Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Research Article

Changes in Arterial to End Tidal CO_2 Difference During Repairing Heart Surgery: Cyanotic Versus Acyanotic Congenital Heart Diseases

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ARTICLE INFO

Article history:
Received 29 January 2025
Revised 21 February 2025
Accepted 05 February 2025

Keywords:
Congenital heart defects;
Pulmonary gas exchange;
Cardiac surgical procedures;
Arterial blood gases;
Hemodynamics

ABSTRACT

Background: End-tidal carbon dioxide ($EtCO_2$) can approximate the arterial pressure of carbon dioxide ($PaCO_2$) in children without underlying congenital heart defects. However, $EtCO_2$ may underestimate $PaCO_2$ in these children, especially during repair procedures. The $PaCO_2$ to $EtCO_2$ difference (Δ $PaCO_2$-$EtCO_2$) may be significant in children with congenital heart disease (CHD) and can be notably influenced by surgical procedures. Postoperatively, the Δ $PaCO_2$-$EtCO_2$ might not remain consistent; thus, arterial blood gas (ABG) analysis may need to be repeated regardless of capnography findings. This hypothesis was tested in our study on children with cyanotic and acyanotic heart defects undergoing corrective surgeries.

Methods: In this cross-sectional study, hospital records of all children under 12 years of age with ASA II-III and cyanotic or acyanotic heart defects who were candidates for elective angiography were reviewed. $EtCO_2$ was measured by lateral aspiration capnography. Simultaneous measurements of $EtCO_2$ and $PaCO_2$ were collected before and after the intervention.

Results: Significant changes were observed in serum HCO_3 concentration and the PaO_2/FiO_2 ratio, both of which significantly decreased after the repair surgery. However, the change in Δ $PaCO_2$-$EtCO_2$ remained insignificant postoperatively. In the cyanotic group, in addition to a significant reduction in serum HCO_3 value and an increase in the PaO_2/FiO_2 ratio after the intervention, we found a significant decrease in Δ $PaCO_2$-$EtCO_2$.

Conclusion: Arterial blood gas analysis during repair surgery should be repeated in the cyanotic congenital heart defects group due to the intraoperative variability of Δ $PaCO_2$-$EtCO_2$, but not in the acyanotic heart defects group due to the stability of this difference. Therefore, $EtCO_2$ assessed by capnography can estimate $PaCO_2$ in children with acyanotic heart defects, but not in those with cyanotic heart defects.

The authors declare no conflicts of interest.
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Introduction

Direct measurement of $PaCO_2$ by arterial blood sampling is the gold standard for assessing ventilation efficacy. End-tidal carbon dioxide ($EtCO_2$) monitors the maximum expired carbon dioxide concentration during a respiratory cycle. As the standard of care in the operating room, it is a continuous, non-invasive method for $PaCO_2$ monitoring [1]. However, several patient-related factors can affect the correlation between EtCO2 and arterial pressure of carbon dioxide ($PaCO_2$) [2]. The difference in $PaCO_2$ between blood (alveolar capillaries) and alveolar gases in children without cardiovascular disease is usually small, making EtCO2 a reliable estimator of $PaCO_2$. Yet, this pressure difference can increase in patients with cardiovascular diseases, attributed to an abnormal ratio of physiological dead space to tidal volume and increased venous mixing.

The ratio of physiological dead space to tidal volume primarily determines the pressure difference between $EtCO_2$ and $PaCO_2$ in individuals with normal cardiovascular function. In such cases, venous mixing is numerically less significant due to the small difference between CO_2 pressure in the vein and the mixed artery, as well as the small size of the shunt. Patients with congenital heart disease (CHD) exhibit variable ventilation-to-perfusion ratios, leading to an abnormal physiological dead space-to-tidal volume ratio and abnormal venous mixing, affecting the pressure difference between $EtCO_2$ and $PaCO_2$ [3]. $PaCO_2$ closely approximates $EtCO_2$ pressure during anesthesia in children with normal cardiovascular function [4].

