Background: The identification of biomarkers for predicting morbidity and mortality, particularly in pediatric population undergoing cardiac surgery will contribute toward improving the patient outcome. There is an increasing body of literature establishing the clinical utility of hyperlactatemia and lactate clearance as prognostic indicator in adult cardiac surgical patients. However, the relationship between lactate clearance and mortality risk in the pediatric population remains to be established. Objective: To assess the role of lactate clearance in determining the outcome in children undergoing corrective surgery for tetralogy of Fallot (TOF). Methods and Study Design: A prospective, observational study. Setting: A tertiary care center. Study Population: Two hundred children undergoing elective surgery for TOF. Study Method: Blood lactate levels were obtained as baseline before operation (T0), postoperatively at admission to the cardiac intensive care unit after surgery (T1), and then at every 6 h for the first 24 h of Intensive Care Unit (ICU) stay (T6, T12, T18, and T24, respectively). The lactate clearance in the study is defined by the equation \( \frac{(\text{lactate initial} - \text{lactate delayed})}{\text{lactate initial}} \times 100\% \). Lactate clearance was determined at T1–T6, T1–T12, T1–T18, and T1–T24 time interval, respectively. The primary outcome measured was mortality. Secondary outcomes measured were the duration of mechanical ventilation, duration of inotropic requirement, and duration of ICU stay. Results: Eleven out of the two hundred patients enrolled in the study died. Nonsurvivors had higher postoperative lactate concentration \((P < 0.05)\) and low-blood lactate clearance rate during 24 h \((P < 0.05)\) in comparison to the survivors. Lactate clearance was significantly higher in survivors than in nonsurvivors for the T1–T6 period \((19.55 \pm 14.28 \text{ vs.} 5.024 \pm 27.79\%, \ P = 0.009)\) and remained significantly higher for each studied interval in first 24 h. Multivariate logistic regression analysis of statistically significant univariate variables showed early lactate clearance to have a significant relationship with mortality. Patients with a lactate clearance >10%, relative to patients with a lactate clearance <10%, in the early postoperative period, had improved outcome and lower mortality. Conclusion: Lactate clearance in the early postoperative period (6 h) is associated with decreased mortality rate. Patients with higher lactate clearance (>10%) after 6 h have improved outcome compared with those with lower lactate clearance. Key words: Lactate; Lactate clearance; Mortality; Pediatric; Postoperative

INTRODUCTION

There is a continuing need of identifying a biomarker for predicting mortality after cardiac surgery, especially in pediatric patient. Lactate, a product of anaerobic metabolism has been established as a good diagnostic, therapeutic, and prognostic marker of global tissue hypoxia.\(^1\) However, recent studies...
have shown that single measurement of lactate level has limited clinical utility for outcome prediction.\[^2\] Persistent elevated lactate in postoperative patients has shown to be associated with an increased mortality rate.\[^3\] As soon as the lactate is cleared from the body, the mortality decreases. Hence, serial measurement of lactate over time giving lactate clearance is a better biomarker for mortality that absolute lactate level.

Lactate clearance is shown to be a better biomarker for predicting mortality in critically ill adult patients;\[^4-6\] however, very few studies are there in the literature proving its utility in pediatric patients. The purpose of this study is to determine the clinical utility of lactate clearance as early as 6 h in the postoperative period as a predictor of mortality. We have hypothesized that lactate clearance in the early postoperative period is a predictor for mortality in children undergoing elective surgery for tetralogy of Fallot (TOF).

**METHODS**

After approval from the institute ethics committee and obtaining informed consent from the legally accepted representative of the children, this study was conducted from January 2013 to January 2015, on children weighing 5–20 kg undergoing elective corrective surgery on cardiopulmonary bypass (CPB) for TOF. The study design was a prospective observational study. Patients with pre-existing congestive cardiac failure, hemodynamic instability or need of inotropic support before the operation, elevation of any parameters preoperatively indicating systemic hypoperfusion, coagulopathy, renal failure (serum creatinine >2 mg/dl, anuria, or oliguria requiring dialysis), hepatic dysfunction (aspartate aminotransferase >40 U/L, alanine aminotransferase >40 U/L), local or systemic infection or inflammation (fever, leukocytosis, tachycardia, or tachypnea), any additional cardiac anomaly (absent pulmonary valve syndrome, pulmonary atresia, branch pulmonary artery stenosis, atrioventricular conduction disturbance and pink TOF), patients undergoing conduit repair, and reoperation were excluded from the study.

