

ORIGINAL ARTICLE

Intraoperative lactate levels and postoperative complications of pediatric cardiac surgery

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Summary

Objectives: Correlate arterial lactate levels during the intraoperative period of children undergoing cardiac surgery and the occurrence of complications in the postoperative period.

Aim: Arterial lactate levels can indicate hypoperfusion states, serving as prognostic markers of morbidity and mortality in this population.

Background: Anesthesia for cardiac pediatric surgery is frequently performed on patients with serious abnormal physiological conditions. During the intraoperative period, there are significant variations of blood volume, body temperature, plasma composition, and tissue blood flow, as well as the activation of inflammation, with important pathophysiological consequences.

Methods/Materials: Chart data relating to the procedures and perioperative conditions of the patients were collected on a standardized form. Comparisons of arterial lactate values at the end of the intraoperative period of the patients that presented, or not, with postoperative complications and frequencies related to perioperative conditions were established by odds ratio and nonparametric univariate analysis.

Results: After surgeries without cardiopulmonary bypass (CPB), higher levels of arterial lactate upon ICU admission were observed in patients who had renal complications (2.96 vs 1.31 mM) and those who died (2.93 vs 1.40 mM). For surgeries with CPB, the same association was observed for cardiovascular (2.90 mM × 2.06 mM), renal (3.34 vs 2.33 mM), respiratory (2.98 vs 2.12 mM) and hematological complications (2.99 vs 1.95 mM), and death (3.38 vs 2.40 mM).

Conclusion: Elevated intraoperative arterial lactate levels are associated with a higher morbidity and mortality in low- and medium-risk procedures, with or without CPB, in pediatric cardiac surgery.

Introduction

Anesthesia for pediatric cardiac surgery is often performed on critically ill patients with abnormal physiological conditions. It has long been known that the

elevation of arterial lactate levels in critically ill patients is associated with a higher incidence of morbidity, including death (1,2). Even in those patients considered hemodynamically stable in the postoperative period of high-risk procedures (normal blood

pressure without vasoactive drugs and urine output above $0.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$), the mortality is significantly higher in patients with hyperlactatemia (3). It is believed that, in such situations, the elevation of arterial lactate levels represents a state of anaerobic metabolism serving as a laboratory marker that can indicate situations of tissue hypoperfusion before clinical manifestations of organ dysfunction become apparent (1–3).

In the specific case of cardiac surgery, the elevation of arterial lactate levels is also associated with worse prognoses in both adults and children (4–8). However, most studies performed in pediatrics evaluated this association in the postoperative period after high-risk procedures without specifying the morbidity that occurred. Little is known of this relationship in routine procedures of lower complexity and the intraoperative capacity of this marker for predicting different types of complications. We hypothesized that even in these less complex procedures, the intraoperative elevation of arterial lactate levels may indicate situations with increased risk of complications after surgery. This study aims, therefore, to examine the levels of intraoperative arterial lactate levels in children undergoing cardiac surgery of low and moderate risk and compare them according to the perioperative conditions and the occurrence of infectious, cardiovascular, respiratory, renal, hematological, and neurological complications.

Materials and methods

After approval by the Ethics and Medical Research Committee, we retrospectively studied 160 consecutive cardiac surgeries performed on children of different ages up to 16 years of age at São Rafael and Ana Nery hospitals in Salvador, Brazil in 2007 and 2008. The procedures selected for the study were all procedures of types 1, 2, and 3 following the classification of Risk Adjustment for Congenital Heart Surgery (RACHS-1) (9).

The perioperative variables were collected on a standardized form with information on demographics, preoperative conditions, type and complexity of the procedure performed, employment and duration of cardiopulmonary bypass (CPB), and use of blood components. All patients underwent arterial catheterization for continuous arterial blood pressure measurement and collection of blood samples. Diuresis, insensible losses, and the volume of crystalloid and colloid administered were included in the final calculation of fluid balance. The weight of compresses and gauzes, vacuum volume, estimated loss during CPB, and volume of blood products administered were used to calculate the blood balance.

Similar protocols of blood flow rate during CPB, based on a weight chart, were used in both hospitals. Under normothermia (37°C), average values of $200 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ were used in children with 3 kg or less with a progressive reduction of the relative flow to $75 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ to those with 30 kg or more. The blood flow rate was individually and constantly adjusted, within tolerated upper and lower limits, according to the targeted mean arterial pressure for the core temperature (30–70 mmHg during normothermia or rewarming phase and 20–60 mmHg during cooling), clinical-surgical conditions (existence of shunts and collateral circulations), venous return to the CPB reservoir, and tissue perfusion parameters (aimed to maintain arterial lactate under 2.5 mm and oxygen saturation in the CPB venous line above 70%). Patients who required prolonged low flow states (below the tolerated lower limits) or total circulatory arrest under deep hypothermia were not included in this analysis.

