

Ali Jabbari (MD, MPH)^{1,2}
Nadia Banihashem (MD)^{1,2}
Ebrahim Alijanpour (MD)²
Hamid Reza Vafaey (MD)³
Hakimeh Alereza (MD)²
Seyed Mozafar Rabiee (MD)²

1- Department of Anesthesiology and Intensive Care, Golestan University of Medical Sciences, Golestan, Iran.

2- Department of Anesthesiology and Intensive Care, Babol University of Medical Sciences, Babol, Iran.

3- Department of Surgery, Cardiac Surgery Branch, Babol University of Medical Sciences, Babol, Iran.

*** Correspondence:**

Nadia Banihashem, Department of Anesthesiology and Intensive Care, Babol University of Medical Sciences, Babol, Iran.

E-mail: ans_dep@yahoo.com

Tel: 0098 111 2238296

Fax: 0098 111 2238296

Received: 10 Nov 2012

Revised: 21 Jan 2013

Accepted: 25 Feb 2013

Serum lactate as a prognostic factor in coronary artery bypass graft operation by on pump method

Abstract

Background: Lactic acidosis in cardiac surgical patients is a manifestation of systemic inflammation and excess pro-inflammatory cytokine production. This investigation was designed to integrate basic concepts about lactate acidosis with a clinically used of serum lactate in patients under coronary artery bypass surgery (CABG) by on pump method.

Methods: From August to September 2012, 15 patients scheduled for routine cardiac surgery entered to our sample and followed up two weeks. Lactate concentration in arterial blood sample was studied. Method of surgery duration of cardiopulmonary bypass, aorta cross clamp timing, hemodynamic parameters, inotrope dosage and patient outcome were documented. The data were collected and analyzed.

Results: The mean age of the patients was 62±14 years. The patients with a poor outcome had significantly higher lactate levels in ABG samples ($p<0.001$). ABG lactate levels did not correlate with the magnitude of intra-operative bleeding or volume of packed cell transfusion ($p>0.05$). The PH of ABG samples did not generally correlate with the ABG lactate concentration ($r=0.116$, $p=0.68$). Increased lactate concentration was reliably associated with patient hemodynamic parameters, inotrope dosage, duration of on pump time and aorta cross clamp time.

Conclusion: This study demonstrates a correlation between serum lactate levels and patient prognosis after CABG surgery by on pump method.

Keywords: Serum lactate, Prognosis, Coronary artery bypass graft

Caspian J Intern Med 2013; 4(2):662-666

Lactic acid is a strong organic acid that readily dissociates in water to H⁺ and the lactate anion (1). It is a major end product of glucose metabolism. The concentration of lactic acid in the blood is a balance between production and clearance (2). In normal, healthy individuals, this balance is optimally maintained, but cardiac surgery, particularly in patients who have been supported on cardiopulmonary bypass could alter this balance (3-5). Increased lactic acid production is a characteristic metabolic consequence of hypoxia, but lactic acidosis can also develop under nonhypoxic conditions (6). The predominant feature of these conditions could be inability to utilize pyruvate in oxidative metabolism pathways or impaired hepatic utilization (6-9). Hypoperfusion and hypothermia during coronary artery bypass graft (CABG) surgery decreased liver function and therefore most of the patients exhibit a progressive increase in plasma lactate during cardiopulmonary bypass (CPB).

Although, progression on lactic acidosis is seen as a potential indicator of inadequate organ perfusion, lactic acid accumulation in cardiac surgical patients could be a result of excess lactic acid production and was not related to altered carbohydrate metabolism or liver hypo perfusion (2, 10). Lactate serum level can give an indicator of the metabolic status during CPB and it is associated with excess mortality among patients (11, 12).

Based on our clinical experience, we hypothesized that although there are many factors that influenced the serum plasma level during a CABG surgery, it has a serious prognostic effect on predicting the outcome of the operation. In other words, lactate serum level inferred by arterial blood gas (ABG) considered playing an important role in patient's prognostic forecast under coronary artery by-pass graft by on pump method. This investigation was designed to integrate basic concepts about lactate acidosis with a clinically used of serum lactate in patients under CABG surgery.

Methods

In this 15 patients scheduled for routine cardiac surgery in our progressive open heart surgery center with uneventful surgical procedures entered to our sample and were followed over a two week period. The patient's demographic characteristics and history of myocardial infarction, hypertension, congestive heart failure, vascular surgery, and diabetes were collected. We extracted the patient's data from his/her medical folder, retrospectively and followed them up prospectively.