In cyanotic children, the right-to-left shunt significantly impacts gas exchange. The addition of venous blood, relatively low in oxygen and high in carbon dioxide, to the heart ventricle not only decreases arterial oxygen saturation but also increases arterial PCO_2 to levels higher than PCO_2 in the pulmonary, alveolar, and end capillaries [5]. This reduction in carbon dioxide removal efficiency is a direct consequence of a right-to-left shunt, leading to changes in both $EtCO_2$ and $PaCO_2$ [6]. Right-to-left shunt also reduces pulmonary blood flow, potentially causing alveolar perfusion, further increasing alveolar dead space, and affecting the pressure difference between $EtCO_2$ and $PaCO_2$ [7].

Measuring the pressure difference between $EtCO_2$ and $PaCO_2$ can reveal the effects of hypoperfusion in children with cyanotic and acyanotic CHD. $EtCO_2$ values, assessed by capnography, and $PaCO_2$, determined by arterial blood gas (ABG) analysis, are physiologically related with a slight difference. However, this difference appears significant in children with both cyanotic and acyanotic CHD [8]. This significant difference in parameters assessed by capnography and ABG may become more pronounced in patients undergoing cardiac repair surgeries for CHD [9]. At the start of each operation, an ABG is typically taken and compared with capnography, often making further ABG analysis unnecessary until the operation's end. Nonetheless, based on clinical observations, we aimed to demonstrate that the difference between $EtCO_2$ and $PaCO_2$ may not remain fixed postoperatively. Hence, ABG may need to be repeated independently of capnography findings. This hypothesis was tested in children with both cyanotic and acyanotic CHD undergoing corrective surgeries.

Methods

In this cross-sectional study, we included hospital-recorded files of all children under 12 years of age with ASA II-III who had cyanotic or acyanotic congenital heart defects (CHDs) and were candidates for elective angiography at the Pediatric Medical Center of Tehran University of Medical Sciences until the end of 2018. The university ethics committee approved the study, and written consent was obtained from the patients' parents (IR.TUMS.CHMC.REC.1397.082). The exclusion criteria included reluctance of the child's parents to cooperate in the project, high pulmonary artery pressure (close to systemic blood pressure), significant intraoperative bleeding, and prolonged angiography time that could lead to changes in arterial blood gas results. Cardiac angiography, which requires an arterial blood sample during the operation, formed the basis for patient selection, and there were no ethical concerns regarding obtaining the arterial blood sample.

Initially, 0.5 mg/kg midazolam syrup was administered to the patients. Once they had calmed down, the patients were taken to the catheterization laboratory. After standard monitoring was installed and oxygen was started via a mask, 0.5 to 2.0 µg/kg fentanyl was injected, and anesthesia was induced with 1 to 2 mg/kg of propofol. After achieving sufficient depth of anesthesia, endotracheal intubation was performed, and the patients were connected to a ventilator. If necessary, an arterial line was established using 22 or 24-gauge arterial catheters from the patient's radial artery. Anesthesia was maintained with 1.5% isoflurane, and the dose of fentanyl was repeated at one-hour intervals if needed. Arterial blood samples were obtained through the arterial line and analyzed using the ABG device (Gem Premier 3000). $EtCO_2$ was measured by lateral aspiration capnography. Simultaneous measurements of $EtCO_2$ and $PaCO_2$ were collected before and after the intervention and compared, considering two subgroups of children with cyanotic or acyanotic CHDs.

Statistical Analysis

For statistical analysis, results were presented as mean ± standard deviation (SD) for quantitative variables and summarized by frequency (percentage) for categorical

variables. To assess the difference in study parameters after the operation compared to the intervention, the paired t-test or Wilcoxon test was used. Additionally, we employed a multivariable linear regression model to determine the main correlates of the EtCO2-PaCO2 difference postoperatively. Statistical analysis was performed using SPSS version 23.0 for Windows (IBM, Armonk, NY, USA).