Arterial lactate was analyzed in an automatic processor of gas analysis of the same make and model in the hospitals surveyed (ABL 700 Radiometer Medical, Copenhagen, Denmark) with values expressed in mm. Blood samples were obtained after arterial catheter placement and upon intensive care unit (ICU) admission for all patients. Other specimens were obtained at different points in management of each case according to the discretion of the surgical team. Because a more frequent sampling would be expected from the sicker cases, an analysis based on the mean or maximum lactate level during surgery could be biased. So, for the purpose of this study, we decided to analyze the lactate levels on admission to the ICU.

Postoperatively, the occurrence of death and complications was recorded, from the description of events in medical records until the discharge of the patient from the hospital. The types of complications that occurred were registered in groups by pre-established definitions. Infection: confirmed or suspected cases of an infection site with the administration of antibiotics. Cardiovascular complications: arrhythmias, total atrioventricular block, cardiac Tamponade, vasoactive drugs for a period exceeding 24 h (continuous infusion of norepinephrine and/or epinephrine), use of inotropic drugs for a period exceeding 24 h (infusions of dopamine below $15 \text{ mcg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ or any value for continuous infusion of dobutamine or milrinone), low cardiac output, and systemic hypertension with application of sodium nitroprusside to control pressure for a period exceeding 24 h. Respiratory complications: embolism, pulmonary edema, mechanical ventilation for more than 48 h after surgery and acute lung injury. Renal complications: acute renal failure (elevation greater than or

Table 1 Demographics and perioperative variables

Variable	Values
Age (months)	36 (8/96)
Weight (kg)	13 (6.23/22.15)
Gender	Masculine: 85 (53%)
Prematurity	Premature: 5 (3%)
Associated disease	Yes: 90 (56%)
Type of procedure	Elective: 130 (81%)
Use of CPB	Yes: 78 (49%)
Intraoperative transfusion	Yes: 100 (62.5%)
Duration of CPB (min) ^a	70 (45/107)
Aortic clamping time (min) ^a	55 (30/80)
Intraoperative diuresis (ml·kg ⁻¹)	3.67 (2.0/5.5)
Final fluid balance (ml)	+140 (-25/+300)
Final blood balance (ml)	+20 (-140/+120)

Age, weight, duration of CPB and aortic clamping, intraoperative diuresis, fluid and blood balances expressed in median, 1st and 3rd quartiles.

Gender, prematurity, associated disease, type of surgery, use of CPB, and intraoperative transfusion were expressed in absolute and relative frequencies.

^aSurgeries with CPB.

Table 2 Distribution of procedures according to categories of adjusted surgical risk (RACHS-1) with rates of complications, use of cardiopulmonary bypass (CPB), mean, and standard deviation of the arterial lactate levels upon ICU admission (mM).

Surgical risk	Number of cases	Use of CPB (%)	Rate of complications (%)	Arterial lactate level upon ICU admission
RACHS-1 1	51 (32%)	28.0 ^a	56.0 ^b	1.77 (-1.40) ^c
RACHS-1 2	51 (32%)	79.6 ^a	87.8 ^b	2.55 (±1.77) ^c
RACHS-1 3	58 (36%)	39.7 ^a	84.5 ^b	1.80 (±1.53) ^c

^aComparison between groups of surgical risk for the use of CPB – *P* < 0.001

^bComparison between groups of surgical risk for morbidity – *P* < 0.001

^cComparison between groups of surgical risk for lactate level upon ICU admission – *P* = 0.002

equal to two times the baseline serum creatinine) and/or requiring dialysis. Neurological complications: coma, seizures, neurological deficit, and cerebral vascular accident. Hematological: coagulopathy (prothrombin time and partial thromboplastin time greater than two times normal and/or fibrinogen <100 mg·dl⁻¹ and/or platelet count less than 80 000 mm⁻³), hemorrhage with or without coagulopathy, and the need to return to the surgical center.