The patients were admitted to a dedicated cardiac surgical intensive care unit after surgery but, patient care was not modified for the purpose of the study. Cardiopulmonary bypass was performed using an open system primed with 1200 mL of Hartmann's solution and roller pumps.

Lactate concentration in arterial blood gas sample was studied in these 15 patients during surgery. All patients were paralyzed and under mechanical ventilation through cuffed Oro-tracheal tube so that P_aCO_2 was kept at 35.0 ± 5.0 mm Hg and P_aO_2 at 110 ± 10 mm Hg (mean \pm standard deviation). One protocol was used for anesthesia induction and maintenance for all patients.

The first ABG sample was drawn at the artery line preparation time as a base line and sampling was done every 30 minutes during the surgery and after the operation every 6 hours, and hemodynamic parameters and inotropic requirement dosage were recorded at the end of cardiopulmonary bypass, on arrival in the intensive car. The duration of postoperative mechanical ventilation and the blood loss in the first day after surgery were recorded.

The nature of the surgical procedure, duration of cardiopulmonary bypass and the minimum temperature on cardiopulmonary bypass (CPB), hemoglobin concentrations on cardiopulmonary bypass that corresponded with these

blood gases and duration of aorta cross clamp time were documented. The patient's outcome was evaluated by post operation intubation time, GCS and hemodynamic parameters, days of ICU (Intensive care Unit) admission, patient ambulation and out of bed time and post operation echo cardiograph. The uncomplicated patient stayed in ICU for 72 hours after CABG routinely, and then they were transferred to post ICU.

Because of our small sample size, we could not evaluate some of our parameters statistically but generally, continuous variables were analyzed with t-test. The relation between lactic acid levels and duration of surgery, cross-clamp time, total inotrope dosage and transfusion volume was analyzed using t-test where appropriate. For categorical covariates, the comparison was studied using a chi square test or Fisher's exact test. The association between an individual outcome and lactic acid levels was examined by t-test, then the interaction between hemodynamic parameters and change in lactic acid levels with time was evaluated by Pearson's correlation coefficient. The significance level was defined as a p value less than 0.05.

Results

Fifteen patients aged 62 ± 14 years were enrolled during the study period. They were observed and followed for about two weeks. There were 9 males and 6 females in our patients (table 1).

Table 1. Characteristics of 15 patients' who underwent CABG

Variables	mean \pm SD
Age (years)	62 \pm 14
Weight (kg)	62 \pm 24
High (cm)	164 \pm 9
BMI	23.13 \pm 2.25
Ejection fraction (EF %)	40 \pm 15
Cross-clamp time (min)	54 \pm 14
Cardiopulmonary bypass time (min)	86 \pm 16
Grafts per patient	3 \pm 1

The patients with a poor outcome had significantly higher lactate levels in ABG samples ($p < 0.001$). Table 2 shows the relationship between serum lactate level and hemodynamic parameters. The patient with serum lactate

level over 5 had an apnea period after extubation and suffered from neurologic damage. The patients with serum lactate level between 3-5 needed aorta balloon pump after the surgery and they were admitted 1 week in ICU. One patient with serum lactate level between 2 and 3 showed arrhythmia and she was transferred to Cardiac Care Unit for more medical treatment. Table 3 shows patients' outcome according to serum lactate

ABG lactate levels did not correlate with the magnitude of intra operative bleeding or hemoglobin concentration (Hb) before the surgery or volume of packed red blood cell transfusion ($p>0.05$). The decreasing rate of ABG lactate concentration was lower in patients with a poor outcome.

The patients showing favorable outcome had a significant decrease in lactate levels 12 hours after injury. This decrease was not observed in patients with a poor outcome. PH of ABG samples did not generally correlate with the ABG lactate concentration in patients under CABG ($r=0.116$, $p=0.68$); however, in a few patients with ventricular ejection fraction below 30% and patient with a valve repaired, a correlation was noted to be ($r=0.786$, $p=0.042$).

Increased lactate concentration in ABG samples was reliably associated with the patient's hemodynamic parameters ($r=0.686$, $p=0.03$), total inotrope dosage ($r=0.549$, $p=0.02$); and duration of on pump time ($r=0.742$, $p=0.03$) and cross-clamp time ($r=0.467$, $p=0.04$).

