

# Serum lactate as mortality and morbidity marker in infants after Jatene's operation

Lactato sérico como marcador de morbimortalidade no pós-operatório de operação de Jatene em lactentes

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Abstract

Objective: To assess the morbidity and mortality after Jatene's operation using lactate as the main marker.

Methods: We performed a historical cohort with infants admitted in a pediatric intensive care unit during 1995 to 2005 who underwent this surgery. We assessed the preoperative, immediate (IPD), third hour (3h), six hour (6h) and first day (POD1) serum lactate as well as other factors such as sepsis, increased bleeding, low cardiac output syndrome, presence of complication, renal insufficiency, pulmonary hypertension, cardiac arrythmias, chylothorax, myocardial ischemia, and seizures and also information about length of PICU stay and death.

Results: The mean age of 76 patients was  $14.59\pm19.09$  days, birth weight  $3.128\pm0.48$  kg Forty-four patients had the diagnosis of simple transposition of great arteries. The circulatory bypass time was  $143.78\pm28.77$  minutes and aortic clamping time of  $87.68\pm22.3$  minutes and LOS of  $20.28\pm15.62$  days. Twenty four (31.58%) died during hospital

stay. Lactate increased in IPD, returning to baseline at 24 hours. Patients who died raised and maintained IPD lactate higher. The 3h lactate best discriminated mortality with area under the curve of 0.68 (CI 0.54 to 0.83) P=0.035. However, considering a cutoff point for lactate greater or equal to 5.8 mmol/dl in the 3-h PO, we obtained only 67% sensitivity and specificity of 64% for mortality. There is positive correlation between number of complications and lactate. The low cardiac output syndrome with an odds ratio (OR) of 7.67 (2.38-24), increased bleeding with OR 2.91 (1.07-7.94) and respiratory complication with OR 1.67 (1.35-2.05) are risk factors when combined.

Conclusion: After Jatene's operation, morbidity and mortality can be assessed with the serum lactate levels, suggesting increased values in the third hour is suggestive of a worse prognosis.

 ${\it Descriptors:}$  Transposition of great vessels. Lactic acid. Morbidity. Mortality.

This study was carried out at Intensive Care Unit at Pediatric Cardiologic Service at Santo Antônio Children's Hospital, Complexo Hospitalar Santa Casa de Porto Alegre, Porto Alegre, RS, Brazil.

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### Resumo

Objetivo: Avaliar a morbidade e mortalidade após a operação de Jatene utilizando a dosagem de lactato sérico como principal marcador.

Métodos: Foi realizada uma coorte histórica com lactentes da UTI no período de 1995 a 2005 submetidos a essa cirurgia. Foram avaliados o lactato do pré-operatório, pós-operatório imediato (POI), da terceira hora de PO (3ªh), sexta hora (6ªh) de PO e do 1º dia de PO; bem como outros fatores como sepse, sangramento aumentado, síndrome de baixo débito, insuficiência renal, hipertensão pulmonar, arritmias cardíacas, quilotórax, isquemia miocárdica, convulsões e outras complicações. Também foram coletadas informações referentes ao tempo de internação na UTI e ao desfecho (se o paciente morreu ou teve alta da UTI).

Resultados: A média de idade dos 76 pacientes foi de 14,59  $\pm$  19,09 dias, peso ao nascimento de 3,128  $\pm$  0,48 kg. Quarenta e quatro pacientes tinham o diagnóstico anatômico exclusivo de transposição de grandes artérias. O tempo médio de CEC foi de 143,78  $\pm$  28,77 minutos, de pinçamento de 87,68  $\pm$  22,3 minutos e de internação na UTI de 20,28  $\pm$  15,62 dias. Vinte

quatro (31,58%) pacientes foram a óbito. O lactato aumentou no POI, retornando aos níveis basais em 24h. Os pacientes que foram a óbito apresentaram e mantiveram a partir do POI níveis de lactato mais elevados. O lactato da 3ªh foi o que melhor discriminou mortalidade, área sob a curva 0,68 (IC 0,54-0,83) P=0,035. Entretanto, considerando um ponto de corte para o lactato maior ou igual a 5,8 mmol/dl na 3ªh de PO, obteve-se apenas sensibilidade de 67% e especificidade de 64% para mortalidade. Existe correlação positiva entre o número de complicações e os níveis de lactato. A síndrome de baixo débito com *odds ratio* (OR) de 7,67 (2,38-24), sangramento aumentado com OR de 2,91 (1,07-7,94) e complicações respiratórias com OR de 1,67 (1,35-2,05) são fatores de risco de óbito quando somados.

