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ORIGINAL ARTICLE

Can postoperative serum lactate levels predict mortality in infants after open heart surgery?

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Abstract

Objective: Complex cardiac surgery is a cause of high morbidity and mortality in newborn infants.Elevated lactate levels after congenital cardiac surgery are indicative of tissue hypoperfusion and are associated with increased morbidity and mortality.Serial lactate measurements are crucial in monitoring prognosis in this patient group. Monitoring lactate levels is important in the management of patients after congenital heart surgery to predict and prevent adverse events.

Methods: Between July 2017 and December 1, 2022, the data of 115 patients aged 0-1 year who were followed up and treated at a pediatric cardiovascular surgery center, treated surgically, and underwent cardiopulmonary bypass during surgery were retrospectively evaluated.

Results: Twenty-two (19%) of the patients died in the postoperative period. The median (IQR) VIS score at 24 hours postoperatively was 27 (5-45), which was significantly higher than 12 (5-22) in survivors (p=0.01). When lactate levels were evaluated, preoperative lactate levels were higher in the group with mortality in the first 3 postoperative days, and the change in lactate levels at 24 hours postoperatively and initial lactate levels at 24 hours were higher (p<0.01). A 2-unit increase in lactate was found to predict mortality with a sensitivity of 77.8% and specificity of 99.13%.

Conclusion: Increased lactate levels are frequently encountered in the postoperative period and are associated with increased mortality and morbidity.

Keywords: Lactat; congenital heart surgery; cardiopulmonary bypass; mortality

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Introduction

Complex cardiac surgical procedures are operations with high mortality in the treatment of congenital heart diseases. Factors including clamping of the aorta, deep hypothermia and cardiopulmonary bypass increase mortality in this clinically unstable patient group [1,2].

Some factors that increase mortality after congenital heart surgery in newborns have been identified. Low gestational week, low birth weight, single ventricle physiology, and the type of surgery performed have been associated with morbidity and mortality in the postoperative period [3]. However, intraoperative and postoperative features also affect mortality in these patients.

Lactate increases in the case of inadequate oxygen supply to tissues or in the case of anaerobic energy metabolism as a result of impaired tissue perfusion. Lactate is produced in erythrocytes, skeletal myocytes, perivenous hepatocytes and skin and metabolized by the liver and kidney [4,5]. Elevated lactate levels may be associated with tissue hypoperfusion (type A hyperlactatemia) or decreased lactate clearance without impaired tissue hypoperfusion (type B hyperlactatemia) [6,7]. Studies showing that lactate clearance increases with age are available; therefore, it is important to determine lactate levels associated with poor prognosis in infants [8].

In terms of predicting prognosis and early intervention, especially lactate elevation continues to be a subject of research in this patient group. Determining the factors associated with lactate elevation after congenital heart surgery may reduce the frequency of associated morbidity and mortality as well as standardization in the follow-up of patients.

The aim of this study was to determine the association of lactate elevation in the postoperative period with morbidity and mortality after congenital heart surgery.

Materials and Methods

Between July 1, 2017 and December 1, 2022, we retrospectively evaluated the data of 115 patients between the ages of 0 and 1 year who were followed up and treated in a pediatric cardiovascular surgery center, treated surgically and underwent cardiopulmonary bypass during surgery.

Diagnoses, ages, body weights, operative times, aortic clamping times (minutes), cardiopulmonary bypass times (minutes) and postoperative 0 and 24 hours serum lactate levels were recorded from the patients' files. Short- and mid-term morbidities, sepsis and pulmonary hypertension, and length of hospitalization were also recorded. Initial leukocyte and platelet counts, hemoglobin levels, albumin and coagulation parameters (PTZ, INR and APTT) were recorded in the postoperative period.

Vasoactive inotrope score (VIS*) in the first 24 hours was recorded.

* Inotrope score (IS) = dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100 X epinephrine dose (mcg/kg/min)

*Vasotropic inotropic score (VIS) = IS + 10 X milrinone dose (mcg/kg/min) + 10,000 X vasopressin dose (U/kg/min) + 100 X norepinephrine dose (mcg/kg/min)

Serum lactate levels measured at preoperative, first postoperative and 24th hour were recorded. In the postoperative period, the difference between the initial lactate level and the lactate level measured at 24 hours was calculated. Mortality times in the postoperative period were also recorded for infants who died. The relationship between the change in postoperative serum lactate levels and those discharged in the first 72 hours postoperatively and those discharged between days 3-30 was evaluated.

