

Predictive role of intraoperative variables in neonatal cardiac surgery outcomes

Predictive variables in neonatal cardiac surgery

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Abstract

Aim: This study investigates the association of intraoperative variables, including anesthesia and cardiopulmonary bypass (CPB) durations, delta CO₂ (Δ CO₂), and lactate levels, with postoperative morbidity and mortality in neonates undergoing complex congenital cardiac surgery.

Materials and Methods: A retrospective analysis was conducted on 42 neonates who underwent surgery in a single center. Data on demographic characteristics, genetic anomalies, anesthesia and CPB durations, and blood gas parameters (Δ CO₂ and lactate levels at entry [T0], post-CPB [T1], and intensive care unit admission [T2]) were collected. Associations between these variables and major adverse events (MAEs) or mortality were statistically analyzed.

Results: A total of 42 neonatal patients were included in the study. The median age of the patients was calculated as 0.4 ± 0.3 months. The mean weight of the sample was 3.3 ± 0.6 kg, and the median total anesthesia and CPB durations were 378.45 ± 103.67 and 116.86 ± 55.03 minutes, respectively. Δ CO₂ levels at T0 were significantly associated with MAEs ($p < 0.05$), while elevated Δ CO₂ at T0 and T1 was observed in patients who died. Total anesthesia duration was a significant predictor of both MAEs and mortality ($p = 0.014$). Lactate levels, however, showed no significant correlation with either MAEs or mortality at any time point.

Discussion: Prolonged anesthesia and CPB durations, along with elevated Δ CO₂ levels, are key predictors of adverse outcomes in neonates undergoing cardiac surgery. Delta CO₂ may serve as an additional marker for early postoperative risk stratification. Larger prospective studies are warranted to confirm these findings and improve clinical management strategies.

Keywords

Neonatal Cardiac Surgery, Delta CO₂, Anesthesia Duration, Cardiopulmonary Bypass, Morbidity, Mortality

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Introduction

Pediatric cardiac surgery is a high-risk and complex process in all aspects. Numerous factors, from the preoperative period to the intensive care phase, influence morbidity and mortality. During pediatric cardiac surgery, particularly in neonates, tissue hypoxia and postoperative organ failure are among the leading causes of mortality. Advanced monitoring techniques and rapid therapeutic interventions based on the results of arterial and venous blood gas analyses are critical in the follow-up process. Various parameters indicating impaired tissue perfusion/oxygenation have been investigated to identify patients at high risk of mortality and morbidity following surgery.

Hemodynamic strategies and treatments aimed at maintaining or improving tissue oxygenation and/or perfusion during and after surgery have been shown to positively affect postoperative outcomes. Early detection and correction of tissue oxygenation/perfusion deficiencies, particularly in patients with diminished physiological reserves, are crucial to preventing adverse outcomes. The delta carbon dioxide (ΔCO_2) value reflects whether CO_2 produced in peripheral tissues is adequately cleared through venous blood flow. It is not influenced by pulmonary venous desaturation, intracardiac shunting, anemia, or insufficient inspiratory oxygen, which can impair oxygen delivery. Studies have explored the association between ΔCO_2 values and reduced tissue perfusion in cardiac surgeries. While ΔCO_2 has been shown to be a useful parameter for assessing tissue perfusion in adult patients, studies investigating its prognostic significance in neonates undergoing pediatric cardiac surgery are limited [1, 2]. Given the increased susceptibility of pediatric patients undergoing open-heart surgery to early postoperative complications, developing and assessing advanced diagnostic methods for these patients is essential.

In this study, we aimed to investigate the effectiveness of perioperative anesthesia and cardiopulmonary bypass (CPB) durations, central venous-to-arterial partial carbon dioxide pressure differences (ΔCO_2), and lactate levels in predicting postoperative mortality and morbidity in neonates undergoing cardiac surgery. By analyzing the findings, we also aim to propose new clinical routines and contribute to the literature.