Conclusão: Após a operação de Jatene, a morbidade e a mortalidade podem ser avaliadas com auxílio da dosagem de lactato sérico, sugerindo que valores aumentados na terceira hora são sugestivos de pior prognóstico.

Descritores: Transposição dos grandes vasos. Ácido láctico. Morbidade. Mortalidade.

### INTRODUCTION

The postoperative period of cardiac surgery in children deserves special attention, where care and monitoring of its evolution in the Intensive Care Unit is essential. However, monitoring of consumption and release of oxygen limited in children after surgical repair of congenital heart disease because of difficulties in measuring cardiac output and lack of confidence in venous saturation monitoring in patients with residual intracardiac communication [1].

In recent years, the serum lactate levels have been used as a prognostic marker of confidence in children during the postoperative period of congenital heart disease, especially in the unstable phase. Recent studies have shown a strong correlation between high lactate levels and an increased risk of morbidity and mortality [1-6].

The inadequate distribution of oxygen to the tissues is reflected by lactic acidosis, a result of anaerobic metabolism. Lactic acidosis is frequently found among critically ill patients, including children, in the postoperative period of cardiothoracic surgery. An increase in lactate levels resulting from systemic hypoperfusion and tissue hypoxia. However, in some patients, increase of lactate levels is not explained only by these two aspects. For example, some drugs such as oral hypoglycemic agents, ethanes, catecholamines and  $\beta 2$  bronchodilators may cause an increase in serum lactate levels [1,2,7,8].

Among the cyanotic congenital heart disease, transposition of great arteries (TGA) is the leading surgical pathology of total correction in the neonatal period [9-11]. Surgical treatment for correction of TGA can be accomplished using several different techniques: Rastelli, Mustard and Senning [3,12,13]. However, after the successful completion of anatomic correction created by Jatene, this has been used in several centers [14].

Because high serum lactate levels in postoperative period of cardiac diseases serve as a guide to the risk of mortality and morbidity, it is justified to assess its levels in patients who underwent surgical correction of TGA by Jatene's operation.

Therefore, the aim of this study was to assess serum lactate as a prognostic marker of mortality and morbidity in the early postoperative period up to 28 days in patients who underwent surgery for correction of TGA by Jatene's operation in the immediate postoperative period at 3<sup>rd</sup> and 6th hour and at 1<sup>st</sup> postoperative day postoperatively in the first 10 years of our case group, from 1995 to 2005.

### **METHODS**

We performed a historical cohort with pediatric patients with TGA who underwent cardiac surgery for correction with Jatene's operation in the period from July 1995 to December 2005. The study site was the Intensive Care Unit

(ICU) of the Service of Pediatric Cardiology at Santo Antônio Children's Hospital at Irmandade Santa Casa de Misericórdia of Porto Alegre.

We included pediatric patients undergoing cardiac surgery for correction of TGA in this period. Patients who did not have enough clinical information to meet the data needed for research or who died in a period less than 24 hours postoperatively were excluded, the latter were excluded because the aim was to identify postoperative factors related to death, the preoperative and surgical factors were not assessed.

The study was accepted and approved by the Research Ethics Committee of Santa Casa de Misericórdia of Porto Alegre under Protocol number 1435/06 and by the Research Ethics Committee of the Universidade Luterana do Brasil under the Protocol number 2006-406H. Patients included in the study had their data collected and anonymity was respected.

The anatomical diagnosis of patients was performed by the same team through transthoracic echocardiography. All surgical corrections were performed by the same team of pediatric cardiac surgeons of the service. Cardiopulmonary bypass (CPB) was performed in all patients, using a membrane oxygenator with low filling volume (priming), venous reservoir Lucchese-Braile (which allows a volume infusion of around 50 ml) and on-line oximetry using C DI-100-3M equipment, with optical sensor in the venous line mounted with the perfusion circuit.