Our primary outcome was to evaluate the relationship between the rapid change in serum lactate levels in the postoperative period and short- and mid-term mortality. Our secondary outcome was to evaluate the relationship between the change in serum lactate levels and short- and mid-term morbidity and the need for respiratory support.

Ethics committee approval was obtained from the local ethics committee.

Statistical Analysis

Statistical Package fort he social Sciences 22 statistical program was used for statistical analysis.

Demographics, patient characteristics and outcomes were expressed as a median for continuous variables and frequency (%) for categorical variables. Univariate and multivariate logistic regression analyses were performed to assess the association between the primary explanatory variable and the composite outcome. In univariate modeling, p < 0.01 was considered statistically significant. Since our data were not normally distributed, median and interquartile range (IQR) 25th and 75th percentiles were used. Data obtained by measurement were expressed as mean ± standard deviation, data obtained by counting were expressed as %, p < 0.01 was considered significant. Chi-square and Spearman correlation test were used to analyze the data.

ROC analysis was used to assess the significance of lactate measurements as significant independent predictors of the composite outcome in multivariate modeling and the area under the curve showing significance was determined. Sensitivity, specificity, positive predictive value and negative predictive value were calculated at various lactate thresholds. Kaplan Meier test was used for survival analysis.

Results

A total of 115 patients were included in the study. The median age (IQR 25-75) was 106.00 (14-240) days and the median body weight was 4.28 (4.28-6.3).

Mean cardiopulmonary bypass time was 144 minutes (IQR 25-75) and mean aortic clamping time was 94 minutes (IQR 25-75). Preoperative sepsis was diagnosed in 23(18.4) patients.

The mean postoperative VIS score was 17 (10-26.5). Demographic and clinical characteristics of the patients are shown in Table 1.

The most common diseases were ventricular septal defect with 37 (32%) and transposition of the great arteries with 32 (26%).Other cardiac anomalies are coarctation of aorta(%4,3), hypoplastic left heart syndrom (%8,7),

Table 1. Demographic and clinical characterics of the patients

	N=115
Age, day*	106.00 (14-240)
Body weightt, kg*	4.28 (4.28-6.3)
Gender, male, n (%)	69(60)
Pulmonary hypertension, n (%)	42(36.6)
Sepsis, n (%)	23(18.4)
Cardiopulmonar bypass, minute*	144 (105-192)
Cross clemp time, minute*	94 (66-128)
Preoperative serum lactate level, mg/dl	2.05 (1.5-3.1)
1st postoperative serum lactate level, mg/dl	2.9 (1.96-4.92)
Postoperative 24th hour serum lactate levels, mg/dl	3.5 (2.2-6)
VIS*	17 (10-26.5)
Duration of surgery, hour**	5 (4-6.5)
Hospital stay, day	24 (14-34)
Mortality, n (%)	22 (19)

*VIS: Vasoactive inotrope score **Median (IQR 25-75)

Table 2. Factors effects mortality

	Mortality group (n=22)	Survivors (n=93)	p
Body weight, kg*	3250 (3037-4057)	5300 (3492-6775)	<0.01
Age, day*	13 (13-21)	180 (21-270)	<0.01
Gender, E (%)	12 (54)	57 (61)	0.36
Cross clamp time, min*	113 (72-153)	93 (66-125)	0.12
Cardiopulmonary bypass, min*	184 (140-251)	138 (103-181)	0.09
Duration of surgery, hours*	6.75 (5-9.1)	4.5 (4.5-6)	<0.01
24th hour VIS score	27 (5-45)	12 (5-22)	0.01
First postoperative lactate, mmol/L*	7.9 (3.3-12)	2.8 (1.9-4.2)	<0.01
White Blood Count (10^3 /L)**	11.7± 4.6	12.2 ±5	0.63
Hematocrit (%)**	38 ±9.5	38± 5.6	0.84
Platelet count (10^3 /L)**	145 ± 106	175 ±95	0.18
Prothrombin time (sec)**	24.7 ± 11.9	16.8 ± 4.2	<0.01
INR**	2.1± 0.7	1.5 ± 0.4	<0.01
Activated prothrombin time (sec)**	58 ± 20	38 ± 12	<0.01
Albumin, g/dl**	28.7± 6.1	33.8± 5.1	<0.01
Hospital stay *(day)	13 (6-21)	25 (20-34)	0.04