Materials and Methods

This retrospective observational study was designed to evaluate the impact of intraoperative variables on postoperative mortality and morbidity in patients operated on in our pediatric cardiac surgery unit. We planned to retrospectively review all neonates aged 0–1 month, regardless of sex, who underwent congenital heart surgery with cardiopulmonary bypass (CPB) between January 1, 2023, and January 1, 2024. Of the 87 patients during this period, those with incomplete blood gas data ($n = 45$) were excluded, resulting in a total of 42 cases included in the study.

Upon admission to the operating room, patients routinely undergo electrocardiography (ECG), non-invasive blood pressure, and pulse oximetry monitoring, followed by induction with midazolam (0.1 mg/kg), fentanyl (1 $\mu\text{g}/\text{kg}$), ketamine (1 mg/kg), and rocuronium bromide (0.6 mg/kg). Subsequently, cefazolin (30 mg/kg IV) and methylprednisolone (3 mg/kg IV)

are administered as standard protocol. After intubation, central venous catheters (CVCs) and arterial cannulas are placed by experienced anesthesiologists specializing in pediatric cardiac anesthesia.

Routine arterial and central venous blood gases are collected simultaneously via these cannulas at three time points: entry (T0), after cardiopulmonary bypass (T1), and upon admission to the pediatric cardiac intensive care unit (T2). All patients are transferred to the pediatric cardiac intensive care unit postoperatively as part of standard care.

This retrospective observational study recorded central venous-to-arterial partial carbon dioxide pressure differences (ΔCO_2) and lactate levels at these three time points for neonates. Postoperative follow-up included evaluating major adverse events (e.g., acute kidney injury, seizures, arrhythmia), the need for extracorporeal membrane oxygenation (ECMO), length of hospital and intensive care unit (ICU) stays, and mortality.

The data collected aimed to compare total anesthesia and CPB durations, perioperative ΔCO_2 values, and lactate levels, assessing their association with postoperative mortality and morbidity in neonates undergoing cardiac surgery.

Statistical Analysis

Descriptive statistics summarized the sample, with means and standard deviations (SD) for parametric data, medians, minimum (MIN), and maximum (MAX) values for non-parametric data, and frequencies (n) and percentages (%) for categorical variables. The Shapiro-Wilk test assessed numerical data normality.

Inferential statistics analyzed group differences and relationships. For normally distributed data, independent t-tests were used for two-group comparisons, and ANOVA for more than two groups. For non-normal data, the Wilcoxon rank-sum test and Kruskal-Wallis test were applied. Categorical data were analyzed using chi-square tests or Fisher's exact test for small sample sizes.

Correlations were evaluated with Pearson's coefficient for normal distributions or Spearman's rank/Kendall's tau for non-normal or non-linear data, with Kendall's tau preferred for small samples ($n < 30$).

Ethical Approval

This study was approved by the Ethics Committee of University of Health Sciences Türkiye, Basaksehir Cam and Sakura City Hospital (Date: 2024-01-17, No: 15).

Results

A total of 42 neonatal patients were included in the study. Of these, 28 (66.67%) were male, and 14 (33.33%) were female. The median age of the patients was calculated as 0.4 ± 0.3 months. The mean height and weight of the sample were 50.52 ± 3.09 cm and 3.3 ± 0.6 kg, respectively. Genetic anomalies were absent in 38 (90.48%) patients and present in 4 (9.52%). The median total anesthesia duration was 378.45 ± 103.67 minutes, and the median CPB duration was 116.86 ± 55.03 minutes.

The median lactate level at admission (T0) was 1.86 ± 1.6 mmol/L, and the mean ΔCO_2 value at T0 was 8.31 ± 4.99 mmHg. At the point of CPB cessation (T1), the median lactate level increased to 3.8 ± 1.79 mmol/L, while the mean ΔCO_2 value

was 7.04 ± 4.13 mmHg. Upon ICU admission (T2), the median lactate level further increased to 4.5 ± 2.84 mmol/L, and the mean ΔCO₂ value was 10.87 ± 5.15 mmHg. The demographic and perioperative descriptive characteristics of the patients are summarized in Table 1.

