. Belpomme et al. [22] reported that wide variations in gradients exist between PaCO_2 and PetCO_2 values that depend on patient conditions. They concluded that the PetCO_2 technique is not useful in pre-hospital ventilation management (bias up to 8.6 mm Hg). On the contrary, Yanagidate et al. [10] concluded capnograph can provide vital information about CO_2 retention and respiratory depression and can serve as an apnea monitor in spontaneously breathing patients. Some research reported that transcutaneous PtcCO_2 monitoring can continuously and reliably measure PaCO_2 in pediatric and geriatric patients during surgery [8,23,24]. But some research found the results from transcutaneous PtcCO_2 have been shown to be delayed [7,8]. Furthermore, some studies were controversial in terms of the reliability of PtcCO_2 [7,25,26]. Therefore the relationships and differences between PetCO_2 and PtcCO_2 methods and PaCO_2 method should be made clear.

Our study compared PetCO_2 and PtcCO_2 methods with PaCO_2 method. Results showed that measurements by transcutaneous methods on patients undergoing general anesthesia were in good agreement with PaCO_2 measurements (3.8 ± 1.85 mm Hg, n.s.). The PetCO_2 method also had acceptable results (-3.9 ± 1.95 mm Hg, n.s.). We found the trend PtcCO_2> PaCO_2>PetCO_2 from the result. It was the overall trend, which was based upon means of PCO_2 at each time point. Although some individual trend differed from the trend listed above. We found that PtcCO_2 was over estimated compared with PCO_2 and PetCO_2 was underestimated compared with PCO_2 most of the time. PtcCO_2 measurements were almost all in the positive direction beside PaCO_2 while PetCO_2 were in the negative direction. So we supposed that combining these two methods measured value would offset the error between them. This is the original idea when we carried out the experiment. We synthesized PetCO_2 and PaCO_2 measurements into a linear regression model and obtained the equation Pet_tcCO2=7.24+0.36×PetCO_2+0.46×PtcCO_2, R^2=0.66, p<0.01.

The experiment result showed the trend that PtcCO_2 was higher than PaCO_2. The main reason was that the sensor temperature improved local perfusion (capillary arterialization) and increased

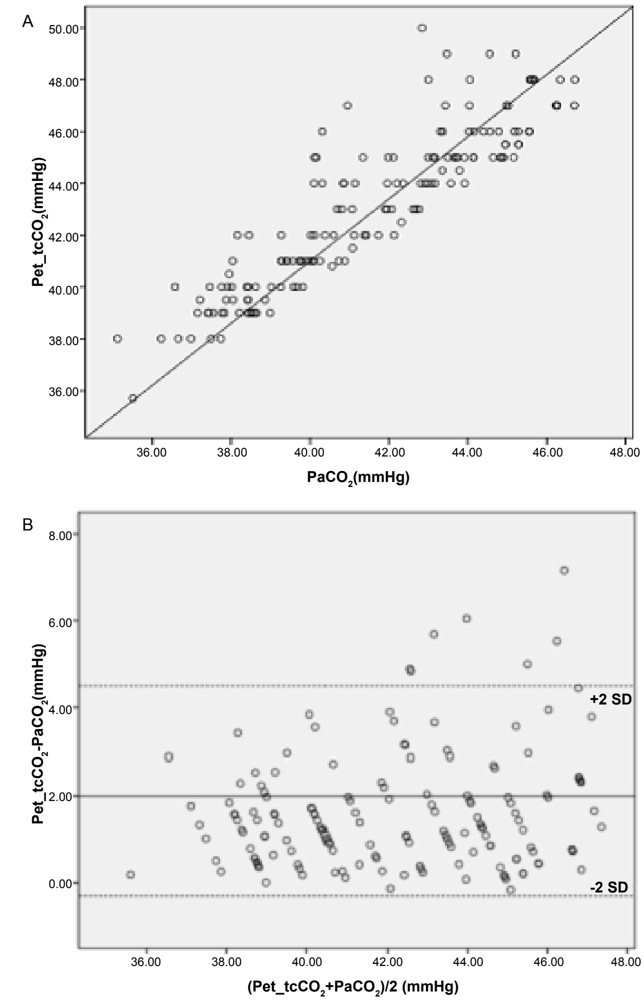

Figure 4: (A) Correlation between PaCO_2 and Pet_tcCO_2 shows a coefficient R^2=0.66. Regression analysis: PaCO_2 = 0.83 × Pet_tcCO_2+5.47. (B) Bias and LOA between PaCO_2 and simultaneously measured Pet_tcCO_2 measurements. The solid line represents the mean of the differences (= bias) between PaCO_2 and PetCO_2 (2.0 mmHg). The dashed lines are equivalent to 2SDs of the means (= LOA).

