Non-Invasive Measurement of Arterial pH During Cardiopulmonary Bypass

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Abstract—Blood pH is an essential parameter to determine the patient's acid-base status during cardiopulmonary bypass. To date, continuous pH measurement is usually done by continuous blood sampling using an expensive disposable sensor. This paper shows the feasibility of measuring arterial pH from the partial pressure of carbon dioxide (P_aCO_2) using arterial blood gas analysis. Further, the effect of hyperglycemia on pH estimation is included to show the necessity of combining glucose monitoring with P_aCO_2 monitoring. 245 blood samples from patients who underwent cardiopulmonary bypass were used. Patients with renal failure were excluded from the study. In this study, three groups of samples were included, A: all blood samples, B: blood samples with glucose $\leq$ 200 mg/dL, and C: blood samples with glucose > 200 mg/dL. A linear approximation based on the least-squares criterion was used to derive the best-fit equation. Our results indicate that there is no significant difference among the models. Further, there is a significant association between arterial pH and P_aCO_2 with a p-value < 0.001 and RMSE of about 0.04. The present findings highlighted that arterial pH could be estimated from P_aCO_2. Additionally, hyperglycemia did not affect the hypothesis of the general relationship between pH and P_aCO_2.

Keywords—cardiopulmonary bypass, arterial pH, glucose, P_aCO_2, ordinary least square

1 Introduction

Blood gases are routinely measured to evaluate the patient's physiological state during cardiopulmonary bypass (CPB). Usually, this is done by laboratory blood sampling over a specified period (usually 30 min) or by using an inline blood gas monitoring system. The latter is considered better as it enables the perfusionists for real-time patient management [1]–[3]. However, this system is limited due to the high cost of disposable sensors. The blood oxygenation balance primarily depends on the oxygen supply and carbon dioxide (CO_2) removal, thus regulating blood pH. CO_2 is a part of the bicarbonate buffer system, which works through reactions to reduce the effects of excessive or insufficient CO_2 that would make pH acidotic or alkalotic. In the presence of an excess of CO_2, bicarbonate ions leave the Red Blood Cells (RBCs) and enter the plasma in response to the increment of CO_2 in the blood, thus causing the generation of hydrogen cations and bicarbonate anions. To maintain electrical balance, chloride ions enter the RBCs. The bicarbonate is either excreted by kidneys or reabsorbed and returned to the blood. The hydrogen ions (H^+) combine with ammonia and they are released into the urine. This reduction in H^+ ions raises the blood pH [4]. Compared to H^+ ions, CO_2 has a higher fat solubility, which makes the acid-base changes caused by respiratory acidosis and alkalosis faster than those caused by metabolic acidosis or alkalosis in the extracellular and intracellular fluids. Therefore, when pH changes are caused by the respiration process rather than metabolism, they are expected to have a more significant impact on the tissue [5]. Human body physiology is altered during CPB, and it is often associated with significant physiological disturbances [6], [7]. Most patients under CPB tend to have high levels of blood glucose despite the absence of any medical history of diabetes [8]. Hyperglycemia is associated with cardiac surgery with or without CPB due to the administration of glucogenic catecholamines [9]. Recent anesthesia protocols suggested that intraoperative blood glucose levels greater than 200 mg/dL are regarded to be hyperglycemic and should be treated [10]. Previous studies revealed that blood glucose affects the strong ion difference (SID) by increasing dilution of extracellular substance [11], which in turn affects the acid-base balance based on Stewart's physicochemical equations of acid-base balance [12]. Consequently, the blood glucose level affects the acid-base balance, and SID disturbance is accompanied by respiratory compensation [13].

Recently, machine learning methods are widely used in medical filed for the detection [14], diagnosis [15], and classification [16] of diseases.

Reporting the strong associations between pH and partial pressure of carbon dioxide (PCO_2), few studies were conducted for measuring blood pH from PCO_2 along with other variables. Matsui et al. (2006) estimated arterial pH using linear regression of the concentration of exhaled gases (CO and CO_2) and vital signs (heart rate, respiratory rate, and surface temperature) that were measured using non-contact methods in hypovolemic animals. The results depicted a significant association between the variables [17]. Bulucu et al. (2014) conducted a study of 21,586 patients considering venous blood gas analyses to predict the venous pH from the bicarbonate and carbon dioxide content. It was found that there is a strong correlation between the estimated and measured venous blood pH [18]. However, the bicarbonate is already calculated in modern blood gas analysis machines using Henderson–Hasselbalch equation [19]–[21].