To cardioplegia, a blood sample was dissolved in a St. Thomas solution with added potassium, in doses of 10ml/ kg. All patients who underwent surgery were cooled to values between 21 and 28°C of central temperature during surgery. Postoperatively, patients remained intubated and mechanically ventilated in pressure controlled mode (Sechrist Infant Ventilator® Model IV – 100B), with positive inspiratory pressure of about 18-22 cm H<sub>2</sub>O, fraction of inspired oxygen of 0.21-0.3, positive end expiratory pressure of 3-5 cmH<sub>2</sub>O and a ventilatory rate of 15-25 breaths/minute. Fifty-one (67.1%) patients returned to surgery with sternotomy opened. Patients were sedated with continuous morphine at a dose of 0.02 mg/kg/h. All patients from surgery received support from one or more vasoactive drugs (dopamine, 5-15 μg/kg/min and milrinone 0.37-0.75 μg/kg/ min for an indefinite period in accordance with their hemodynamic status; nitroglycerin 1 µg/kg/min for 24 hours).

The information needed for the study were obtained from medical records and computerized systems of consultation for each patient. The variables of interest used in the study were: gender, age (in days), weight (kg), length of ICU stay (days), anatomic diagnosis by transthoracic echocardiography (TGA, TGA and IC, TGA and aortic changes, TGA and other anatomical defects) and date of

surgery. The serum lactate levels at preoperative, immediate postoperative, 3rd postoperative hour, 6th postoperative hour and 1st postoperative day periods was collected as a routine service by the nursing staff and sent to the central laboratory.

Data from the intraoperative (CPB time and aortic clamping time) were recorded in the chart by the anesthesiologist responsible for the surgery. Complications developed during the ICU were classified according to the following criteria: sepsis (systemic inflammatory response syndrome + suspected or proven infection), increased bleeding (>5ml/ kg/h at the first 24 hours), low output syndrome (mean arterial pressure <40 mmHg + serum lactate> 2 mmol/L + central venous oxygen saturation <70% + diuresis <0.5 ml/kg/h), respiratory complications (atelectasis, pneumonia, pneumothorax, prolonged mechanical ventilation and/or high obstruction), renal failure (requiring peritoneal dialysis), pulmonary hypertension (pulmonary arterial systolic pressure > 50% of systemic systolic arterial pressure), arrhythmias (atrioventricular block, sinus bradycardia and/ or supraventricular tachycardia), chylothorax (pleural effusion with triglyceride > 150 mg/dl and the predominance of lymphocytes), myocardial ischemia (serum troponin > 0.1 with elevation or ST-segment depression) and seizures (tonicclonic movements). Information was also collected concerning the time of hospitalization, death and discharge from ICU.

Serum lactate was analyzed by arterial gasometry sample using the potentiometric method, using as reference values from 5.7 to 2.0 mg/dL or 0.63 to 2.44 mmol/L. The equipment used for measurements was Radiometer ABL 700®.

Quantitative data were described as mean and standard deviation and qualitative data by frequency and percentage. The analysis of quantitative variables with normal distribution were analyzed using Student's t test and for nonparametric test was used the Mann Whitney test. For qualitative data, we used the chi-square test. Comparison of lactate levels at different times was performed by analysis of variance (ANOVA). The measure of association for risk of death was obtained by the odds ratio and in logistic regression model were placed only variables whose odds radio was above 1. The trend measure used was the confidence intervals between 5% and 95%. The Pearson's correlation test was used for the number of complications and the level of serum lactate. A P value <0.05 was considered statistically significant. Comparison of lactate levels according to mortality and morbidity was obtained by the ROC curve. The area under the curve was significantly greater than 0.5. The cutoff point was one in which it was possible to obtain greater sensitivity and specificity, and was calculated for different times postoperatively. For data analysis we used SPSS, version 12.0 for Windows.

# **RESULTS**

From July 1995 to December 2005, 2,626 cardiac surgeries were performed at the Pediatric Service of Cardiology at Santo Antônio Children's Hospital. Of these, 106 were for repair of TGA through Jatene's operation. Seventeen (16.04%) patients were excluded because they died less than 24 hours postoperatively. Of the 89 patients, 10 patients had no record of serum lactate in their medical record and three did not have their medical records found. The mean age of the 76 study patients was  $14.59 \pm 19.09$  days (minimum 1 and maximum of 113 days), the mean birth weight of  $3.128 \pm 0.48$  kg (minimum 1.9 and maximum of 4.2 kg) and 49 (64.47%) were male. Forty-four (57.9%) patients had a unique anatomical diagnosis of TGA, including the association of patent ductus arteriosus (PDA) and patent foramen ovale (PFO).