Anesthetic and surgical management were standardized in all patients including the anesthesia and surgical team members. All operations were performed by the same anesthesia and surgical team to eliminate the influence of anesthesia and surgical techniques on varying postoperative clinical outcome of the patients. The standard American Society of Anesthesiologists monitoring was used in all children along with invasive arterial pressure monitoring, central venous pressure monitoring, and transesophageal echocardiography. All children were premedicated with intramuscular morphine 0.1 mg/kg and phenergan 0.05 mg/kg, and anesthesia was induced with an inhalation technique using oxygen-air-sevoflurane, 2–5 μg/kg of fentanyl, and 1.0 mg/kg of rocuronium bromide to facilitate tracheal intubation. Anesthesia was maintained with oxygen-air-sevoflurane of 0.5–2%, and intermittent doses of fentanyl, midazolam, and vecuronium. CPB was conducted on all children using a membrane oxygenator (Medtronic, Anaheim, CA), nonocclusive roller pumps, and moderate hypothermia (28–30°C). The CPB circuit was primed in all cases with 20 mL/kg of lactated Ringer's solution, 1 mL/kg of sodium bicarbonate 7.5% (w/v), 0.5 g/kg of mannitol 20% (w/v), and 100 U/kg of heparin. Packed red blood cells were added on CPB, and conventional ultrafiltration was performed during the rewarming phase of CPB to maintain a hematocrit value of 30%. Myocardial protection was achieved using a blood cardioplegia solution in a dose of 20 mL/kg. CPB flows were maintained between 120 and 200 mL/kg/min. Post-CPB, appropriate inotrope, and dilators were used to maintain the patient's hemodynamics.

Patients were transferred to the Cardiac Intensive Care Unit (ICU) after surgery. The sample for lactate was obtained at T0 (after induction of anesthesia), T1 (at shifting to ICU), T6 (after 6 h of ICU stay), T12 (after 12 h of ICU stay), T18 (after 18 h of ICU stay), and T 24 (after 24 h of ICU stay), respectively. T0 establishes the baseline values and T1, T6, T12, T18, and T24 establishes the change in lactate value at ICU. Lactate analysis was performed with commercial gas analyzer (ABL 835 Flex, radiometer Copenhagen, Denmark). The lactate clearance is defined by the equation \((\frac{\text{lactate}_{\text{initial}} - \text{lactate}_{\text{delayed}}}{\text{lactate}_{\text{initial}}} \times 100\%)\). A positive value indicates a decrease in lactate blood concentration and its clearance from the body, and a negative value indicates the inability to clear lactate from the blood circulation. Lactate clearance is determined at T1–T6, T1–T12, T1–T18, and T1–T24.

For all patients, the primary outcome measured was mortality, and the secondary outcomes measured were; the duration of mechanical ventilation, the duration of inotropic requirement, and the length of ICU stay. The duration of mechanical ventilation was defined as the number of hours the child remained intubated after shifting to the ICU. The criteria for tracheal extubation was conscious and responsive patient, adequate motor
power, peripheral skin temperature >33°C, stable hemodynamic parameters, no continuing bleeding, \( \text{PaO}_2 > 60 \text{ mmHg}, \text{PaCO}_2 < 40 \text{ mmHg}, \) and electrolytes within normal limits. The duration of inotropic requirement was defined as the number of hours the patient required inotropes. The length of ICU stay was defined as the as the number of hours between the date of surgery and ICU discharge. A vasoactive inotrope score was calculated based on the type and dosage of inotrope utilized using the following formula designed to account for relative potencies of various inotropes.\(^7\)

\[
(\text{[dopamine + dobutamine] } \mu\text{g/kg/min} \times 1) + (\text{milrinone } \mu\text{g/kg/min} \times 20) + (\text{[epinephrine + norepinephrine] } \mu\text{g}/\text{kg/min} \times 100)^2
\]

### Statistical analysis

The data were entered in Microsoft Excel format (Microsoft, Redmond, WA, USA) and analyzed using SPSS version 15 software (SPSS, Chicago, IL, USA). 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. Univariate and multivariate regression analysis were performed accordingly. A \( P < 0.05 \) was considered statistically significant.