Table 2. Arterial serum lactate level and hemodynamic parameters in studied patients'

Time	hemodynamic parameters			serum lactate level (mmol/L)
	Systolic BP (mmHg)	Diastolic BP (mmHg)	HR (bpm)	
Artery line preparation (zero time)	127±36	76±23	78±31	0.83±0.29
30th min from beginning	96±41	65±18	84±17	0.87±0.33
15th min of cardio pulmonary bypass (on pump time)	-	-	-	2.84±1.68
End of the cardio pulmonary bypass (off pump time)	-	-	-	3.48±2.23
End of the surgery	86±21	45±9	88±26	4.28±2.48
ICU admission time	92±18	52±11	89±24	4.33±2.56
2 h after ICU admission	98±27	58±13	90±18	3.87±2.17

Table 3. Outcome of the patients according to serum lactate levels

Out come	Number of patient	Serum lactate level (mmol/L)
good		
Expected outcome (uncomplicated)	10	≤ 2
Long time arrhythmia	1	2-3
acceptable		
Post operation (ICU discharge) CCU admission	1	2-3
Long time ICU admission, use of aortic balloon pump	1	3-4
Long time ICU admission, use of aortic balloon pump	1	4-5
poor		
Neurologic sequela	1	≥ 5

Discussion

Epinephrine increases cardiac output by increasing contractility and heart rate, and it is frequently employed in moderate or severe impaired in cardiac contractility. It may be administered during CABG as a continuous or bolus injection to rapid stimulation for increasing ventricular contractility (13). Epinephrine and other potent beta-

adrenergic agonists may cause lactic acidosis. At high continuous infusion doses, they could cause considerable vasoconstriction and raised serum acetate. Lactic acidosis has been reported with epinephrine administration after cardiopulmonary bypass besides; some authors believe that serum lactate levels are related to total dose of vasoconstrictors prescription during the surgery (13, 14). Totaro

and Raper reported that 6 of 18 patients who received epinephrine after cardiopulmonary bypass developed lactic acidosis (13). The present results in this study showed that there were associations between total inotrope dosage and lactate concentration in ABG samples.

Several experiments demonstrated that the addition of banked blood to pump prime may elevate prime potassium, bradykinin and lactate levels (15). We did not see the correlation between volume of packed red blood cell transfusion and serum lactate level during our study. Maybe our small sample size affected our results.

Inadequate tissue perfusion and oxygenation is manifested by decreased arterial PH and saturation and increased lactate production (16, 17). This investigation demonstrated that serum lactate concentration in ABG samples was reliably associated with patient hemodynamic parameters but did not generally correlate with PH of arterial blood sample although lactic acidosis is often associated with a high anion gap and is generally defined as a lactate level >5 mmol/L and a serum pH <7.35 but in CABG surgery may be due to bicarbonate prescription during the operation, there was no association between arterial blood PH and serum lactate level (16).

Some evidence suggests that surgical factors such as prolonged cardiopulmonary bypass during CABG surgery act as a trigger to precipitate systemic inflammation (18). The duration of cardiopulmonary bypass and cross-clamp time may have accounted for postoperative lactic acidosis and the changes in lactic acid level over time was associated with the carriage of TNF-mediated systemic inflammation rather than hypo perfusion (3, 18). Our finding emphasizes on this subject.

In pediatric cardiac surgery, lactic acidosis is a powerful predictor of outcome. Greater lactic acid serum levels are associated with adverse outcome including excess mortality (19). Lactate level was used as a prognostic indicator in a study and the outcome was favorable if it normalized within 48 hours (16). Jansen et al. suggested that the use of blood lactate monitoring for risk-stratification in critically ill patients and the recent evidence suggests that the elevated lactate and decreased lactate clearance are important for prognostication (7, 20). Based on our observations, we consider the profiles of ABG lactate concentration defined in relation to the patients' clinical course and outcome. ABG lactate levels that are persistently high or that increase over time indicate the patient's deterioration.

We concluded that blood lactate measurement in patients under cardiac surgery was accurate by arterial blood sampling but adequate understanding of interaction between metabolic pathways and stress factors was required for its correct interpretation (21). The serial measurements of serum lactate level provided the important prognostic information. This study demonstrated a combination of serum lactate level to the patients' prognosis after CABG surgery by on pump method. The serial assessment of arterial blood gas for lactate and acid-base status in patients under CABG operation is useful in the evaluation of prognosis and clinical course.

The small size of this study and our focus on the patients' serum lactate level excluded any possibility of study on the interaction between probable confounding factors and outcome. The accurate and expanded results could not be achieved in the present report, due to the unavailability of some data. More studies with appropriate sample size are needed to evaluate the factors that impact on serum lactate level and its value on the outcome of patients under CABG surgery.