Odds ratio, with respective 95% confidence intervals, for the occurrence of each type of complication were obtained according to the lactate level observed upon ICU admission. The Mann–Whitney test was used to compare lactate levels according to prematurity,

Table 3 Mean and standard deviation of the arterial lactate upon ICU admission (mM) according to prematurity, type of surgery, type of anesthesia, and use of CPB during the procedure

Perioperative condition	Arterial lactate level upon ICU admission		<i>P</i>
	mean and standard deviation		
Prematurity	Yes: 1.39 (±1.04)	No: 2.04 (±1.54)	0.191
Type of surgery	Emergency: 2.48 (±2.42)	Elective: 1.91 (±1.23)	0.819
CPB	Yes: 2.53 (±1.54)	No: 1.52 (±1.35)	<0.001

Table 4 Frequency of complications after surgeries with and without cardiopulmonary bypass (CPB)

Complication type	Frequency of occurrence	
	Surgeries without CPB (%)	Surgeries with CPB (%)
Infection	15 (18.3)	14 (17.9)
Cardiovascular	20 (24.3)	42 (53.8)
Low cardiac output	5 (6.0)	12 (15.3)
Arrhythmias	5 (6.0)	21 (26.9)
Prolonged use of vasopressor	19 (23.1)	22 (28.2)
Prolonged use of inotrope	16 (19.5)	34 (43.5)
Systemic arterial hypertension	21 (25.6)	9 (11.5)
Respiratory	25 (30.4)	36 (46.1)
Acute pulmonary lesion	4 (4.8)	10 (12.8)
Prolonged mechanical ventilation	22 (26.8)	29 (37.1)
Renal	10 (12.0)	15 (18.3)
Neurological	6 (7.3)	5 (6.4)
Hematological	23 (28.0)	42 (53.8)
Bleeding	4 (4.8)	13 (16.6)
Coagulopathy	12 (14.6)	38 (48.7)
Death	5 (6.0)	8 (10.2)
Combined events	60 (73.1)	63 (80.7)

Occurrence of postoperative complications expressed in absolute and relative frequencies.

type of surgery, and the use of CPB. The Kruskal–Wallis test was used for lactate comparison, and the chi-squares test was performed to evaluate differences in the rate of complications and use of CPB among different categories of surgical risk. A *P* value of less than 0.05 was considered significant.

Results

As shown in Table 1, of the 160 patients studied, 85 were men and 75 women, 90 presented with an associated disease and only five were premature. The median age and weight were 36 months and 13 kg, respectively, with a wide range of variation in the sample (15 days to 16 years old and from 2.3 to 67 kg in weight). The procedures were considered elective in most situations

(81% of cases), and cardiopulmonary bypass (CPB) was used in approximately half of the surgeries (48%) with an average duration of 70 min and aortic clamping time of 55 min. In 62.5% of cases, some type of blood product transfusion was necessary and the patients had a median intraoperative diuresis of $3.67 \text{ ml}\cdot\text{kg}^{-1}$ with an average water and blood balance of +140 ml and +20 ml.

The distribution of procedures according to risk using the RACHS-1 classification was uniform in the sample with approximately one-third of the cases in each category (Table 2). The group RACHS-1 2 showed the highest use of CPB compared to groups 1 and 3 and a higher frequency of complications than group 1 but not in group 3. In the sample studied, group 3 consisted mainly of short palliative procedures without the use of CPB, such as pulmonary artery banding and systemic to pulmonary shunts, while group 2 was represented mainly by cavity procedures with the use of CPB, such as Fallot total correction and surgery for closure of septal defects.

Prematurity and type of surgery had no relationship with the ICU admission values of arterial lactate observed during surgery (Table 3). The use of cardiopulmonary bypass, however, was associated with higher lactate values when compared to the same procedures

without it. In the distribution by surgical risk adjusted (RACHS-1), the highest values of lactate were observed in group 2, instead of presenting increasing values in their respective groups, as expected (Table 2). This probably reflects the higher rate of CPB use in group 2 (79.6%), as the postoperative morbidity was similar in groups 2 and 3 (87.8% and 84.5%, respectively).

As the use of CPB was the main factor influencing the variation in arterial lactate levels during surgery, we chose to subdivide the sample into two groups according to its usage during the procedure. After this subdivision, the ICU admission arterial lactate levels were compared in patients who presented or not with infectious, cardiovascular, respiratory, renal, hematological, neurological, death or any of the listed complications (combined events). Table 4 shows the frequency of these complications in each group.

In surgery without CPB, patients who had renal complications and those who died presented higher values of arterial lactate intraoperatively (Table 5).

In the surgical procedures with the use of CPB, patients presenting with cardiovascular, respiratory, renal and hematological complications, and death showed a higher arterial lactate upon ICU admission than those who did not (Table 6).