### RESULTS

A total of 210 patients undergoing elective surgical repair for TOF between January 2013 and January 2015 were enrolled in the study. Ten patients were excluded as per criteria for exclusion. Of remaining 200 patients eleven died (mortality 5.5%) within first 30 days postoperatively. Five patients died of low-cardiac output, one of bleeding, two of respiratory failure, and three of multiorgan dysfunction.

Univariate analysis comparing the different perioperative parameters of survivors and nonsurvivors is shown in Table 1. The preoperative demographic profile was comparable between the survivors and nonsurvivors. The mean age of the survivor and nonsurvivor was 3.08 ± 1.35 years and 2.56 ± 0.65 years \( (P > 0.05) \), respectively. The two groups were comparable with respect to CPB time, aortic cross-clamp time, urine output, amount of hemofiltration, temperature on CPB, and hematocrit on CPB \( (P > 0.05) \). In the postoperative period, nonsurvivors had prolonged duration of inotrope use \( (54.73 \pm 13.55 \text{ vs. } 23.89 \pm 13.39 \text{ h}, P < 0.001) \), higher vasoactive inotrope score \( (15.36 \pm 3.69 \text{ vs. } 5.67 \pm 3.6, P < 0.001) \), prolonged duration of mechanical ventilation \( (18.82 \pm 8.18 \text{ vs. } 11.19 \pm 4.52 \text{ h}, P < 0.001) \), and ICU stay \( (48.85 \pm 7.26 \text{ vs. } 66.64 \pm 25.46 \text{ h}, P = 0.004) \) in comparison to the survivors.

### Table 1: Univariate analysis between survivor and nonsurvivor

| Parameter                        | Survivor \((n=189)\) | Nonsurvivor \((n=11)\) | \(P\) | OR (95% CI) |
|----------------------------------|----------------------|------------------------|------|-------------|
| Age (years)                      | 3.08±1.35            | 2.56±0.65              | 0.06 | 0.72 (0.49-1.2) |
| Weight (kg)                      | 9.76±2.97            | 9.73±2.32              | 0.96 | 0.76 (0.3-2.1) |
| Gender (male/female)             | 121/68               | 8/3                    | 0.5  | 0.66 (0.17-2.59) |
| Height (cm)                      | 87.36±5.25           | 90.13±4.72             | 0.97 | 0.87 (0.12-3.4) |
| Preoperative hemoglobin (g/100 mL)| 20.23±1.93         | 19.23±1.78             | 0.09 | 0.75 (0.52-1.06) |
| Preoperative oxygen saturation (%)| 70.82±6.62          | 68.12±7.35             | 0.43 | 1.03 (0.94-1.14) |
| Beta blocker (%)                 | 171 (90)             | 10 (90.1)              | 0.96 | 0.95 (0.11-7.85) |
| Coiling (%)                      | 40 (21.2)            | 3 (27.3)               | 0.6  | 0.71 (0.18-2.82) |
| CPB time (min)                   | 90.10±9.253          | 90.73±6.82             | 0.775| 1.00 (0.94-1.07) |
| Clamp time (min)                 | 62.76±4.27           | 64.55±4.65             | 0.23 | 1.10 (0.95-1.28) |
| Temperature on CPB (centigrade)  | 29.91±0.22           | 29.92±0.23             | 0.87 | 1.24 (0.07-9.98) |
| Urine output on CPB (mL)         | 151.43±80.45         | 148.45±15.66           | 0.55 | 0.98 (0.94-1.2) |
| CUF (mL)                         | 78.76±8.51           | 80.45±9.25             | 0.52 | 1.02 (0.95-1.12) |
| Hematocrit on CPB (%)            | 33.51±2.1272         | 34.72±1.67             | 0.5  | 1.31 (0.97-1.76) |
| Duration of inotropic support (h)| 23.89±13.39          | 54.73±13.55            | <0.001*| 1.17 (1.09-1.26) |
| Vasoactive inotropic score       | 5.67±3.6             | 15.36±3.69             | <0.001*| 2.80 (1.53-4.42) |
| Vasopressor use (%)              | 15 (7.9)             | 5 (45.5)               | <0.001*| 0.10 (0.02-0.37) |
| Duration of mechanical ventilation (h) | 11.19±4.52     | 18.82±8.18             | <0.001*| 1.30 (1.10-1.53) |
| Duration of ICU stay (h)         | 48.85±7.26           | 66.64±25.46            | 0.004*| 1.07 (1.02-1.13) |