Acknowledgments

The authors thank their colleagues at the Department of Anesthesiology and Intensive Care of Babol University of Medical Sciences and the Open Heart Intensive Care Unit of Ayatollah Rouhani Hospital for their cooperation.

Funding: Self-funded.

Conflict of interest: None declared.

References

1. Bernal W, Donaldson N, Wyncoll D, Wendon J. Blood lactate as an early predictor of outcome in paracetamol-induced acute liver failure: a cohort study. *Lancet* 2002; 359: 558-63.
2. Khosravani H, Shahpori R, Stelfox HT, Kirkpatrick AW, Laupland KB. Occurrence and adverse effect on outcome of hyperlactatemia in the critically ill. *Crit Care* 2009; 13: R90.
3. Cremer J, Martin M, Redl H, et al. Systemic inflammatory response after cardiac operations. *Ann Thorac Surg* 1996; 61: 1714-20.

4. Raper RF, Cameron G, Walker D, Bowey CJ. Type B lactic acidosis following cardiopulmonary bypass. *Crit Care Med* 1997; 25: 46-51.
5. Haisjackl M, Birnbaum J, Redlin M, et al. Splanchnic oxygen transport and lactate metabolism during normothermic cardiopulmonary bypass in humans. *Anesth Analg* 1998; 86: 22-7.
6. Maillet JM, Le Besnerais P, Cantoni M, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. *Chest* 2003; 123: 1361-66.
7. Vernon C, Letourneau JL. Lactic acidosis: recognition, kinetics, and associated prognosis. *Crit Care Clin* 2010; 26: 255-83.
8. Marko P, Gabrielli A, Caruso LJ. Too Much Lactate or Too Little Liver? *J Clin Anesth* 2004; 16: 389-95.
9. McNelis J, Marini CP, Jurkiewicz A, et al. Prolonged lactate clearance is associated with increased mortality in the surgical intensive care unit. *Am J Surg* 2001; 182: 481-5.
10. Chiolerio RL, Revelly JP, Leverve X, et al. Effects of cardiogenic shock on lactate and glucose metabolism after heart surgery. *Crit Care Med* 2000; 28: 3784-91.
11. Ryan T, Balding J, McGovern EM, et al. Lactic Acidosis After Cardiac Surgery Is Associated With Polymorphisms in Tumor Necrosis Factor and Interleukin 10 Genes. *Ann Thorac Surg* 2002; 73: 1905-11.
12. Davies AR, Bellomo R, Raman JS, Gutteridge GA, Buxton BF. High lactate predicts failure of intra aortic balloon pumping after cardiac surgery. *Ann Thorac Surg* 2001; 71: 1415-20.
13. Totaro RJ, Raper RF. Epinephrine induced lactic acidosis following cardiopulmonary bypass. *Crit Care Med* 1997; 25: 1693-9.
14. James JH, Luchette FA, McCarter FD, Fischer JF. Lactate is an unreliable indicator of tissue hypoxia in injury or sepsis. *Lancet* 1999; 354: 505-8.
15. Ratcliffe JM, Wyse RK, Hunter S, Alberti KG, Elliott MJ. The role of priming fluid in the metabolic response to cardiopulmonary bypass in children less than 15kg body weight undergoing open heart surgery. *Thorac Cardiovasc Surg* 1988; 36: 65-74.
16. Cerovic O, Golubovic V, Spec-Marn A, Kremzar B, Vidmar G. Relationship between injury severity and lactate levels in severely injured patients. *Intensive Care Med* 2003; 29: 1300-5.
17. Husain FA, Martin MJ, Mullenix PS, Steele SR, Elliott DC. Serum lactate and base deficit as predictors of mortality and morbidity. *Am J Surg* 2003; 185: 485-91.
18. Ryan T, Balding J, McGovern EM, et al. Lactic Acidosis After Cardiac Surgery Is Associated With Polymorphisms in Tumor Necrosis Factor and Interleukin 10 Genes. *Ann Thorac Surg* 2002; 73: 1905-9.
19. Duke T, Butt W, South M, Karl T. Early markers of adverse events in children after cardiac operations. *J Thorac Cardiovasc Surg* 1997; 114: 1042-52.
20. Jansen TC, van Bommel J, Bakker J. Blood lactate monitoring in critically ill patients: a systematic health technology assessment. *Crit Care Med* 2009; 37: 2827-39.
21. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med* 2004; 32: 1637-42.