Based on the above-mentioned facts and studies, the idea is to create a technique including the patient's blood gas analysis data, which can predict blood pH from arterial partial pressure of carbon dioxide (P_aCO_2).

To our knowledge, this work represents the first attempt to measure arterial pH noninvasively for patients who are under CPB by analyzing and evaluating the association between arterial pH and P_aCO_2 and creating a model used for arterial pH estimation from P_aCO_2, which can be noninvasively measured using an oxygenator exhaust capnometry [22]. In addition, the impact of hyperglycemia on the model is studied to show whether pH estimation is glucose-dependent or not.

2 Material and methods

2.1 Patients and data collection

In this study, 245 blood samples were involved [23]. These blood samples were taken from 60 patients admitted to Ibn Al-Bitar Specialized Center for Cardiac Surgery in Iraq. The mean patient age was 50.0 years (SD = 22.21, range = 5-85). Sixty-two percent of patients were male. Alpha-stat pH management was used during CPB at a temperature range of 18-37°C. Medtronic® Affinity Fusion oxygenators were used for all patients who underwent coronary artery bypass graft and valve replacement with CPB, from November 2020 to January 2020. Blood samples were routinely taken with heparinized syringes every 30 min and analyzed using RAIOMETER ABL800 FLEX. Acid-base disturbances are common in patients with chronic renal failure [24]; therefore, patients with chronic renal failure were excluded from the study as there are other factors to be considered, such as blood pressure and body surface area, which were not measured during data collection [10]. The study was approved by Ibn Al-Bitar Specialized Center for Cardiac Surgery research committee. All experimental protocols were done according to the declaration of Helsinki and his later amendments.

2.2 Statistical analysis

We started by investigating all the data as per group (A), without taking into account the effect of the elevated blood glucose on pH. For exploring glucose effect, group A was divided into two subgroups based on blood glucose level: group B, which involves blood samples with glucose ≤ 200 mg/dL; and group C includes blood samples with glucose > 200 mg/dL, which is considered as hyperglycemic condition [10]. P_aCO_2 and pH statistics are presented in Table 1. Preliminary, the normality of data was examined using distribution plots (Figure 1) and Shapiro Wilk test (Table 2). Pearson's correlation coefficient was used to measure the strength of association between arterial pH and P_aCO_2.

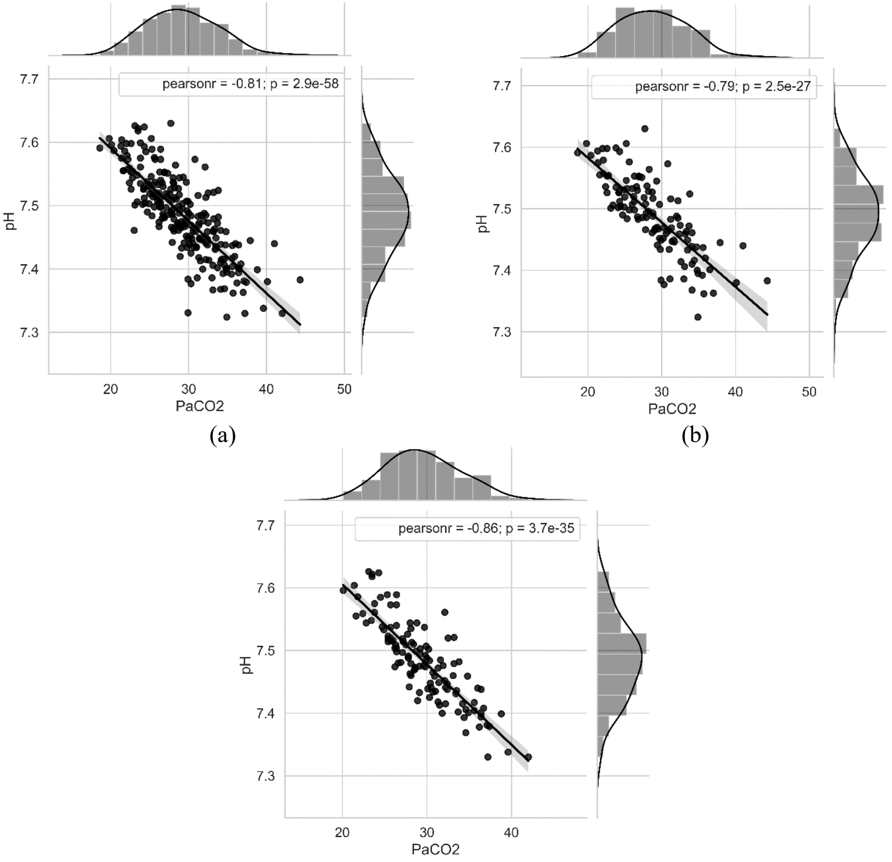
To obtain mathematical models relating P_aCO_2 and pH, we used the linear approximation method based on the ordinary least squares criterion (OLS). The dataset was divided into 70% and 30% for the training and testing set, respectively. The coefficient of determination (R^2), the root mean square error (RMSE) between predicted and measured values, and the coefficient of variance (CV) were used to assess model accuracy. The statistical analysis and model fitting was implemented using Python Sklearn library.