*\(P<0.05\) is significant. Values are expressed as mean±SD. \(P<0.05\) is considered significant. CPB: Cardiopulmonary bypass, ICU: Intensive Care Unit, SD: Standard deviation, CUF: Conventional ultrafiltration, OR: Odds ratio, CI: Confidence interval
The initial lactate values measured before the surgical intervention (T0) were comparable in both survivors and nonsurvivors (1.61 ± 0.44 mmol/L vs. 1.9 ± 0.56 mmol/L; P = 0.08). The initial lactate values measured at admission to ICU (T1) was 3.99 ± 1.33 mmol/L in survivor compared to 5.11 ± 1.77 mmol/L in nonsurvivors (P = 0.065). Thereafter, the lactate values measured at every 6 h interval was found to be significantly higher in nonsurvivors than in survivors (3.16 ± 1.12 mmol/L vs. 4.87 ± 1.88 mmol/L at T6, 2.95 ± 1.09 mmol/L vs. 4.7 ± 1.76 mmol/L at T12, 2.7 ± 1.07 mmol/L vs. 4.77 ± 1.91 mmol/L at T18, and 2.5 ± 1.11 mmol/L vs. 4.9 ± 2.08 mmol/L at T24, P < 0.05 for each studied period) [Table 2].

The mean blood lactate concentration obtained by averaging the lactate value during the first 24 h was significantly lower in survivors than in nonsurvivors (3.07 ± 1.03 mmol/L vs. 4.8 ± 1.08 mmol/L; P = 0.008) [Table 2].

In survivors, the mean postoperative blood lactate concentration decreased significantly with time in comparison to the nonsurvivors [Figure 1].

Lactate clearance was significantly higher in survivors than in nonsurvivors for the T1–T6 period (19.55 ± 14.28 vs. 5.24 ± 27.79%, P = 0.009) and remained significantly higher for each studied interval in first 24 h (24.59 ± 16.81% vs. 6.41 ± 32.19; P = 0.003 for T1–T12, 30.77 ± 25.44% vs. 2.17 ± 13.83%; P = 0.002 for T1–T18, 35.89 ± 29.07% vs. 3.16 ± 16.38%; P = 0.001 for T1–T24) [Table 3].

On multivariate analysis comparing survivors and nonsurvivors, duration of ventilation, duration of ICU stay, use of vasopressor, and lactate clearance were found to be significantly associated with mortality (P < 0.05). It is found that lactate clearance as early as 6 h in the postoperative period can significantly predict mortality [Table 4].

The role of lactate clearance: Patients with initial lactate levels (T1) > 2.5 mmol/L were taken for comparison as initial lactate values in the normal range would not provide any meaningful data. Fifty-one patients with initial lactate level < 2.5 mmol/L were accordingly excluded. Four patients of this subgroup showed an increase in lactate level during 24 h (lactate increased to 3.6–6.5 mmol/L), but all of them had survived. However, subgroup analysis was not performed because of the small number of patients. Further investigation may be needed in patients whose initial lactate level is in the normal range but increases during the early postoperative period. The subgroup with high initial lactate (n = 149) was divided into high- and low-lactate clearance group. We took lactate clearance at 6 h for subgroup formation as it was the earliest period at which it was found to be significant on multivariate analysis of our data. The cut-off was taken as 10% depending on previously published data.[2] Thereby, the two subgroups formed were (a) high-lactate clearance group in which repeat lactate decreased by 10% or more from initial and (b) low-lactate clearance group in which lactate decreased by < 10% from initial at 6 h postoperatively.