Statistical analyses revealed significant associations between

Table 1. Demographic and Clinical Numerical Variables for Patients

Variables	Median(min-max)	Mean±IQR
Age (months)	0.3 (0.1-1)	0.4 ± 0.3
Height (cm)	50 (41-58)	50.52 ± 3.09
Weight (kg)	3.3 (1.9-4.6)	3.3 ± 0.6
Anesthesia duration time (min)	350 (195-630)	378.45 ± 98.75
CPB time (min)	115 (27-309)	116.86 ± 66
Entry (T0) CO ₂ (Delta)	8.05 (0.5-17.9)	8.31 ± 6.32
Entry (T0) Lactat	1.4 (0.5-10.4)	1.86 ± 1.35
Post CPB period (T1) CO ₂ (Delta)	6.85 (0.5-18.7)	7.04 ± 4.23
Post CPB period (T1) Lactat	3.55 (0.8-10.4)	3.8 ± 1.45
ICU (T2) CO ₂ (Delta)	10.9 (0.1-23)	10.87 ± 5.15
ICU (T2) Lactat	4 (1.3-16)	4.5 ± 2.35
ICU stay duration (day)	14 (4-95)	18.64 ± 12
Hospital stay duration (day)	22 (4-102)	25.60 ± 11.75

Table 2. Comparative Analyses for Major Adverse Reaction(MAR) Subgroups

	Overall (n = 42)	MAR (-) (n = 32)	MAR (+) (n = 10)	p
Age (months)				
Mean ± SD	0.4 ± 0.3	0.41 ± 0.31	0.39 ± 0.29	0.832
Median (Min-Max)	0.3 (0.1 - 1)	0.3 (0.1 - 1)	0.25 (0.2 - 1)	
Weight (kg)				
Mean ± SD	3.3 ± 0.6	3.36 ± 0.56	3.11 ± 0.7	0.259
Median (Min-Max)	3.3 (1.9 - 4.6)	3.3 (1.9 - 4.6)	2.9 (2.2 - 4.4)	
Anesthesia duration time (min)				
Mean ± SD	378.45 ± 103.67	344.22 ± 75.32	488 ± 109.17	<0.001
Median (Min-Max)	350 (195 - 630)	335 (195 - 555)	482.5 (365 - 630)	
CPB time (min)				
Mean ± SD	116.86 ± 55.03	104.34 ± 47.81	156.9 ± 59.86	0.007
Median (Min-Max)	115 (27 - 309)	96 (27 - 230)	138.5 (85 - 309)	
Entry (T0) CO₂ (Delta)				
Mean ± SD	8.31 ± 4.99	7.46 ± 4.98	11.05 ± 4.09	0.045
Median (Min-Max)	8.05 (-1.4 - 17.9)	6.75 (-1.4 - 17.5)	10.6 (5.6 - 17.9)	
Entry (T0) Lactate				
Mean ± SD	1.86 ± 1.65	1.88 ± 1.84	1.79 ± 0.85	0.496
Median (Min-Max)	1.4 (0.5 - 10.4)	1.35 (0.5 - 10.4)	1.8 (0.6 - 3.2)	
Post CPB period (T1) CO₂ (Delta)				
Mean ± SD	7.04 ± 4.13	6.61 ± 4.36	8.39 ± 3.08	0.240
Median (Min-Max)	6.85 (-1 - 18.7)	5.95 (-1 - 18.7)	8.4 (3.9 - 14.8)	
Post CPB period (T1) Lactate				
Mean ± SD	3.8 ± 1.79	3.59 ± 1.73	4.46 ± 1.9	0.209
Median (Min-Max)	3.55 (0.8 - 10.4)	3.45 (0.8 - 10.4)	3.55 (2.2 - 7.7)	
ICU (T2) CO₂ (Delta)				
Mean ± SD	10.87 ± 5.15	10.67 ± 5.04	11.53 ± 5.7	0.649
Median (Min-Max)	10.9 (0.1 - 23)	10.9 (0.1 - 23)	10.3 (4.7 - 22.5)	
ICU (T2) Lactate				
Mean ± SD	4.5 ± 2.84	4.12 ± 2.13	5.71 ± 4.35	0.400
Median (Min-Max)	4 (1.3 - 16)	4 (1.3 - 9.8)	4.1 (1.3 - 16)	

anesthesia duration, CPB duration, T0 ΔCO₂ values, and the occurrence of major adverse events (p < 0.05, Table 2). A significant relationship was also found between total anesthesia duration and mortality (p = 0.014). However, no significant associations were observed between mortality and variables other than anesthesia duration (p > 0.05). Interestingly, ΔCO₂ values at T0 and T1 were higher in patients who experienced mortality, although the results did not reach statistical significance. The detailed analysis of these findings is presented in Table 3.