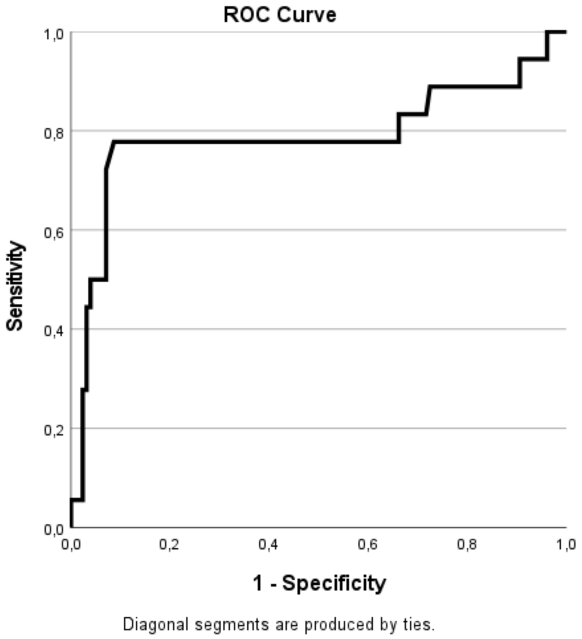
*median (IQR 25-75) **mean±standart deviation VIS: Vasoactive inotrope score

Table 3. Comparison of lactate levels and lactate changes in infants with and without mortality

	Postop mortality in the first 72 hours (N=11)	Postop mortality in 3-30 days (N=11)	Survivors (n=93)	p
Preoperative serum lactate level, mg/dl	4.3 (1-8)	-1.1 (-2.2-2)	-1.1 (-2.9- -0.1)	P^1:<0.01 P^2:0.62
1st preoperative serum lactate level, mg/dl	2.8 (2.1-3.55)	1.8 (1.2-3.1)	1.95 (1.5-2.95)	P^1:0.59 P^2:0.27
Postoperative 24th hour serum lactate levels, mg/dl	9.8 (7.95-16.5)	4.7 (2.9-8.4)	4.2 (2.65-6.6)	P^1: <0.01 P^2:0.55
Postoperative 24th hour-first serum lactate level difference	14.9 (10-21)	4.5 (2.7-8)	3.2 (1.9-4.5)	P^1: <0.01 P^2:0.48

***median (IQR 25-75) **P^1: Postoperative mortality in the first 72 hours & Survivors**
p^2: Postoperative mortality in 3-30 days& Survivors

Figure 1. ROC analysis showing the relationship between mortality and lactate change



tetralogy of Fallot (6.9%), total abnormal pulmonary venous return (6.9%) , pulmonary atresia (0,8%), truncus arteriosus (0,8%) and complete atrioventricular defect (7,8%).

Twenty-two (19%) of the patients died in the postoperative period. When the infants with mortality were compared with the survivors, the mortality group had younger age and lower body weight ($p < 0.01$ and $p < 0.01$, respectively). Cardiopulmonary bypass time and operation time were longer and postoperative serum lactate levels were higher in the group with mortality (Table 2). There was no significant correlation between mortality and aortic cross-clamping time (p=0.12). There was no significant correlation between thrombocytopenia and mortality (p>0.01), whereas high prothrombin time, activated partial thromboplastin time and INR were significantly associated with mortality (p<0.01).

The median (IQR) VIS score at 24 hours postoperatively was 27 (5-45), which was significantly higher than 12 (5-22) in the survivors (p=0.01) (Table 2).

When lactate levels were evaluated, in the group with mortality in the first 3 postoperative days, preoperative lactate levels were higher, and the change in lactate levels at postoperative 24h and 24h-first lactate levels were higher (p<0.01). However, no significant difference was observed between the group who died after day 3 and the survivors in terms of lactate levels and lactate changes (Table 3).

The ROC analysis showing the relationship between change in serum lactate levels and mortality during the first 3 days is shown in Figure 1. The AUC was 0.78 and a 2-unit increase in lactate was found to predict mortality with 77.8% sensitivity and 99.13% specificity. The Kaplan-Meier test evaluated the relationship between mortality and time of death in the postoperative period; the median (IQR) day of death was 4.5 (2-12.3) days (p=0.029).

Discussion

Advances in congenital heart surgery techniques have gained momentum in recent years. However, data on preoperative and postoperative follow-up of patients in neonates are still insufficient. In this group with high mortality and morbidity rates, mortality and morbidity rates can be reduced by analyzing the parameters used in the follow-up of patients well and intervening at the right time.