Table 1. Statistical information (Mean ± standard deviation) of blood samples

Group	Blood samples	pH	P_aCO_2 (mmHg)	Glucose (mg/dL)
A	245	7.488± 0.067	28.966±0.067	195.5078±48.025
B	125	7.492±0.0669	28.743±4.835	160.768±25.103
C	120	7.484±0.066	29.499±4.403	237.816±27.667

Table 2. Shapiro Wilk test results for pH and P_aCO_2

Groups	Parameters	Test Statistic (W)	P-Value
A	pH	0.99607	0.75231
	P_aCO_2	0.99243	0.19792
B	pH	0.99342	0.83635
	P_aCO_2	0.98851	0.39337
C	pH	0.99349	0.85271
	P_aCO_2	0.99281	0.79517



(a)

(b)

(c)

Fig. 1. Joint plot showing both histogram distribution of pH and P_aCO_2 and a scatter plot along with the regression line to illustrate the association between the two parameters for (a) group A, (b) group B, and (c) for group C

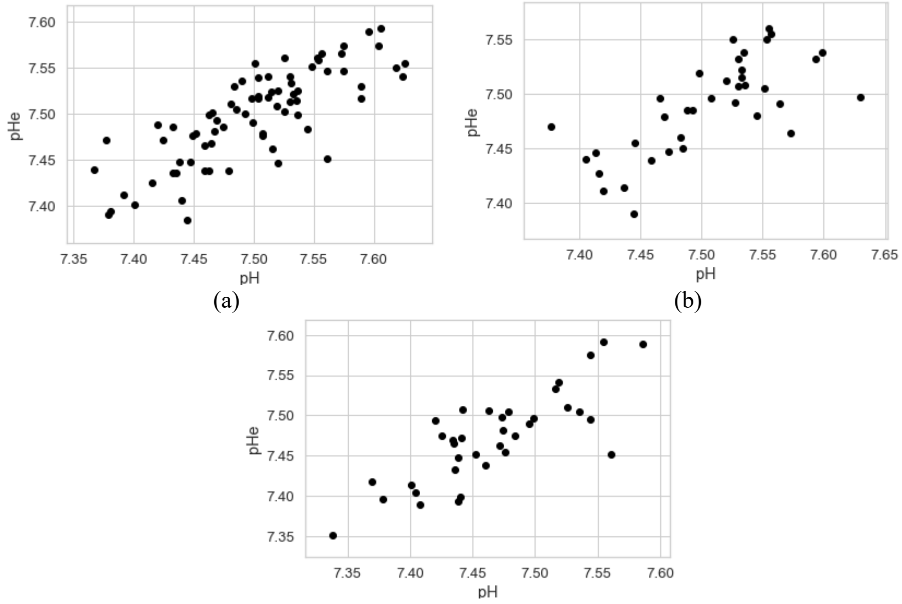
3 Results

As shown in Table 1, blood glucose level nearly has no impact on the variability of blood pH (±0.067 units). Blood pH shows a linear relation with P_aCO_2 where Pearson's correlation coefficient suggests a high negative correlation (-0.81, -0.79, and -0.86 for groups; A, B, and C, respectively) as reported in Figure 1.

The OLS results are presented in Table 3, and the relationship between estimated and real pH is illustrated in Figure 2. The slope (Coef) represents the reduction in pH with each unit increase in P_aCO_2 (towards acidity). In the group A dataset, the association between P_aCO_2 and pH as the linear best-fit equation is in the form: pH = 7.837-0.01198 × P_aCO_2, with RMSE of 0.040 units and R^2 of 0.607. Further, the CV of groups B and C are equal. To assess model performance, the distribution of residuals was graphically evaluated using quantile-quantile (Q−Q) plot (Figure 3).