Discussion

Our study is one of the rare contributions in the literature focusing on morbidity and mortality prediction in neonates undergoing complex congenital cardiac surgery. The high average total anesthesia duration, CPB time, and overall mortality rate in our study highlight the complexity of the patients' pathologies.

We identified prolonged anesthesia duration as a predictive parameter for major adverse events and mortality. This may be attributed to the unique vulnerability of this sensitive population, consisting of neonates under 5 kg, where extended intraoperative times may lead to temperature fluctuations, heightened inflammatory responses, intravascular volume changes, and tissue perfusion disorders. Similar associations

Table 3. Comparative Analyses for Mortality Subgroups

	Overall (n = 42)	Mortality (-) (n = 35)	Mortality (+) (n = 7)	p
Age (months)				
Mean±SD	0.4 ± 0.3	0.37 ± 0.28	0.57 ± 0.36	0.166
Median (Min-Max)	0.3 (0.1 - 1)	0.3 (0.1 - 1)	0.5 (0.2 - 1)	
Weight (kg)				
Mean±SD	3.3 ± 0.6	3.37 ± 0.59	2.94 ± 0.57	0.085
Median (Min-Max)	3.3 (1.9 - 4.6)	3.3 (1.9 - 4.6)	3 (2.2 - 3.9)	
Anesthesia duration time (min)				
Mean±SD	378.45 ± 103.67	356.29 ± 82.4	489.29 ± 133.27	0.014
Median (Min-Max)	350 (195 - 630)	335 (195 - 560)	525 (335 - 630)	
CPB time (min)				
Mean±SD	116.86 ± 55.03	108.29 ± 46.08	159.71 ± 78.05	0.056
Median (Min-Max)	115 (27 - 309)	106 (27 - 230)	150 (72 - 309)	
Entry (T0) CO₂ (Delta)				
Mean±SD	8.31 ± 4.99	7.67 ± 4.92	11.54 ± 4.23	0.059
Median (Min-Max)	8.05 (-1.4 - 17.9)	7.3 (-1.4 - 17.9)	11.2 (7 - 17.3)	
Entry (T0) Lactat				
Mean±SD	1.86 ± 1.65	1.95 ± 1.77	1.41 ± 0.75	0.478
Median (Min-Max)	1.4 (0.5 - 10.4)	1.4 (0.6 - 10.4)	1.2 (0.5 - 2.3)	
Post CPB period (T1) CO₂ (Delta)				
Mean±SD	7.04 ± 4.13	6.53 ± 4.13	9.57 ± 3.34	0.075
Median (Min-Max)	6.85 (-1 - 18.7)	6 (-1 - 18.7)	10.2 (4.1 - 14.8)	
Post CPB period (T1) Lactat				
Mean±SD	3.8 ± 1.79	3.71 ± 1.83	4.26 ± 1.57	0.295
Median (Min-Max)	3.55 (0.8 - 10.4)	3.3 (0.8 - 10.4)	3.6 (3.3 - 7.7)	
ICU (T2) CO₂ (Delta)				
Mean±SD	10.87 ± 5.15	10.67 ± 5.39	11.86 ± 3.89	0.585
Median (Min-Max)	10.9 (0.1 - 23)	10.5 (0.1 - 23)	11.7 (7.5 - 19.1)	
ICU (T2) Lactat				
Mean±SD	4.5 ± 2.84	4.19 ± 2.27	6.01 ± 4.73	0.344
Median (Min-Max)	4 (1.3 - 16)	4.1 (1.3 - 9.8)	3.9 (2.5 - 16)	

between CPB duration and morbidity or mortality have been demonstrated in studies on adult patients [3, 4]. Likewise, studies on pediatric populations have reported correlations between CPB duration and mechanical ventilation, ICU stay length, and postoperative complications (5, 6).