Congenital heart surgery involves complex surgical procedures. Intraoperative clamping of the aorta, deep hypothermia and cardiopulmonary bypass disrupt the physiologic balance of the newborn and cause difficulties in patient management in the postoperative period [1,2].

Although the surgical procedure is facilitated by mechanical interruption of blood flow from the aorta, systemic organ perfusion is affected. Impaired perfusion of organs causes hypoxia at the tissue level. This is manifested by elevated lactate levels in the laboratory. Elevated lactate is associated with high mortality and morbidity [5]. Therefore, lactate is used as an important parameter to predict the development of morbidity and mortality in adult and pediatric age groups[9,10].

In a study including neonates, a peak lactate level of 7.3 mmol/l or greater was found to be significantly associated with the presence of a major residual lesion. Overall, the study highlights the potential of hyperlactataemia as a predictor of adverse outcomes post-cardiac surgery in neonates with congenital heart disease. The two-variable model and peak lactate levels can help in prognosticating the risk and identifying patients who may require intervention [5].

In a single-center retrospective study in the adult age group, the data of a total of 1290 patients were retrospectively evaluated. The patients were divided into three groups as <2 mmol/l, 2-5 mmol/l and >5 mmol/l according to their initial lactate levels after cardiopulmonary bypass. Lactate levels >5 mmol/l were evaluated as severe hyperlactatemia and found to be associated with prolonged hospital stay, renal damage, liver damage and increased mortality in these patients [10]. In another study, the relationship between lactate level and mortality in the postoperative period in 432 neonates was examined. In single ventricle patients, lactate values of 7.8mmol/L and above in the first 48 hours and in the first 12 hours after intensive care unit admission were found to be associated with mortality [5]. In our study, the lactate value in the first 24 hours in patients with mortality was 6 mmol/L and above, in accordance with existing studies.

In a study comparing lactate levels and postoperative outcomes in 231 patients under one year of age, high lactate levels were found to be risky in terms of mortality and morbidity [11]. In this study, it was concluded that serum lactate level is an ideal marker for patient follow-up and treatment decision.

The relationship between lactate levels and mortality in patients who underwent Norwood procedure for hypoplastic left heart disease was investigated. A total of 221 patients were included in the study in which 6-year data were collected from a single center. In these patients, serial lactate measurements in the first 72 hours were compared with 7th and 30th day mortality rates. The results showed that failure to reduce blood lactate levels below 6.76 mmol/L in the first 24 hours was highly predictive of mortality on day 30 [12].

The risk classification for congenital heart disease in pediatric patients (RACHS-1) is a classification system used to predict mortality and morbidity in congenital heart surgery[13]. In a study by Hazan et al. the difference between lactate levels in patients with the same RACHS-1 score was found to be associated with mortality. It was concluded that combining RACHS-1 scoring with serial lactate measurements would provide a more comprehensive approach to predict survival in patients and direct appropriate interventions and treatments [14].

Early or late elevation of serum lactate level is as important as serial measurement. In a study conducted in an adult age group, early lactate elevation was defined as a lactate level above 3 mmol/L in the first hour postoperatively. In this study, a positive correlation was found between early lactate elevation and aortic clamping time. In addition, late lactate elevation was found to be independent of intraoperative characteristics and more benign as a result of this study [15]. In our study, especially death in the first 3 days and 24-hour lactate change in the postoperative period were important. A 2-unit increase in lactate level was found to predict mortality with 77.8% sensitivity and 99.13% specificity.

In our study, postnatal age and weight were lower in the group with mortality, and thrombocytopenia and coagulopathy were significantly more frequent in the group with mortality. We associated this with the severity of the inflammatory response of patients to complex cardiac surgical procedures in the neonatal period.

Cardiovascular bypass surgery in the infant period is associated with particularly high mortality and morbidity. Our study is especially important because it includes infants and newborns.

In conclusion, elevated lactate levels are frequently encountered in the postoperative period and are associated with increased mortality and morbidity. In our study, the relationship between elevated lactate levels and mortality was emphasized especially in patients under 1 year of age.

Close monitoring of lactate levels after congenital heart surgery can predict mortality and allow earlier interventions. However, prospective studies with a high number of patients are needed especially to evaluate newborns.

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Conflict of interests

None.

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Ethical Standards

All procedures were in accordance with the Declaration of Helsinki. Ethical approval was received from the Gazi Yasargil Training and Research Hospital Ethics Committee, Diyarbakır, Turkey.

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