Table 2: Serial blood lactate level between survivors and nonsurvivors

| Parameter                  | Survivor (n=189) | Nonsurvivor (n=11) | P    | OR (95% CI) |
|----------------------------|------------------|--------------------|------|-------------|
| Preoperative lactate (T0)  | 1.61±0.44        | 1.9±0.56           | 0.08 | 2.7 (0.82-8.99) |
| Initial lactate (T1)       | 3.99±1.33        | 5.11±1.77          | 0.065| 1.88 (1.14-3.08) |
| Lactate at 6 h (T6)        | 3.16±1.12        | 4.87±1.88          | 0.013*| 1.67 (1.23-2.02) |
| Lactate at 12 h (T12)      | 2.95±1.09        | 4.72±1.76          | 0.008*| 3.59 (1.9-6.7) |
| Lactate at 18 h (T18)      | 2.7±1.07         | 4.77±1.91          | 0.006*| 3.39 (1.9-6.03) |
| Lactate at 24 h (T24)      | 2.5±1.11         | 4.9±2.08           | 0.003*| 3.03 (1.8-5.02) |
| Mean postoperative lactate | 3.07±1.03        | 4.8±1.80           | 0.008*| 3.64 (1.96-6.76) |

*P<0.05 is significant. Values are expressed as mean±SD. P<0.05 is considered significant. SD: Standard deviation, OR: Odds ratio, CI: Confidence interval

Table 3: Lactate clearance rate between survivors and nonsurvivors during 1st 24 h

| Parameter                  | Survivor (n=189) | Nonsurvivor (n=11) | P    | OR (95% CI) |
|----------------------------|------------------|--------------------|------|-------------|
| Lactate clearance (T1-T6)  | 19.55±14.28      | 5.24±27.79         | 0.009*| 0.93 (0.89-0.98) |
| Lactate clearance (T1-T12) | 24.59±16.81      | 6.41±32.19         | 0.003*| 0.94 (0.90-0.99) |
| Lactate clearance (T1-T18) | 30.77±25.44      | 2.17±13.83         | 0.002*| 0.96 (0.92-1) |
| Lactate clearance (T1-T24) | 35.89±29.07      | <3.16±16.38        | <0.001*| 0.94 (0.90-0.98) |

*P<0.05 is significant. Values are expressed as mean±SD. P<0.05 is considered significant. SD: Standard deviation, OR: Odds ratio, CI: Confidence interval
Both the groups were comparable with respect to age, sex, height, and weight. However, the incidence of preoperative coiling was higher in low-lactate clearance group (36.6% vs. 15.7%, \( P = 0.007 \)). Duration of inotropic support required (24.19 ± 13.28 vs. 30.78 ± 18.49, \( P < 0.001 \)), vasoactive inotropic score (6.247 ± 4.18 vs. 12.34 ± 5.69, \( P < 0.001 \)), duration of ICU stay (48.85 ± 7.26 vs. 66.64 ± 25.46, \( P = 0.004 \)), duration of mechanical ventilation (11.29 ± 4.73 vs. 14.56 ± 6.73, \( P < 0.001 \)) were significantly lower in the high-clearance group compared with the low-clearance group. Both low- and high-clearance groups had similar baseline lactate (\( T_0 = 1.65 ± 0.51 \) vs. 1.59 ± 0.4, \( P = 0.48 \)) and initial lactate values (\( T_1 = 4.65 ± 1.07 \) vs. 4.78 ± 0.93, \( P = 0.47 \)); however, the high-clearance group had lower lactate value at 6 h and throughout the 24-h study period (\( P = 0.001 \)). The high-clearance group had a relatively lower in-hospital mortality rate compared with the low-clearance group (1.9% vs. 22%, \( P = 0.03 \)) [Table 5 and Figure 2].