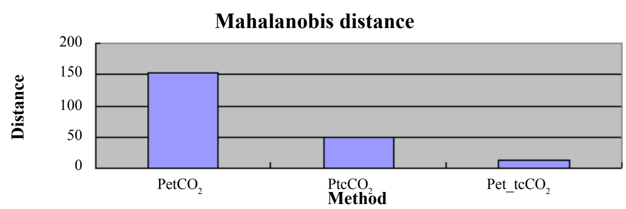

Figure 5: The Mahalanobis distance between PetCO_2 and PaCO_2 was 83.4 , PtcCO_2 and PaCO_2 was 51.3, Pet_tcCO_2 and PaCO_2 was 21.6, respectively. Pet_tcCO2 was found to be more similar than PetCO_2 and PtcCO_2 methods.

local production of carbon dioxide in the tissue, which leads to falsely high measurements [14]. On the contrary, $PetCO_2$ measurement was always underestimated compared with PCO_2 because gas from lung units that were ventilated but not perfused (alveolar dead space or high ventilation-perfusion ratio units) contains little or no carbon dioxide. When this gas was mixed with the gas from „normal" lung units, the resultant concentration of carbon dioxide was reduced in the expired gas. This phenomenon accounts for the fact that $PetCO_2$ was lower than $PaCO_2$ [27]. Many authors have reported the relationship between $PetCO_2$ and $PaCO_2$ during anesthesia. Nunn and Hill [28] reported that mean $PaCO_2$ exceeded mean $PetCO_2$ by 4.5 to 4.7 mm Hg during anesthesia, with either controlled or spontaneous respiration.

Most investigators focused their reports on the accuracy and precision of $PtcCO_2$ or $PetCO_2$, whereas the reliability of them were not or less discussed. We combined used of $PtcCO_2$ and $PetCO_2$ these two methods and this can not only help to improve the accuracy and precision but also help to improve the reliability. Bland-Altman analysis was used in the present study to measure the agreement between Pet_tcCO_2 and $PaCO_2$. Previous studies showed that a difference of 5 mm Hg or less between $PaCO_2$ and other noninvasive measurements was a clinically acceptable difference [19,29,30]. The mean of Pet_tcCO_2 sub $PaCO_2$ difference was 2 mm Hg, which indicated that there was no difference between Pet_tcCO_2 and $PaCO_2$. The Mahalanobis distance between Pet_tcCO_2 and $PaCO_2$ was 21.6 which was smaller than $PtcCO_2$ and $PetCO_2$, which meant Pet_tcCO_2 was more similar to $PtcCO_2$ and $PetCO_2$. The scatter diagram of Pet_tcCO_2 and $PaCO_2$ showed that 7 points were outside of the acceptable range. While the scatter diagram of $PetCO_2$ and $PaCO_2$ showed that 6 points were outside of the acceptable range. In fact, no new equipment was used to measure the PCO_2 so that the precision could not be improved by this method.

The combined Pet_tcCO_2 technology can be easily applied to Clinical application. Pet_tcCO_2 model could be constructed as software embedded into the original anesthesia machine or ventilator equipment. Most of the existing monitoring devices have a digital output interface. $PetCO_2$ and $PtcCO_2$ data can be easily collected and put into the processing equipment such as the anesthesia machine or ventilator equipment. $PetCO_2$ and $PtcCO_2$ act as the input variables, clinicians can see the Pet_tcCO_2 value shown from the software. Because the measure methods of $PtcCO_2$ by transcutaneous and $PetCO_2$ by end-tidal carbon dioxide are monitored normally, no additional cost will be needed to carry out the new approach.

Although this combine method could improve higher accuracy for the measurement of PCO_2 in general anaesthesia on adult patients, the two different devices need to be used on the patients. For those who do not need these devices for real time monitor, the costs will be increased. But for the serious patients who want to have a ideal way to monitor PCO_2 and release pain, this technology is acceptable.

When preparing to use this new method of measuring PCO_2, it is important to consider the patients' basic health condition. Care should be taken to ensure that the patients' face mask should not leak gas. Transcutaneous capnometry has already been established in clinical applications. In order to make the combine module simple, findings from this study were based on patients with stable cardiac statuses, stable body temperatures, no lung disease, and normal capnograms. Thus, further experiment should be carried out on patients with severe respiratory failure to be monitored using this approach. The sample size of this study was relatively small. Comparisons of complication rates for the two different monitoring techniques will require larger patient numbers because complications in patients undergoing procedural sedations were rare in the emergency department studied. Thus, this study would need to be conducted with a larger sample size to prove its results. With small data sets, the use of artificial intelligent technology, such as support vector machines, can be used to train and obtain model parameters that realize individuation monitors and improve accuracy.

Conclusions

The combined use of transcutaneous and end-tidal methods could help improve the accuracy and precision of PCO_2 measurements. Results of this study demonstrate that the Pet_tcCO_2 approach of combining $PetCO_2$ and $PtcCO_2$ techniques is a new technology for PCO_2 measurement in general anaesthesia on adults patients who have no serious lung disease.

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