Table 5 Comparison of arterial lactate levels upon ICU admission (mm) in patients with and without postoperative complications after surgery without cardiopulmonary bypass

Complication type	Arterial lactate level upon ICU admission		OR	IC 95%	P
	No	Yes			
Infection	1.35 ± 1.06	1.85 ± 1.76	1.31	0.90–1.90	0.152
Cardiovascular	1.37 ± 1.29	1.82 ± 1.43	1.26	0.88–1.81	0.195
Low cardiac output	1.38 ± 1.19	2.09 ± 1.79	1.36	0.94–1.96	0.101
Arrhythmias	1.50 ± 1.37	1.81 ± 0.91	1.14	0.67–1.93	0.621
Prolonged use of vasopressor	1.36 ± 1.25	1.99 ± 1.56	1.35	0.93–1.95	0.110
Prolonged use of inotrope	1.38 ± 1.20	2.04 ± 1.74	1.34	0.93–1.93	0.115
Systemic arterial hypertension	1.65 ± 1.48	1.14 ± 0.78	0.57	0.26–1.24	0.160
Respiratory	1.40 ± 1.36	1.78 ± 1.30	1.21	0.86–1.72	0.266
Acute pulmonary lesion	1.51 ± 1.37	1.78 ± 0.97	1.12	0.62–2.03	0.696
Prolonged mechanical ventilation	1.39 ± 1.32	1.85 ± 1.38	1.25	0.88–1.78	0.209
Renal	1.31 ± 0.81	2.96 ± 2.80	1.89	1.15–3.12	0.012
Neurological	1.52 ± 1.37	1.46 ± 1.05	0.96	0.46–1.99	0.912
Hematological	1.33 ± 1.20	2.01 ± 1.61	1.40	0.95–2.07	0.083
Bleeding	1.45 ± 1.33	2.85 ± 1.09	1.46	0.94–2.26	0.086
Coagulopathy	1.38 ± 1.25	1.90 ± 1.57	1.28	0.89–1.83	0.169
Death	1.40 ± 1.20	2.93 ± 2.20	1.56	1.03–2.36	0.033
Combined events	1.36 ± 0.84	1.58 ± 1.49	1.15	0.73–1.84	0.533

Values are expressed as mean and standard deviation, odds ratio (OR), and 95% confidence interval (IC 95%) for the occurrence of the specified complications.

Bold values represents statistical significance.

Arterial lactate level upon ICU admission					
Complication type	Occurrence		OR	IC 95%	<i>P</i>
	No	Yes			
Infection	2.40 ± 1.40	2.81 ± 1.79	1.18	0.87–1.60	0.282
Cardiovascular	2.06 ± 0.94	2.90 ± 1.81	1.60	1.04–2.46	0.030
Low cardiac output	2.11 ± 0.95	3.15 ± 2.00	1.69	1.12–2.53	0.011
Arrhythmias	2.41 ± 1.49	2.84 ± 1.64	1.18	0.86–1.61	0.291
Prolonged use of vasopressor	2.20 ± 1.23	3.32 ± 1.90	1.61	1.11–2.35	0.012
Prolonged use of inotrope	2.14 ± 0.97	3.00 ± 1.93	1.54	1.05–2.26	0.026
Systemic arterial hypertension	2.61 ± 1.61	1.96 ± 0.68	0.67	0.31–1.33	0.240
Respiratory	2.12 ± 1.08	2.98 ± 1.82	1.56	1.05–2.31	0.026
Acute pulmonary lesion	2.46 ± 1.56	3.00 ± 1.39	1.21	0.83–1.75	0.310
Prolonged mechanical ventilation	2.23 ± 1.16	3.01 ± 1.92	1.42	1.01–2.00	0.046
Renal	2.33 ± 1.36	3.34 ± 1.94	1.44	1.02–2.02	0.036
Neurological	2.47 ± 1.41	3.38 ± 2.88	1.31	0.84–2.05	0.222
Hematological	1.95 ± 0.79	2.99 ± 1.81	1.99	1.20–3.33	0.008
Bleeding	2.36 ± 1.47	2.91 ± 1.64	1.24	0.91–1.70	0.165
Coagulopathy	2.10 ± 1.02	2.95 ± 1.83	1.56	1.04–2.34	0.029
Death	2.40 ± 1.24	3.38 ± 2.74	1.38	1.02–1.97	0.047
Combined events	1.95 ± 1.05	2.66 ± 1.60	1.62	0.87–3.00	0.124

Values are expressed as mean and standard deviation, odds ratio (OR), and 95% confidence interval (IC 95%) for the occurrence of the specified complications.