### Table 4: Multivariate analysis between survivors and nonsurvivors

| Parameter                      | OR   | 95% CI         | \( P \)  |
|-------------------------------|------|----------------|---------|
| Duration of ventilation       | 1.488| 1.14-1.937     | 0.004*  |
| Duration of ICU stay          | 1.08 | 1.02-1.14      | 0.03*   |
| Use of vasopressor            | 35.19| 3.02-409.96    | 0.02*   |
| Lactate clearance (T1-T6)     | 0.955| 0.912-1.001    | 0.006*  |
| Lactate clearance (T1-T24)    | 0.924| 0.876-0.974    | 0.001*  |

*\( P < 0.05 \) is significant. OR: Odds ratio, CI: Confidence interval, ICU: Intensive Care Unit

**Figure 1:** Mean postoperative blood lactate concentration in survivors and nonsurvivors

**Figure 2:** Kaplan–Meier survival analysis in patients with lactate clearance of >10% versus <10% at 6 h postoperatively
Very few pediatric studies have analyzed the serial lactate measurements and lactate clearance as indicators for mortality after cardiac surgery. To our knowledge, this is the first study that has been done to correlate lactate clearance with mortality, at different time interval, within first 24 h in TOF patients undergoing intracardiac repair. In our study, we found that lactate clearance as early as 6 h in the postoperative period is a predictor of mortality in children undergoing cardiac surgery.

The search for an ideal biomarker for predicting adverse outcome following pediatric cardiac surgery continues. Heart rate, blood pressure, oxygen delivery, periphery-core temperature gradient, mixed venous oxygen saturation, etc., are not established as indicators of outcomes after cardiac surgery. Plasma lactate is a conventional indicator of tissue hypoxia and has been widely used in the management of critically ill patients. Hyperlactatemia has been correlated with mortality in adults, children, and neonates. However, the predictive role of plasma lactate on mortality has been extensively studied in critically ill adults only. In pediatric patients, the predictive value of lactate concentration on postoperative mortality is supported by some studies; however, a few authors like Hatherill et al.,[13] and Munoz et al.[14] have reported low- positive predictive role. Kalyanaraman et al.[8] reported that both initial and peak lactate levels had a poor positive predictive value for mortality in children undergoing repair or palliation of congenital cardiac defects. The cut-off value of lactate that correlate with mortality is widely debated. Basaran et al.[15] found that a cutoff of 4.8 mmol/L for mean serum lactate in infants after cardiac surgery can predict mortality and morbidity. In our study, we also found that postoperative lactate...
levels were significantly elevated in nonsurvivors during the first 24 h when compared with survivors.

Interpretation of single lactate measurements has several limitations as an increased single lactate level might indicate mechanisms other than cellular hypoxia-like increased lactate production via catecholamine-driven pathways or decreased lactate clearance due to hepatic dysfunction. Serial lactate measurements over time have been shown to be useful as predictors of outcome in patients with severe sepsis and septic shock. Early lactate clearance has been associated with improved outcome in adult patients with severe sepsis and septic shock[2] but its role in pediatric cardiac surgical patients still needs to be evaluated. Charpie et al.[16] found that an increase in lactate level of more than 0.75 mmol/L/h is a predictor of poor outcome in neonates undergoing complex cardiac surgery with a positive predictive value of 100%, sensitivity of 89%, and specificity of 100%. Huang et al.[17] concluded that lactate clearance can be correlated with survival in postcardiac arrest children after the return of spontaneous circulation with the help of extracorporeal membrane oxygenation. They found that postextracorporeal cardiopulmonary resuscitation nonsurvivors had higher lactate level and lower clearance in the first 24 h. Rocha et al.[18] evaluated lactate trend in infants after Jatene’s operation and found that increased serum lactate from the 3rd h in the postoperative period can assess mortality. In our study, we found that early lactate clearance, as defined by the percentage of lactate cleared over the first 6-h in the postoperative period can predict in-hospital mortality in postcardiac surgery patients. We also found that patients with high-lactate clearance of more than 10% from its baseline value in 6 h required less duration of ventilation, less inotropic requirement, vasopressor therapy, and had less duration of ICU stay.

Our study has a few clinically significant implications. Low-lactate clearance in the early postoperative period will be helpful for clinical risk stratification of critically ill pediatric patients. Serum lactate can thereby be used as an easily available biomarker for early interventional strategy or goal-directed therapy. The comparison between survivors and nonsurvivors showed a discrepancy regarding numbers. A post hoc power analysis of the data could not be performed in this study. Ongoing numbers in prospective studies are warranted.