Other anatomical defects found associated to TGA were interventricular communication (IC) in 24 (31.6%) patients and aortic changes (Aoc) in 8 (10.5%) patients. Regarding transoperative period, the mean CPB time was  $143.78\pm28.77$  minutes (minimum 91 and maximum 276 minutes) and mean time of clamping (clamp) of  $87.68\pm22.3$  minutes (minimum 43 and maximum 140 minutes). The length of stay in ICU lasted an average  $20.28\pm15.62$  days and the shorter time of 2 days and the longest 80 days (Table 1). Fifty-two (68.42%) patients were discharged from the ICU and 24 (31.58%) died during this period.

The variables of patients were compared according to their outcomes in the ICU and are presented in Table 2. The data show that none of the variables had significant *P* value

Table 1. Characteristics of infants undergoing Jatene's operation between 1995 and 2005 (n = 76)

between 1995 and 2005 (n = $76$ )		
Characteristics	Data	
Male %	64.47	
Age, days*	$14.59 \pm 19.09$	
Weight, kg *	$3.128 \pm 0.48$	
Length of stay, days *	$20.28 \pm 15.62$	
Anatomic diagnosis		
$TGA (PDA + PFO), \%(n^{\circ})$	57.9(44)	
TGA + IC, %(n°)	31.6(24)	
$TGA + Aoc, \%(n^{o})$	10.5(8)	
Transoperative		
CPB, min*	$143.78 \pm 28.77$	
Clamping, min*	$87.68 \pm 22.3$	

<sup>\*</sup> Data presented by mean and standard deviation. TGA = Transposition of Great Arteries, PDA = Patent Ductus Arteriosus, PFO = Patent Foramen Ovale; IC = Interventricular communication; Aoc = aortic changes; CPB = cardiopulmonary bypass time

when compared to patients who died or lived. Only a tendency to death was found in patients who stayed longer in CPB, with a P = 0.05.

Postoperatively, 51 (67.1%) patients returned to surgery with sternotomy opened. Only seven (9.21%) patients had no type of complication after surgery, 22 (28.9%) had one complication, 26 (34.2%), two complications, 14 (18.4%), three complications, six (7.9%), four complications and 1 (1.3%), five complications. The most frequent complications developed by patients in the postoperative period during the time of ICU admission are shown in Table 3.

Table 2. Age, weight, length of ICU, CPB, clamping and serum lactate in infants who underwent Jatene's operation: comparison of deaths and live

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Variables	Death	Discharge from ICU	P
Age, days <sup>T</sup>	$11.63 \pm 12.41$	$15.96 \pm 21.46$	0.27
Weight, kg <sup>T</sup>	$3.15 \pm 0.45$	$3.12 \pm 0.51$	0.81
Time of ICU, days <sup>T</sup>	$16.75 \pm 19.84$	$21.9 \pm 13.15$	0.25
Preop lactate*+	$4.11 \pm 5.65$	$4.36 \pm 4.4$	0.85
IPO lactate*+	$6.73 \pm 3.78$	$6.63 \pm 4.11$	0.91
Lactate at 3rd hour*+	$7.42 \pm 4.96$	$5.73 \pm 3.03$	0.13
Lactate at 6th hour*+	$7.14 \pm 5.5$	$5.56 \pm 4.3$	0.25
Lactate at 1st PO day*	<sup>+</sup> 4.56 ± 4.75	$2.84 \pm 1.98$	0.16
CPB, min <sup>T</sup>	$156.04 \pm 41.17$	$138.12 \pm 18.7$	0.05
Clamping, min <sup>T</sup>	$90.5 \pm 24.31$	$86.38 \pm 21.44$	0.48

