Original Article

Evaluation of Blood Lactate Level as Predictor of Early Adverse Outcome after Cardiac Surgery under Cardiopulmonary Bypass

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Abstract:

Background: We examined the hypothesis that high blood lactate level in intensive care unit patient after adult cardiac surgery under cardiopulmonary bypass is associated with early adverse outcome. The objective of this study was to evaluate whether high blood lactate level after cardiac surgery is a predictor of the early outcome after adult cardiac surgery under cardiopulmonary bypass.

Methods: This prospective observational study was carried out in the department of Cardiac Surgery at National Institute of Cardiovascular Disease (NICVD), Dhaka from July, 2013 to April 2014. A total number of 100 patients who underwent cardiac operation with cardiopulmonary bypass were enrolled in this study as per inclusion and exclusion criteria. Patients were divided into two groups according to their blood lactate level 6 hours after transferintensive care unit. Peroperative variables and postoperative variables were observed and recorded during the hospital course of patient. Categorical variables were analyzed by Chi-Square test and Fisher's exact test and continuous variables were analyzed by 't' test. Multiple Binary Logistic Regression Analysis of predictors for each of the outcome variables was done.

Results: Blood lactate levels ≥3mmol/L 6 hours after transfer to intensive care unit were present in 57(57%) patients. Multiple logistic regression analysis showed higher blood lactate level was an independent predictor for early postoperative low output syndrome (OR 9.073, 95% CI 2.819 – 29.207, p = < .0001), pulmonary complication (OR 5.734, 95% CI 1.814 – 18.122, p = .003), neurological deficits (OR 9.725, 95% CI 1.111 - 85.147, p = .040), renal dysfunction (OR 7.393, 95% CI 1.855-29.469, p = .005), arrhythmia (OR 10.512, 95% CI 1.902 – 58.108, p = .007) and wound infection (OR 7.742, 95% CI 1.418 - 42.259, p = .018).

Conclusions: High blood lactate level 6 hours after transfer to intensive care unit is an independent predictor for worse outcomes in adult patients after cardiac surgery under cardiopulmonary bypass.

Keywords: Lactate, cardiopulmonary bypass.

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Introduction:

High blood lactate level is a well-recognized marker of circulatory failure, and its severity has been associated with morbidity and mortality in different clinical conditions.[1,2] After cardiac surgery, hyperlactatemia (HL) is relatively common and is associated with morbidity and mortality.[3,4]

Elevated lactate concentrations in the immediate postoperative period reflect unmet metabolic demand and may be associated with poor outcome.[5] Irrespective of its origin, hyperlactatemia and its persistence have been demonstrated to be an early indicator of worse outcome in cardiac surgical patients.[6] Prolongation of lactate clearance is associated with increasing mortality and failure of a patient to normalize lactate is associated

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with 100% mortality.[7] The evolution of the lactate concentration after therapeutic management is able to predict the outcome more accurately.[8]

Lactate represents a useful and clinically obtainable surrogate marker of tissue hypoxia and disease severity, independent of blood pressure.[9] Persistently elevated lactate has been shown to be better than oxygen transport variables (oxygen delivery, oxygen consumption, and oxygen extraction ratio) as an indicator of mortality rate. Among septic shock patients, only survivors had a significant decrease in lactate concentrations over the course of the disease. In contrast, non survivors had significantly higher lactate concentrations during both the initial and final phases of shock.[10]

Various preoperative factors or comorbidities may create the right environment for HL during CPB. Age, female gender, congestive heart failure, low left ventricular ejection fraction, hypertension, atherosclerosis, diabetes, preoperative hemoglobin value, redo or complex surgery, and emergency procedures were found to be risk factors for HL.[11] Cardioplegic cardiac arrest and extracorporeal circulation (ECC) result in systemic inflammation, cardiac damage, myocardial stunning, hemodynamic instability, tissue edema, bleeding diathesis and finally multiorgan dysfunction.[12,13]Cardioplegic arrest induces anaerobic myocardial metabolism with a net production of lactate from glycolysis. Persistent lactate release during reperfusion suggests a delayed recovery of normal aerobic metabolism and may lead to depressed myocardial function.[14]

Lactate level 6 hours after intensive care unit (ICU) admission is an independent predictor of postoperative complications including 30-day all-cause mortality and severe morbidity after cardiac surgery in adult patients.[15] In patients with clinical shock, associated with tachycardia, hypotension, cold and clammy skin and decreased urine output, lactate levels have been referred to as the best objective indicator of the severity of shock.[16]

High blood lactate levels are associated with tissue hypo perfusion and may contribute to postoperative adverse outcome. Hyperlactatemia and its persistence have been demonstrated to be an early indicator of worse outcome in cardiac surgical patients. National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh is a high volume center and a considerable number of cardiac surgeries are performed under cardiopulmonary bypass. Hence, it is an ideal place for investigating lactate level.