CONCLUSION

Lactate clearance in the early postoperative period is an independent predictor of mortality in pediatric cardiac surgical patients. It is inexpensive, easy to do, and a reliable predictor of patient outcome.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Levy B. Lactate and shock state: The metabolic view. Curr Opin Crit Care 2006;12:315-21.
2. Nguyen HB, Rivers EP, Knoblich BP, Jacobsen G, Muzzin A, Ressler JA, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. Crit Care Med 2004;32:1637-42.
3. Meregalli A, Oliveira RP, Friedman G. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. Crit Care 2004;8:R60-5.
4. Odom SR, Howell MD, Silva GS, Nielsen VM, Gupta A, Shapiro NI, et al. Lactate clearance as a predictor of mortality in trauma patients. J Trauma Acute Care Surg 2013;74:999-1004.
5. Wu JF, Wu RY, Chen J, Ou-Yang B, Chen MY, Guan XD. Early lactate clearance as a reliable predictor of initial poor graft function after orthotopic liver transplantation. Hepatobiliary Pancreat Dis Int 2011;10:587-92.
6. Marty P, Roquilly A, Vallée F, Luzi A, Ferré F, Fourcade O, et al. Lactate clearance for death prediction in severe sepsis or septic shock patients during the first 24 hours in intensive care unit: An observational study. Ann Intensive Care 2013;3:3.
7. Gaiés MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med 2010;11:234-8.
8. Kalyanaraman M, DeCampili WM, Campbell AI, Bhalala U, Harmon TG, Sandiford F, et al. Serial blood lactate levels as a predictor of mortality in children after cardiopulmonary bypass surgery. Pediatr Crit Care Med 2009;9:285-8.
9. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, Lima AP, et al. Early lactate-guided therapy in intensive care unit patients: A multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med 2010;182:752-61.
10. Nguyen HB, Kuan WS, Batech M, Shrikhande P, Mahadevan M, Li CH, et al. Outcome effectiveness of the severe sepsis resuscitation bundle with addition of lactate clearance as a bundle item: A multi-national evaluation. Crit Care 2011;15:R229.
11. Cheung PY, Chui N, Joffe AR, Rebeyka IM, Robertson CM; Western Canadian Complex Pediatric Therapies Project, Follow-up Group. Postoperative lactate concentrations predict the outcome of infants aged 6 weeks or less after...
intracardiac surgery: A cohort follow-up to 18 months. J Thorac Cardiovasc Surg 2005;130:837-43.

12. Saugstad OD. Is lactate a reliable indicator of tissue hypoxia in the neonatal period? Acta Paediatr 2002;91:17-9.

13. Hatherill M, Sajjanhar T, Tibby SM, Champion MP, Anderson D, Marsh MJ, et al. Serum lactate as a predictor of mortality after paediatric cardiac surgery. Arch Dis Child 1997;77:235-8.

14. Munoz R, Laussen PC, Palacio G, Zienko L, Piercey G, Wessel DL. Changes in whole blood lactate levels during cardiopulmonary bypass for surgery for congenital cardiac disease: An early indicator of morbidity and mortality. J Thorac Cardiovasc Surg 2000;119:155-62.

15. Basaran M, Sever K, Kafali E, Ugurlucan M, Sayin OA, Tansel T, et al. Serum lactate level has prognostic significance after pediatric cardiac surgery. J Cardiothorac Vasc Anesth 2006;20:43-7.

16. Charpie JR, Dekeon MK, Goldberg CS, Mosca RS, Bove EL, Kulik TJ. Serial blood lactate measurements predict early outcome after neonatal repair or palliation for complex congenital heart disease. J Thorac Cardiovasc Surg 2000;120:73-80.

17. Huang S, Wu ET, Chen YS, Ko WJ, Wang SS. The blood lactate clearance following extracorporeal cardiopulmonary resuscitation for pediatric patients with in hospital cardiac arrest. Circulation 2011;124:A13130.

18. Rocha TS, Silveira AS, Botta AM, Ricachenevsky CP, Dalle Mulle L, Nogueira A. Serum lactate as mortality and morbidity marker in infants after Jatene’s operation. Rev Bras Cir Cardiovasc 2010;25:350-8.