Data presented by mean and standard deviation. ICU time = Length of stay in ICU; Preop Lactate = serum lactate preoperatively; IPO Lactate = lactate levels in the immediate postoperative period; Lactate at 3rd h = serum lactate at the 3rd postoperative hour; Lactate at 6th h = serum lactate at the 6th postoperative hour; Lactate at 1st PO = lactate levels at 1st postoperative day, CPB = cardiopulmonary bypass time. \* Serum lactate concentration presented in mmol/L. Mann + Whitney. T Student

Table 3. Distribution of early complications after Jatene's operation (n = 76)

operation (n = 70)	
Types of complications	No. of patients/%
None	7 (9.2)
Sepsis	29 (38.2)
Increased bleeding	27 (35.5)
Low Output	18 (23.7)
Respiratory	16 (21)
Renal failure	14 (18.4)
Pulmonary Hypertension	11 (14.5)
Arrhythmias	7 (9.2)
Chylothorax	6 (7.9)
Myocardial Ischemia	6 (7.9)
Seizures	4 (5.3)

There is a positive correlation between the number of complications and lactate levels in the IPO (r=0.23) at  $3^{rd}$  hour (r=0.33) at  $6^{th}$  hour (r=0.32) on  $1^{st}$  PO day (r=0.28), except preoperatively.

Separating the patients into two groups, those with TGA with IC and Aoc, and those who had only TGA, or that is, without IC, it was observed that the serum lactate preoperatively and in the IPO was higher in patients who had TGA without IC (Table 4).

There was no increased risk of complications in patients with IC, according to Table 5.

There is an increased risk of death in patients with increased bleeding, low output and respiratory complications (Table 6). However, only low output is an independent risk factor when placed in a logistic regression model.

The mean serum lactate preoperatively was  $4.28 \pm 4.78$  mmol/L, in the immediate postoperative,  $6.66 \pm 3.98$  mmol/L; at 3rd postoperative hour,  $6.26 \pm 3.8$  mmol/L, at the 6th postoperative hour,  $6.03 \pm 4.7$  mmol/L and at 1st postoperative day,  $3.27 \pm 2.98$  mmol/L. Comparing the levels of serum

Table 4. Serum lactate after Jatene's operation comparison between simple TGA and TGA + IC and Aoc

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Periods	TGA	TGA+IC+Aoc	P
Preop	$5.29 \pm 5.79$	$2.73 \pm 1.75$	0.001
IPO	$7.22 \pm 4.67$	$5.91 \pm 2.70$	0.006
3rd h	$6.18 \pm 3.29$	$6.38 \pm 4.45$	0.423
6th h	$6.02 \pm 4.68$	$6.04 \pm 4.80$	0.850
1st PO	$3.44 \pm 3.31$	$3.03 \pm 2.50$	0.661

Serum lactate values presented by mean and standard deviation (mmol/L). TGA = Transposition of Great Arteries, IC = Interventricular communication; Aoc = Aortic changes; Preop = preoperative; IPO = immediate postoperative; 3rd  $h = 3^{rd}$  postoperative hour, 6th  $h = 6^{th}$  postoperative hour;  $PO = I^{st}$  postoperative day

Table 5. Presence of IC as a risk factor for complications after Jatene's operation

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Complications	Odds Ratio	P
Sepsis	1.19 (0.47 – 3.05)	0.44
Increased bleeding	1.32(0.52 - 3.39)	0.12
Low output	1.52(0.53 - 4.40)	0.25
Respiratory	1.08(0.36 - 3.31)	0.55
Renal failure	2.11(0.65 - 6.84)	0.17
Pulmonary Hypertension	1.80(0.49 - 6.51)	0.32
Arrhythmias	0.42(0.07 - 2.24)	0.26
Chylothorax	1.42(0.27 - 7.50)	0.5
Myocardial Ischemia	1.41 (0.27 - 7.50)	0.5
Seizures	0.44 (0.04 - 4.40)	0.44
Open Sternum	1.89 (0.69 – 5.16)	1.0

lactate in the preoperative period with the IPO, from the 3rd hour and the 6th hour, the levels of the  $1^{st}$  postoperative day with the IPO, from the 3rd hour and the 6th hour, and the 3rd hour with the 6th hour there was a significant statistical difference with a P < 0.01 (Figure 1).