One of the strengths of our study lies in utilizing simple but effective parameters, such as lactate and ΔCO_2 , to provide valuable insights into the recovery process of neonates post-surgery. Additionally, by focusing on specific time intervals (T0, T1, T2), we could track changes in these parameters, offering a novel perspective on early detection of tissue oxygenation and perfusion impairments.

In our study, ΔCO_2 values at T0 were associated with major adverse events, and elevated ΔCO_2 values at T0 and T1 were more pronounced in patients who died, suggesting that ΔCO_2 may serve as an important indicator of impaired tissue oxygenation. However, no significant relationship was observed between ΔCO_2 values at T2 and adverse outcomes. This may reflect the effect of intraoperative corrective interventions on tissue oxygenation and the repair of congenital cardiac defects. In the adult cardiac surgery literature, some studies have failed to demonstrate ΔCO_2 's utility in predicting major adverse events or mortality (7-9). Negative findings have been reported by Morel et al. and Huette et al., who noted that various parameters influencing tissue perfusion can complicate the interpretation of ΔCO_2 [10, 11]. Factors such as CPB itself, endothelial dysfunction, and microcirculation alterations may directly or indirectly contribute to complications, complicating the interpretation of outcomes. However, other studies have yielded positive results; for example, Mukai et al. reported that ΔCO_2 measured at the end of cardiac surgery was a moderate predictor of postoperative major adverse events and mortality [12].

Similar to our findings, studies on neonates and infants have shown that elevated ΔCO_2 values at admission are strongly associated with poor prognosis [1, 2]. Gong et al. also demonstrated a negative correlation between ΔCO_2 and cardiac index (CI) in infants undergoing CPB for complex congenital heart surgery [13]. Based on these findings, we believe that ΔCO_2 can serve as an additional measure for early postoperative risk stratification in neonates undergoing cardiac surgery. Nevertheless, further studies with larger cohorts are needed to validate this hypothesis.

Regarding lactate, no significant relationship was observed between lactate levels and tissue perfusion in our study. The association between lactate levels at all time points and major adverse events or mortality was insignificant. Although earlier studies linked lactate levels and clearance to outcomes in pediatric cardiac surgery [14-16], more recent research has indicated that elevated lactate levels in CPB patients may not necessarily reflect tissue hypoxia [17, 18]. For instance, Hakim et al. found an association between lactate levels and morbidity but not mortality [19].

We also believe that lactate alone is not a sufficient parameter for predicting postoperative mortality and morbidity in neonates undergoing cardiac surgery. It may be influenced by factors beyond tissue hypoxia, warranting further investigation.

Limitation

One of the major limitations of our study is its retrospective

design, which inherently limits the ability to establish causal relationships. Additionally, the exclusion of patients with incomplete blood gas data reduced the sample size, potentially impacting the robustness of our findings. The small sample size (42 patients) further restricts the generalizability of the results. Another limitation is the single-center nature of the cohort, comprising neonates younger than 30 days. This specificity limits the applicability of our findings to other cardiac disease populations or similar cohorts in different institutions.

Future large-scale, multicenter, prospective studies are needed to validate these findings in broader populations and improve their generalizability. Such research would provide a more comprehensive foundation for integrating these parameters into routine clinical practice.

Conclusion

Our study highlights the roles of anesthesia duration, CPB duration, and ΔCO_2 in predicting postoperative complications following neonatal cardiac surgery. These findings provide valuable insights into the integration of these parameters into clinical monitoring and suggest new approaches to managing neonates undergoing cardiopulmonary bypass.

ΔCO_2 , in particular, may serve as a potential component in postoperative complication scoring systems for this population, offering a basis for future research. However, validating these findings in larger studies and improving their generalizability is essential. This underscores the need for prospective, multicenter research to establish the reliability of these parameters in broader clinical settings.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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