Results

A total of 34 patients with acyanotic CHD and 30 with cyanotic CHD undergoing cardiac repair surgeries were assessed for pulmonary and hemodynamic parameters preoperatively and postoperatively. The baseline characteristics of the two groups are summarized in (Table 1). The average age of participants in the acyanotic and cyanotic CHD groups was 32.55 ± 22.35 months and 8.16 ± 15.02 months, respectively. The most common underlying condition in the acyanotic CHD group was patent ductus arteriosus (PDA), found in about two-thirds of the patients, while the most common condition in the cyanotic group was pulmonary stenosis in 40.0% of the patients. Consequently, the most common repair procedures in the two groups were PDA closure and PDA stenting, respectively.

Changes in study parameters after the procedure, compared to before, in both study groups are shown in (Table 2). In the acyanotic group, significant changes were observed in serum HCO_3 concentration and PaO_2/FiO_2 ratio, both of which were significantly reduced after the repair surgery. However, changes in other parameters, especially $PaCO_2$, $EtCO_2$, and the difference between $PaCO_2$ and $EtCO_2$, remained insignificant postoperatively. In the cyanotic CHD group, in addition to significant reductions in serum HCO_3 value and increases in the PaO_2/FiO_2 ratio after the intervention, we found a substantial increase in PaO_2, a decrease in $PaCO_2$, an increase in $EtCO_2$, and a reduction in the difference between $PaCO_2$ and $EtCO_2$ (Table 2).

Therefore, changes in $EtCO_2$ and $PaCO_2$ were aligned in cyanotic CHD patients. In the cyanotic CHD group, no association was found between PaO_2 and the difference between $PaCO_2$ and $EtCO_2$ before surgery (beta=-0.047, SE=0.036, P=0.221), and this association remained insignificant after the surgical intervention (beta=-0.079, SE=0.052, P=0.152). According to multivariate linear regression models (Table 3,4), the difference between $PaCO_2$ and $EtCO_2$ after the intervention was independent of baseline parameters, including demographics and hemodynamic indices, in both acyanotic and cyanotic CHD groups.

Table 1- Baseline characteristics in the acyanotic and cyanotic groups

Characteristics	Acyanotic group (n=34)	Cyanotic group (n=30)
Gender, %		
Male	16 (47.1)	18 (60.0)
Female	18 (52.9)	12 (40.0)
Mean age, month	32.55±22.35	8.16±15.02
Mean weight, kg	13.11±6.24	6.36±5.61
Underlying disease, %		
AS	4 (11.8)	0 (0)
ASD	4 (11.8)	0 (0)
AVSD + PA	0 (0)	2 (6.7)
CoA	1 (2.9)	0 (0)
PA	0 (0)	4 (13.3)
PDA	22 (64.7)	0 (0)
PDA+ASD	1 (2.9)	0 (0)
Post-ToF PS	0 (0)	2 (6.7)
PS	1 (2.9)	12 (40.0)
Remnant aortic catheter	1 (2.9)	0 (0)
TGA	0 (0)	4 (13.3)
TGA + VSD	0 (0)	2 (6.7)
ToF	0 (0)	2 (6.7)
VSD + PS	0 (0)	2 (6.7)
Repairing procedure, %		
Aortic stenting	1 (2.9)	0 (0)
Aortic valve balloon dilation	4 (11.8)	0 (0)
ASD closure	4 (11.8)	0 (0)
Atrial Septostomy	0 (0)	4 (13.3)
Device removal	1 (2.9)	0 (0)
PDA closure	23 (67.6)	0 (0)
PDA stenting	0 (0)	14 (46.7)
Pulmonary artery stenting	0 (0)	6 (20.0)

Pulmonary valve balloon dilation	0 (0)	4 (13.3)
Pulmonary valve balloon dilation	1 (2.9)	0 (0)
RPA stenting	0 (0)	2 (6.7)