In current practice, lactate is frequently measured usually with the goal of detecting tissue hypoxia during ICU care. However, high blood lactate levels in ICU are getting more importance to predict early outcome after cardiac surgery in recent journals.

Methods:

The study was designed as prospective observational study. It was carried out in the department of Cardiac Surgery from July 2013 to April 2014, at National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh.

The adult patients undergoing elective cardio-pulmonary bypass (CPB) during cardiac surgery at NICVD and fulfilled the inclusion and exclusion criteria were selected. Sampling method was Purposive and convenient.The study protocol was approved by ethical committee of NICVD.

Exclusion criteria were patients with pre-CPB high blood lactate level, emergency surgery, adult complex congenital heart defects, hepatic dysfunction, end-stage renal disease, intraoperative mortality or mortality less than 6 hours after transfer to ICU and patient's refusal for enrollment in the study. Postoperative variables were lactate (mmol/L) after transfer in ICU (6 hours &12 hours after transfer in ICU, blood transfusion units, mechanical ventilation time, low output syndrome (LOS), duration of ICU stay, postoperative Intra-aortic balloon pump requirement, postoperative complications (within 30 days), re-operation for bleeding, neurological deficit,myocardial Infarction, pulmonary complication, arrhythmia, renal dysfunction, wound infection, mortality.

The patients were divided into two groups according to the blood lactate level 6 hours after transfer in ICU after cardiac surgery. Those patients who had less than 3 mmol/L of blood lactate level 6 hours after transfer in ICU were in group A and those patients who had e"3 mmol/L of blood lactate level were in group B.

All patients undergoing cardiac surgery were given general anesthesia with endotracheal intubation and were treated with the standard CPB technique. Five arterial blood samples were drawn: After the anesthetic induction, at the end of CPB, immediately after transfer in ICU (0 hour), and then 6 hours and 12 hours after transfer in ICU. Arterial blood samples were analyzed by blood gas analyzer, model – Siemens RAPIDlab 1265, manufactured by Beckman int. California, USA.

Standard ICU management protocols were used and the patients were subsequently shifted to Post-ICU, ward or cabin and discharged whenever appropriate according to operating consultant's judgment.

Data were collected using a pre designed case record form. Postoperative complications after discharge was recorded during follow up after 1 month.

Results were expressed as means with standard deviation. Potential risk factors were assessed using ax^2 test, Fisher's exact test, *t* test. A forward multiple

logistic regression analysis was then performed to estimate independent predictive factors for complications. For all analysis a *p*-value <0.05 were considered statistically significant. Statistical analysis was performed by using statistical program for social science (SPSS 17.0).

Results:

A total number of 100 patients undergoing elective CPB were recruited for this study.Those patients who had< 3mmol/L of blood lactate level were designed as control group and those patients who had ³ 3 mmol/L of blood lactate level at 6th hour after transfer to ICU were designed as subject group.

Preoperative demographic variables

Table I shows the distribution of study population according to preoperative variables. Majority of patients were in d" 60 years age group (91%), male sex (62%), normal BMI categories (87%), non-diabetic (75%), non-hypertensive (86%), normal lipid profile (83%) and good LVEF status (89%). Difference between two groups is not statistically significant.

Peroperative demographic variables

Table II shows the comparison of operation time, CPB time, aortic cross clamp time and blood transfusion units between groups. The mean Operation time in control group and subject group was 319.02 ± 70.479 and 359.47 ± 83.274 respectively. The difference between the two groups was statistically significant (p = .012). The mean CPB time in control group and subject group is 121.65 ± 43.449 and 141.88 ± 42.312 respectively. The difference between the two groups was statistically significant (p = .021). The mean ACC time in control group and subject group is 72.88 ± 29.124 and 86.32 ± 26.156 respectively. The difference between the two groups was statistically significant (p = .017). The mean Blood transfusion unit in control group and subject group was 2.186 ± 0.4502 and 2.579 ± 0.9248 respectively. The difference between the two groups was statistically significant (p = .012).

Table-I

Preoperative variables distribution of study population (n = 100)