The Mann Whitney test showed no difference in the mean levels of serum lactate of patients who died or were discharged from the ICU in different periods. However, patients who died had a serum lactate preoperatively lower than those who lived, but in the IPO had higher levels than those who lived. These high levels were sustained until the end of the first postoperative day (Figure 2).

Only serum levels of lactate in the 3rd hour discriminate mortality, as shown by the area under the curve > 0.5 with P = 0.035. The levels of serum at 6th hour showed only a trend, with P = 0.052 (Table 7).

Table 6. Risk factors for early death after Jatene's operation

Complications	Odds Ratio	P
Sepsis	1.27 (0.46 – 3.33)	0.43
Increased bleeding	2.91(1.07 - 7.94)	0.031*
Low output	7.67(2.38 - 24.0)	0.000*
Respiratory	1.67 (1.35 - 2.05)	0.001*
Renal failure	1.83(0.56 - 6.00)	0.24
Pulmonary Hypertension	0.79(0.19 - 3.27)	0.52
Arrhythmias	4.29(0.93 - 19.7)	0.06
Chylothorax	5.00(0.85 - 29.5)	0.07
Myocardial Ischemia	5.00(0.85 - 29.5)	0.07
Seizures	0.71 (0.07 - 7.20)	0.63
Open Sternum	1.73 (0.59 - 5.10)	0.23

<sup>\*</sup> Chi-square < 0.05

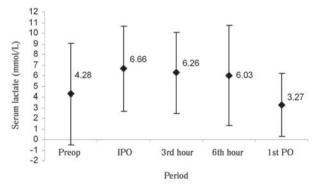


Fig. 1 - Values of serum lactate (mean and standard deviation) in infants after Jatene's operation

Preop = preoperative; IPO = immediate postoperative; 3rd hour = 3rd postoperative hour; 6th hour = 6th postoperative hour; 1st  $PO = 1^{st}$  postoperative day

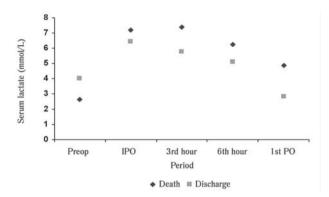


Fig. 2 - Values of serum lactate (mean) after Jatene's operation comparing deaths and live

 $Preop = preoperative; IPO = immediate postoperative; 3rd hour = 3rd postoperative hour; 6th hour = 6th postoperative hour; 1st <math>PO = 1^{st}$  postoperative day

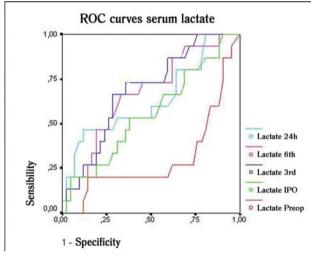


Fig. 3 - ROC curves of serum lactate after Jatene's operation in infants - Preop Lactate = preoperative serum lactate; IPO Lactate = serum lactate in the immediate postoperative period; Lactate 3rd = serum lactate at the 3rd postoperative hour; Lactate 6th = serum lactate at the 6th postoperative hour; Lactate 24h = serum lactate at 1st postoperative day

Table 7. Statistical description of the ROC curves of serum lactate after Jatene's operation in infants

-		Standard		CI (95%)	
Serum lactate	Area	Error	P	Lower	Higher
Preop	0.302	0.086	0.024	0.133	0.472
IPO	0.556	0.088	0.520	0.385	0.728
3rd hour	0.685	0.076	0.035	0.537	0.833
6th hour	0.670	0.079	0.052	0.514	0.826
1st PO	0.635	0.090	0.123	0.459	0.811

CI (95%) = Confidence Interval of 95% Lower = lower limit; Upper = upper limit, preop = preoperative; IPO = Immediate postoperative, 3rd hour = 3rd postoperative hour; 6th hour = 6thpostoperative hour; PO = 1st postoperative day Regarding the outcome of death-ICU discharge, considering a cutoff point for serum lactate  $\geq 5.8$  mmol/L at the 3rd postoperative hour, it was obtained a sensitivity of 67% and specificity 64%.