AS: Aortic Stenosis; ASD: Atrial Septal Defect; CoA: Coarctation of the Aorta; PA: Pulmonary Atresia; PDA: Patent Ductus Arteriosus; PS: Pulmonary Stenosis; RPA: Right Pulmonary Artery; TGA: Transposition of the Great Arteries; ToF: Tetralogy of Fallot; VSD: Ventricular Septal Defect

Table 2- Comparing the changes in the study parameters after operation based on the patient group

Parameter	Acyanotic group (n=34)			Cyanotic group (n=30)		
	Before	After	P value	Before	After	P value
FiO2	0.58±0.30	0.61±0.29	0.258	0.67±0.21	0.60±0.23	0.157
HR	119.20±17.71	115.50±17.96	0.064	125.86±12.83	128.60±15.89	0.46
SBP	85.41±12.56	87.82±13.44	0.143	73.00±15.42	42.60±14.15	0.82
DBP	46.67±8.71	49.05±11.25	0.098	36.86±11.60	37.40±10.76	0.84
MAP	59.58±9.26	62.05±11.59	0.072	49.00±12.28	49.20±11.13	0.925
Pulse pressure	38.73±9.06	38.76±6.98	0.983	36.13±8.56	35.20±8.89	0.801
Arterial PH	7.36±0.06	7.35±0.06	0.588	7.33±0.07	7.32±0.12	0.906
HCO_3	22.61±2.40	21.63±2.70	0.015	23.25±3.16	21.13±3.88	0.001
PaO_2	193.35±118.51	183.44±109.68	0.554	55.00±50.05	71.40±32.35	0.02
$PaCO_2$	40.05±6.91	39.67±6.05	0.728	43.93±7.22	40.20±8.27	0.033
$ETCO_2$	32.67±4.81	32.94±4.92	0.789	25.86±5.13	31.00±4.53	0.001
PaO_2/FiO_2	360.26±156.47	308.51±106.61	0.017	78.27±56.81	129.36±91.46	0.002
Δ $PaCO_2$.$ETCO_2$	7.38±5.71	6.73±6.72	0.537	18.07±6.93	9.20±6.53	0.002

DBP: Diastolic Blood Pressure; HR: Heart Rate; MAP: Mean Arterial Pressure; SBP: Systolic Blood Pressure; P<0.05 was statistically significant.

Table 3- Multivariable linear regression analysis to determine the main determinants of Δ $PaCO_2$.$ETCO_2$ changes after operation in the acyanotic group

Characteristic	Beta	Standard error	95% confidence interval	P value
Male sex	0.245	2.431	-4.772, 5.262	0.921
Age	0.002	0.086	-0.175, 0.179	0.983
Weight	0.089	0.349	-0.631, 0.809	0.801
HCO3	-0.84	0.55	-1.978, 0.29	0.138
SBP	-0.29	1.339	-3.049, 2.477	0.833
DBP	-0.69	2.592	-6.037, 4.664	0.793
HR	0.033	0.094	-0.16, 0.226	0.727
MAP	1.161	3.881	-6.849, 9.17	0.767

DBP: Diastolic Blood Pressure; HR: Heart Rate; MAP: Mean Arterial Pressure; SBP: Systolic Blood Pressure

Table 4- Multivariable linear regression analysis to determine the main determinants of Δ $PaCO_2$.$ETCO_2$ changes after operation in cyanotic group

Characteristic	Beta	Standard error	95% confidence interval	P value
Male sex	2.021	8.365	-18.447, 22.49	0.817
Age	-1.29	1.41	-4.74, 2.161	0.396
Weight	4.253	4.404	-6.524, 15.03	0.372
HCO_3	-0.79	1.291	-3.951, 2.368	0.562
SBP	-0.08	1.048	-2.644, 2.485	0.942
DBP	-0.02	0.353	-0.886, 0.839	0.949
HR	-0.14	1.147	-2.945, 2.667	0.907
MAP	2.021	8.365	-18.447, 22.49	0.817