	Age# Group	Lactate Group (mmol/L)		Total	P Value
		Control group (n = 43) <3	Subject group (n = 57) ≥3		
Age	d" 60 years	39 (90.7%)	52 (91.2%)	91 (91%)	*1.000*
	>60 years	4 (9.3%)	5 (8.8%)	9 (9%)	
Sex	Male	25 (58.1%)	37 (64.9%)	62 (62%)	*0.490*
	Female	18 (41.9%)	20 (35.1%)	38 (38%)	
BMI	Normal & U.weight	39 (90.7%)	48 (84.2%)	87 (87%)	*.340*
	Obese &Overweight	4 (9.3%)	9 (15.8%)	13 (13%)	
DM	Present	11 (25.6%)	14 (24.6%)	25 (25%)	*.907*
	Absent	32 (74.4%)	43 (75.4%)	75 (75%)	
HTN	Present	7 (16.3%)	7 (12.3%)	14 (14%)	*.568*
	Absent	36 (83.7%)	50 (87.7%)	86 (86%)	
Dys-lipidemia	Present	8 (18.6%)	9 (15.8%)	17 (17%)	*.711*
	Absent	35 (81.4%)	48 (84.2%)	83 (83%)	
LVEF	Good	38 (88.4%)	51 (89.5%)	89 (89%)	*1.000*
	Impaired	5 (11.6%)	6 (10.5%)	11 (11%)	

#Data were analyzed using Fisher's Exact test; Level of significance was 0.05.

Table-II

Comparison of Operation time, CPB time, ACC time and Blood transfusion units between groups

Peroperative Variables	Lactate Group (mmol/L)		P Value
	Control group(n = 43) <3 Mean ± SD	Subject group(n = 57) ≥3 Mean ± SD	
Operation time#	319.02 ± 70.479	359.47 ± 83.274	*.012s*
CPB time#	121.65 ± 43.449	141.88 ± 42.312	*.021s*
ACC time#	72.88 ± 29.124	86.32 ± 26.156	*.017s*
Blood transfusion unit#	2.186 ± 0.4502	2.579 ± 0.9248	*.012s*

Data were analyzed using't' test,(n = number of patients, S = significant)

Postoperative measures of adverse outcome

Table III shows the distribution of study population according to postoperative variables. Low output syndrome, prolonged mechanical ventilation time (>24h), neurological deficit, pulmonary complications, arrhythmia, renal dysfunction, wound infection are found statistically significant.

Table 04 shows the multiple binary logistic regression analysis and high lactate level was found to be an independent predictor of postoperative low output syndrome, arrhythmia, pulmonary complications, renal dysfunction, neurological deficits and wound infection. Multiple logistic regression analysis shows higher blood lactate level is an independent predictor for early postoperative low output syndrome (OR 9.073, 95% CI 2.819 – 29.207, p = < .0001), pulmonary complication (OR 5.734, 95% CI 1.814 – 18.122, p = .003), neurological deficits (OR 9.725, 95% CI 1.111 - 85.147, p = .040), renal dysfunction (OR 7.393, 95% CI 1.855-29.469, p = .005), arrhythmia (OR 10.512, 95% CI 1.902 – 58.108, p = .007) and wound infection (OR 7.742, 95% CI 1.418 - 42.259, p = .018).

Table-III

Postoperative variables distribution of study population (n = 100)

	Age# Group	Lactate Group (mmol/L)		Total	P Value
		Control group (n = 43) <3	Subject group (n = 57) ≥3		
Low output syndrome	Present	08 (18.6%)	36 (63.1%)	44 (44%)	*< .0001**
	Absent	35 (81.4%)	21 (36.9%)	56 (56%)	
Prolonged MVT (>24h)	Present	0 (0%)	6 (10.5%)	6 (6%)	*.036**
	Absent	43 (100%)	51 (89.5%)	94 (94%)	
Prolonged ICU stay (>48h)	Present	7 (16.3%)	18 (31.6%)	25 (25%)	*.080*
	Absent	36 (87.7%)	39 (68.4%)	75 (75%)	
Reoperation for bleeding	Yes	0 (0%)	3 (5.3%)	3 (3%)	*.257*
	No	43 (100%)	54 (94.7%)	97 (97%)	
Neurological Deficit	Present	1 (2.3%)	12 (21.1%)	13 (13%)	*.006**
	Absent	42 (97.7%)	45 (78.9%)	87 (87%)	
Perioperative Mi	Present	0 (0%)	5 (8.8%)	5 (5%)	*.068*
	Absent	43 (100%)	52 (91.2%)	95 (95%)	
Pulmonary Complications	Present	9 (20.9%)	31 (54.4%)	40 (40%)	*.001**
	Absent	34 (79.1%)	26 (35.6%)	60 (60%)	
Arrhythmia	Present	4 (9.3%)	19 (33.3%)	23 (23%)	*.005**
	Absent	39 (90.7%)	38 (66.7%)	77 (77%)	
Renal dysfunction	Present	5 (11.6%)	23 (40.4%)	28 (28%)	*.002**
	Absent	38 (88.4%)	34 (59.6%)	72 (72%)	
Wound infection	Present	7 (16.3%)	2 (3.5%)	9 (9%)	*.036**
	Absent	36 (83.7%)	55 (96.5%)	91 (77%)	
Mortality	Present	1 (2.3%)	6 (10.5%)	7 (7%)	*.234*
	Absent	42 (97.7%)	51 (89.5%)	93 (93%)	