# DISCUSSION

The comparison of the patient's characteristics in our sample with those from literature allows us to show that the mean age of our patients  $14.59 \pm 19.09$  days, was slightly higher than those found by Conte et al. [4], which was 7 days and by Zabala Arguelles et al. [5], which was  $8.3 \pm 2.9$  days. Regarding surgery, the mean CPB time found in our study was  $143 \pm 28.77$  minutes and clamping time,  $87.68 \pm 22.3$  minutes. In the study by Zabala Arguelles et al. [5], with 15 patients who underwent surgical correction of TGA without IC, the mean CPB time was  $108 \pm 91$  minutes and clamping  $56 \pm 11$  minutes.

Over half of our patients (64.47%) were males in our sample, as well as in the study of Sharma et al. [15]. Of the 76 patients included in our study, 57.9% of diagnoses of TGA had no associated anatomical defects. In two other studies, one from 2002 and another from 2004, 56.5% and 62.2% had an anatomic diagnosis of TGA without associated defects, respectively [15,16].

In our study, from July 1995 to December 2005, there were 106 surgeries for correction of TGA using the Jatene's operation. In contrast, in a review published in 2002, in a period of 10 years, also in a developing country, 299 surgical corrections of TGA [11] were performed. A Brazilian study only with patients with Taussig-Bing found a mortality rate of 23.8% in this group whose surgical complexity is greater, in our sample we did not perform stratification of death according to type of malformation associated to TGA [17].

The surgical risk of this operation, according to literature, is around 2-5%, although it still presents in some centers, a risk higher than 10%, reaching over 20% of cases [18]. The postoperative outcome of any congenital heart disease depends on three variables: the anatomic-functional situation before the operation, the technique used and postoperative complications.

The experience of the first cases operated at the Dante Pazzanese Institute, where the technique was devised by Jatene et al. [18] in 1975, combined with the first cases operated at InCor, to date from 1987, it was obtained a mortality of 20.7%. However, one study from Minas Gerais showed a hospital mortality of 5.8% after the Jatene's operation, with patients similar to ours in relation to weight, age and associated defects [19].

In national multicenter study, it was observed general hospital mortality of 26%, the period of Jatene's operations was performed from 1975 to 2000. There was no stratification of mortality according the institution. The study included

the following institutions: Hospital da Real e Benemérita Sociedade Portuguesa de Beneficência, Dante Pazzanese Institute of Cardiology, Heart Hospital of the Syrian Sanatorium Association and Heart Institute, the latter two institutions were responsible for 96.4% of cases, respectively 50.7% and 45.7% [20].

Regarding the length of ICU stay, we obtained an average of  $20.28 \pm 15.62$  days, compared with  $2 \pm 1$  days described by Conte et al. [4]. Similar findings were seen in a study from 1998, where the average length of ICU stay was 17.8 days, but in patients who underwent cardiac surgery for several reasons [21].

Of the studies considered, none intended to show a specific variable as a risk factor for death. Among all the variables in our study, only low output proved to be a risk factor for death within the first 24 hours. Although the hospital mortality after the Jatene's operation is higher in Brazil than in reports from the international literature, there are few studies on the determinant factors. Our study is locally pioneering in the attempt to relate postoperative factors, among them the level of serum lactate. The major limitation of our study is the lack of preoperative or transoperative data that might have contributed to high mortality in our group. The low output only determinant factor of death in this sample may have occurred due to pre-desaturation maintained, delayed diagnosis, intraoperative coronary events which were not analyzed.

Other studies have associated death with pulmonary arterial hypertension, sepsis and left ventricular dysfunction [15,16]. In our study, only a tendency to death was found in patients who stayed longer in CPB, with a P = 0.05.

Postoperatively, only seven (9.21%) patients developed no complications. However, 26 (34.2%) patients had two associated complications. The most frequent complication found was sepsis (38.16% of patients). In a study published in 1998 and another in 2002, complications developed postoperatively were similar to those found in our study [21,22].

The mean serum lactate level of our patients preoperatively was  $4.28 \pm 4.78$  mmol/L; in the IPO of  $6.66 \pm 3.98$  mmol/L; at 3rd postoperative hour  $6.26 \pm 3.8$  mmol/L, at 6th postoperative hour  $6.03 \pm 4.7$  mmol/L and at 1st postoperative day  $3.27 \pm 2.98$  mmol/L. As in other studies, serum lactate values show a peak in the IPO with their levels decreasing gradually over the course of 24 hours, to values even lower than the preoperative [2,7,8,16,23].