Bold values represents statistical significance.

Table 6 Comparison of arterial lactate levels upon ICU admission (mm) in patients with and without postoperative complications after surgery with cardiopulmonary bypass

Discussion

Although the relationship between hyperlactatemia and morbidity and mortality in pediatric cardiac surgery has been observed in several studies, most previous work describes the predictive value of this biomarker in the postoperative period of high-risk procedures (6,7,10,11). Our study demonstrated that even in surgeries of low to moderate risk, higher arterial lactate values in the intraoperative period are associated with higher rates of complications.

Although the anaerobic metabolism because of tissue hypoxia is an important cause of elevated arterial lactate, other factors such as the reduction of lactate catabolism owing to low hepatic flow and increased lactate production by β -adrenergic stimulation, especially in skeletal muscles, may also contribute to the hyperlactatemia of the critical patient (12). Whatever the reason, the elevation of arterial lactate is an important marker of loss of compensation of the regulatory mechanisms of tissue blood supply in situations of physiological stress.

In the study, highest levels of arterial lactate at the end of the intraoperative period were associated with higher rates of cardiovascular, respiratory,

renal, and hematological complications in surgeries that required extracorporeal circulation. Systemic and pulmonary vasomotor changes, large decrease of hematocrit, inadequacies in the CPB pump flow, increased oxygen consumption during reheating, and exacerbation of the inflammatory response can lead to discrepancies between metabolic requirements of organ systems and the supply of oxygen to cells and induce states of global and regional anaerobiosis with harmful consequences. Prolonged use of inotropes and vasopressors was significantly more frequent in these patients, possibly representing hypoperfusion states caused by low cardiac output with a negative impact on renal function. Coagulopathy associated with higher lactate levels after surgery with CPB could indicate the formation of thrombi in the microcirculation owing to inadequate anticoagulation and blood exposure to nonendothelial surfaces causing obstruction of blood flow in tissue, hyperfibrinolysis, and increased consumption of clotting factors and platelets.

Higher rates of renal complications and death were observed in patients with higher levels of arterial lactate upon ICU admission after surgery without CPB. This occurrence could represent situations of hemody-

dynamic stress during surgery with secondary effects on an organ system highly sensitive for systemic hypoperfusion, even when temporary, contributing to higher postoperative mortality rates.

Cardiopulmonary bypass, although indispensable for some procedures, is responsible for a series of undesirable pathophysiological alterations that could culminate in the elevation of lactate and organ dysfunction (13). Abraham *et al.* (14) showed that pump flow rates below $100 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ were associated with an odds ratio for the occurrence of hyperlactatemia of 7.67 in a retrospective analysis of low-risk surgical procedures. They also noticed a reduction of these odds by a factor of 0.8343 for each 1 mmHg augment of the mean arterial pressure during CPB. Duke *et al.* (6) compared gastric tonometry, serial hemodynamic assessment with a pulmonary artery catheter, and measurement of oxygen saturation in mixed venous blood and the arterial lactate levels during and after surgery. They noticed that higher blood lactate level was the most consistent predictive variable for major adverse events throughout the early postoperative period. Siegel *et al.* (5) found that elevated lactate levels on admission to the ICU ($>4.2 \text{ mm}\cdot\text{l}^{-1}$) were more likely to be associated with decreased survival after repair of congenital heart defects in children than other perioperative data such as cardiopulmonary and cross-clamp times, estimated blood loss during surgery, and the Pediatric Risk of Mortality (PRISM) score (used to assess the severity of illness in pediatric ICU patients) (15). They also

described a strong positive correlation of these lactate levels with the postoperative duration of intravenous inotropic support and mechanical ventilatory support.

The present study has the limitations expected in a retrospective study. Although positive associations between hyperlactatemia and postoperative complications were observed, we cannot imply causality. Some types of complications studied had low frequencies. Therefore, this study had insufficient power to detect interactions between potentially confounding variables.

The intraoperative and immediate postoperative periods represent an important moment for adopting measures and practices that may favor the clinical course of patients. Elevated arterial lactate levels during pediatric cardiac surgery of low and medium complexity can serve as early indicators for an increased risk of postoperative complications and even death. However, the impact of specific measures to control this marker based on hemodynamic management protocols has not yet been resolved consistently in the literature, and more studies are still needed for its determination.

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Conflict of interest

No conflicts of interest declared.

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