#Data were analyzed using Fisher's Exact test; Level of significance was 0.05.(n = number of patients, * = significant)

Table-IV

Multiple Binary Logistic Analyses of Predictors of Mortality and Morbidity

Morbidity	Variable	OR	95% CI	P value
LOS	High Lactate	9.073	2.819 – 29.207	*< 0.0001**
Arrhythmia		10.512	1.902 – 58.108	*0.007**
Pulmonary Complications		5.734	1.814 – 18.122	*0.003**
Renal Dysfunction		7.393	1.855 – 29.469	*0.005**
Neurological Deficits		9.725	1.111 – 85.147	*0.040**
Wound Infection		7.742	1.418 – 42.259	*0.017**

Discussion:

The present study has demonstrated that a lactate level e" 3mmol/L at 6 hours after transfer to ICU are related to postoperative adverse events and is independently associated with risk of major complication after cardiac surgery. Although the causes of these high lactate levels are numerous and diverse, these results raised the possibility that targeting therapy to reduce or prevent the initial increase in this variable may prevent complications and improve postoperative outcomes.

The distribution of co morbid conditions as diabetes and hypertension among both groups were recorded. Among the study population the difference between the two groups was not statistically significant (p = .907 and p = .568 respectively). Similar non-significant result was found by Hajjar et al.[15]

Outcome after cardiac operation is determined by preoperative characteristics of the patients in addition to intra operative factors such as operation time, CPB time, and ACC time. The difference between the two groups is statistically significant which indicates that operation time; CPB time and ACC time are one of the important causes of hyperlactatemia. Similarly, Rao et al, Hajjar et al, Maillet et aland Ranucci et al stated that there is significant correlation between CPB time and postoperative adverse outcome.[4, 6, 14, 15] Maillet et al and Demers et al also found ACC time as an important peroperative factor that had statistically significant difference between two groups. [11, 14]

In the observation of postoperative outcome, the present study found blood transfusion after transfer to ICUcontrol group and in subject group was statistically significant (p = .012). It was consistent with reports in Hajjar et al.[15]

Rao et alstated that the development of postoperative LOS, in the absence of an intraoperative misadventure revealed a failure of myocardial protection causing persistent anaerobic metabolism and lactate release. In this study regarding low output syndrome the difference between the two groups is statistically significant (p = < .0001).[4]

Maillet et alshowed in previous study that prolong mechanical ventilation and ICU stay found in hyperlactatemia group and was statistically significant and results werenot similar to our study (p = .080).[14] Vincent et al, Bakker et al and Nichol et alshowed a strong positive correlation between blood lactate levels and the risk of morbidity with neurological deficits as in our study (p = .006), but mortality was not statistically significant (p = .234).[8, 10, 18]

In our study, we found significant difference among outcome variables like perioperative MI (p = 0.005), arrhythmia (p = 0.001), renal dysfunction (p = 0.002) and pulmonary complications (p = 0.001). Provenchere et al found statistically significant (p = <0.0001) correlation among CPB duration, low output syndrome, vasoactive drugs, reoperation for bleeding with renal dysfunction after cardiac surgery.[17] Hajjar et al, Malliet et aland Ranucci et alshowed in their studies a strong correlation between high lactate and major complications after cardiac surgery that are similar with current study. The risk estimation among the study variables are analyzed by multiple binary logistic regressions.[6, 14, 15]

Hajjar et alshowed that hyperlactatemia 6 hours after ICU admission is an independent risk factor for worse outcome after cardiac surgery.[15] This study brought a new perspective to the role of lactate monitoring after cardiac surgery.

In our study, multiple logistic regression analysis showed that higher blood lactate level 6 hours after transfer to ICU is an independent predictor for early postoperative low output syndrome (OR 9.073, 95% CI 2.819 – 29.207, p = < .0001), pulmonary complication (OR 5.734, 95% CI 1.814 – 18.122, p = .003), neurological deficits (OR 9.725, 95% CI 1.111 - 85.147, p = .040), renal dysfunction (OR 7.393, 95% CI 1.855-29.469, p = .005), arrhythmia (OR 10.512, 95% CI 1.902 – 58.108, p = .007) and wound infection (OR 7.742, 95% CI 1.418 - 42.259, p = .018) These findings are similar to previous study. In current study, high lactate is not found as independent predictor of mortality.

Conclusion:

Peak blood lactate level of 3 mmol/L or higher at 6th hour after transfer to ICU is associated with an increased risk of perioperative morbidity and is an independent predictor of major postoperative complications after cardiac surgery under cardiopulmonary bypass.

Limitations of the Study

The study has been prospectively designed; but no real randomization has been performed. Finally, it is performed in a single center, which could restrict the generalization of our findings.

Recommendations

Randomized, controlled trials are needed to evaluate the potential benefit of normalizing lactate levels after cardiac surgery.

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