Table 3. Prediction metrics from OLS

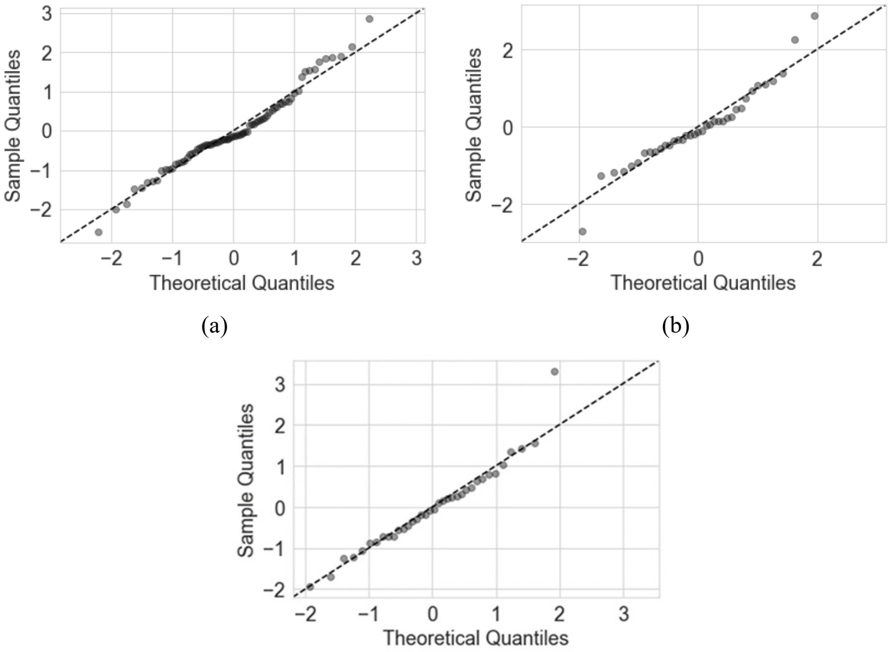
Groups	**A**	**B**	**C**
Coef	-0.01198	-0.01143	-0.01361
Intercepts	7.83798	7.81725	7.88503
p-value	<0.001	<0.001	<0.001
RMSE	0.0404	0.0446	0.0349
R^2	0.6070	0.4060	0.6715
Pearson's r	0.7794	0.6927	0.8315
CV	0.00702	0.00653	0.00653



(a) (b)

(c)

Fig. 2. The association between real and estimated pH for (a) group A (R^2=0.6070, RMSE= 0.0404), (b) group B (R^2=0.0446, RMSE= 0.4060), and (c) for group C (R^2=0.6715, RMSE= 0.0349)



(a)

(b)

(c)

Fig. 3. Q-Q plot of the residuals of the OLS models for (a) group A, (b) group B and (c) for group C

4 Discussion

The relation between elevated blood sugar and acidosis [11] suggested that blood glucose affects pH estimation. The key finding of this study is that for pH monitoring from P_aCO_2, glucose monitoring does not affect the relationship as the results demonstrated that there are no significant differences between groups A, B, and C. The difference between estimated and real pH (reported in Figure 2) is obvious as blood acidity is precisely described by three independent parameters: PCO_2; SID; and total weak acid concentration [25]. R^2 suggests that about 60% of the variance in pH can be explained by P_aCO_2 individually. Our results show that within the range of P_aCO_2 (35–48 mmHg), the OLS is useful to predict pH from P_aCO_2 (p-value < 0.001), and with a bias of 0.04.

5 Conclusion

This paper aimed to show the feasibility of measuring blood pH noninvasively during CPB and if it should be combined with blood glucose monitoring or not. The results clarified that pH could be estimated from P_aCO_2 (p-value < 0.001, RMSE of 0.04, R^2 of 60%) using OLS, and the process is not affected by blood glucose level during CPB.

Eventually, the suggested formulation will be examined using oxygenator exhaust capnometry along with considering the influence of renal failure, to enhance the confidence of the predictive results given via the suggested method, thus facilitating the translation of its applicability for non-invasive arterial pH monitoring. This study is significant for Iraq and the first in the field due to the deficiency in using expensive disposable sensors in cardiac centres.

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7 References

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