Recently, Kalyanaraman et al. [24] showed that the initial and peak lactate are not significantly high in non-survivors of various types of cardiac surgery in children of various ages, however, they are not predictors of mortality. The time when the serum lactate level is above 2 mmol/L for more than 48 hours postoperatively, it predicts mortality in

patients RACHS-1 (Risk Adjustment for Congenital Heart Surgery), with positive predictive value of 60%, sensitivity 50% and specificity of 98%. Another recent study suggests the association of serum lactate > 8 mmol/L with a central venous oxygen saturation < 40% as predictors of mortality with high sensitivity and specificity [25]. There is a correlation between regional oxygen saturation in brain and kidney measured by near-infrared spectrospy and lactate when that is less than 65%, serum lactate levels are greater than or equal to 3 mmol/L in acyanotic patients [26].

Our data demonstrated that only serum levels of lactate from the 3rd hour discriminate mortality, as observed in the ROC analysis, showing an AUC > 0.5 with P = 0.035, different from that found in an article published in 1997 [6]. The levels of serum at 6th hour show only a trend, with P =0.052. In other studies, only after 24 h serum lactate served as a predictor of mortality [3,4]. Considering a cutoff point for serum lactate  $\geq 5.8$  mmol/L at the 3rd postoperative hour for the outcome death-ICU discharge, we obtained a sensitivity of 67% and specificity 64%; although statistically significant, this finding is of little use clinically due to the low sensitivity and specificity. A study published in 2006, with a cutoff of 4.8 mmol/L for serum lactate, showed that patients with levels above those in the early postoperative period had an increased risk of morbidity and mortality [6]. In another study, a serum lactate > 6 mmol/ L in the initial postoperative had a good predictive value for mortality [8].

Our study, as described by Hatherill et al. [8] also shows the serum lactate as a marker of morbidity, as there was positive correlation of their levels with the number of complications developed by patients, except in the preoperative.

Newborns are a group particularly prone to complications in the postoperative period due to changes triggered during CPB due to several factors, including: the effects of hemodilution are more pronounced, reduction of hematocrit and oncotic pressure limits the supply of O<sub>2</sub> and decrease in systemic vascular resistance may compromise tissue perfusion; increased exposure of circulating blood to the non-endothelial surface in the extracorporeal circuit, with exacerbation of systemic inflammatory response with release of cytokines and free radicals, O<sub>2</sub>, leading to direct tissue injury or change in microcirculation. Moreover, the duration of CPB, of myocardial anoxia, the level of hypothermia, the duration of cooling and warming, the strategy of manipulating the pH and hematocrit value may also contribute to hypoperfusion during CPB [27].

Although nonspecific, the increase or change in lactate levels during CPB may be a marker of regional hypoperfusion or increased metabolic demand. The organs that most often produce lactate include brain, intestines, liver, kidney and skeletal muscles [28,29]. Lactic acidosis

results from tissue hypoperfusion, the effect of certain drugs, or native defects of carbohydrate metabolism. The  $O_2$  supply is determined by cardiac output and arterial  $O_2$  content. Anemia and hypoxia decreased arterial  $O_2$  content, but its supply to the tissues tends to be maintained by compensatory mechanisms that increase cardiac output.

When lactic acidosis occurs related to these factors, there is probably concomitant cardiovascular compromise. The decrease of serum lactate on admission in the intensive care was proposed as a potential marker of poor evolution in postoperative pediatric cardiac surgery. In this population, the decrease of lactate should be cause for investigation of conditions leading to tissue hypoperfusion. In general, includes the adaptation of the cardiovascular and respiratory system to changes of blood volume in the postoperative period, the effects of CPB on the organism and the presence of residual defects [27].

In this retrospective study with patients in the postoperative of surgery for correction of transposition of great arteries through Jatene's operation, one can conclude that the serum lactate proved to be a marker of mortality and morbidity. Also, there was an increase in their values in the immediate postoperative period, returning to levels close to those of preoperative in 24 hours. Patients who died showed higher levels of lactate from the immediate postoperative period, and remained so until the end of the 1st postoperative day. Serum lactate at the 3rd hour was what that best discriminated mortality. There is an association between low output syndrome and increased risk of death.

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