DBP: Diastolic Blood Pressure; HR: Heart Rate; MAP: Mean Arterial Pressure; SBP: Systolic Blood Pressure

Discussion

It has been well demonstrated that $EtCO_2$ can approximate $PaCO_2$ in children without congenital heart defects. However, $EtCO_2$ may underestimate $PaCO_2$ in those with cardiovascular defects, especially during repair procedures. In other words, the $PaCO_2$-to-$PETCO_2$ difference may be significant in children with congenital heart disease (CHD), and these changes may be significantly affected by surgical procedures. However, the latter changes have not been definitively proven. It has been previously found that the $PaCO_2$-to-$PETCO_2$ difference is potentially impacted by abnormalities in physiological dead space and venous admixture. Thus, intraoperative manipulations can alter or even modulate

these parameters, but it remains unclear whether the $PaCO_2$-to-$PETCO_2$ difference, along with other hemodynamic parameters, remains constant.

Another important point is whether the nature of CHD as cyanotic or non-cyanotic affects the changes in the $PaCO_2$-to-$PETCO_2$ difference after surgery. As revealed in the present study, among the non-cyanotic CHD group, no significant change in the $PaCO_2$-to-$PETCO_2$ difference was observed. However, a significant decrease in this difference was found in the cyanotic CHD group. In other words, ABG analysis during the operation should be repeated in the cyanotic CHD group undergoing repair surgery. Such results have been similarly shown in some studies but contradicted in others. For instance, Lazzell et al. indicated that the PaCO2-to-PETCO2 difference remained constant in patients with acyanotic and cyanotic CHD with stable pulmonary blood flow (PBF), but not in patients with cyanotic CHD [10]. Choudhury et al. indicated that the $PaCO_2$-to-$PETCO_2$ difference in all cyanotic children and the acyanotic children with severe pulmonary hyperperfusion and pulmonary hypertension was markedly increased compared to that in children with normal conditions [11]. They showed that in cyanotic children, the increase in this difference is produced by the combined effect of low PO_2 and pulmonary hyperperfusion secondary to right-to-left shunting. In acyanotic children, the increased gradient is caused by the combined effects of high pulmonary artery pressure (PAP) values and increased pulmonary perfusion.

In a similar study by Lee et al., the value of $PETCO_2$ and the $PaCO_2$-to-$PETCO_2$ difference differed between both cyanotic and acyanotic groups [12]. The $PETCO_2$ of the cyanotic group was lower than that of the acyanotic group throughout the operation period and did not change significantly after cardiopulmonary bypass. In their experiment, cyanotic children demonstrated a greater $PaCO_2$-to-$PETCO_2$ difference before bypass than the acyanotic group. In the acyanotic group, the $PaCO_2$-to-$PETCO_2$ difference increased significantly after CPB, whereas it remained unchanged in the cyanotic group. Thus, the behavior of the $PaCO_2$-to-$PETCO_2$ difference after surgery seems to differ between the two types of CHDs. Such different behavior may, of course, be individualized and attributed to factors such as the presence of blood shunting from the venous to arterial circulation side and variation in the ventilation-to-perfusion ratio in the lung. The difference in the $PaCO_2$-to-$PETCO_2$ difference between cyanotic and acyanotic children can be attributed to the combined effect of the larger alveolar dead space and larger venous admixture.

Conclusion

The value of the PaCO2-to-PETCO2 difference significantly varies depending on whether the CHD is cyanotic or acyanotic. In acyanotic CHD, the stability of the PaCO2-to-PETCO2 difference can be expected after the repair procedure. However, a reduction in this difference is predicted in cyanotic conditions. Therefore, it is necessary to repeat ABG analysis during surgery to assess the PaCO2 condition and, consequently, the pulmonary condition of children.

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