RELATIONSHIP BETWEEN SERUM LACTATE LEVELS AND MORBIDITY OUTCOMES IN CARDIOVASCULAR PATIENTS AFTER CABG

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ABSTRACT

Objective — *To evaluate the relationship between postoperative serum lactate levels and outcome in patients undergoing open heart surgery and verify the clinical impact of hyperlactatemia(HL) and low lactemia(LL) during CABG in terms of postoperative morbidity and mortality rate.*

Study Design — *Desctiptive study.*

Place and Duration of Study — Sina Heart center (non-university hospital in Isfahan, Iran) from fall 2005 to fall 2006.

Patients and Methods — *Hundred consecutive patients undergoing cardiac surgery with cardiopulmonary bypass were included in the study. Postoperative lactate concentration and other metabolic parameters were determined. Evaluation of lactate concentrations, pH values and base excess during the first 24 postoperative hours were assessed. Hyperlactatemia was defined as a peak arterial blood lactate concentration exceeding 3 mmol/l. Pre and intraoperative factors were tested for independent association with the peak arterial lactate concentration and HL. The postoperative outcome of patients with or without hyperlactatemia was compared.*

Results: — *We found positive effect of time on lactate and pH levels. On day 1, HL and LL patients had comparable lactate concentrations, which remained significantly higher than those of HL patients.*

Conclusions — *HL is frequent after cardiac surgery. Based on our analysis, postoperative measurement of lactate level appears to be clinically useful. A threshold of 3 mmol/L at ICU admission was able to identify a subpopulation of patients at higher postoperative risk. Sequential determinations identified patients at higher risk for major complication and thus the need for closer surveillance of their therapeutic responses and metabolic consequences.*

Key words — Cardiac surgery, Lactate levels, Outcome, Rrisk factor

INTRODUCTION:

Cardiac surgery is an important procedure for many patients with heart diseases. Hyperlactatemia (HL) is well-recognized marker of circulatory failure, and its severity has been associated with mortality in different clinical conditions.[1,2] After cardiac surgery HL is relatively common and is associated with morbidity and mortality.[3,4] During cardiac surgery with cardiopulmonary bypass (CPB) in adult patients, prevalence of HL is almost 10% to 20% and is associated with postoperative morbidity and mortality.[5] At present, the nature of HL during and after cardiac operations is not clear, but the majority of authors tend to attribute this finding to a tissue hypoxia (type A HL) even if type B HL (without tissue hypoxia) has been advocated in some cases.[4,6-9] The main factor leading to a possible organ dysoxia during the surgery is hemodilution degree.[10,11] Some studies have suggested an independent association between low PH and mortality.[12] Despite this apparently reasonable assumption, no scientific evidence of an association between

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HL and mortality, morbidity and hospitalization exists in Iran. The present study was designed to verify the clinical impact of HL during CABG in terms of postoperative morbidity and mortality.

PATIENTS AND METHODS:

This was an observational study conducted in Sina Heart center (non-university hospital in Isfahan, Iran) from fall 2005 to fall 2006. We prospectively studied 92 unselected, consecutive patients undergoing cardiac surgery with normothermic CPB during a 12-month period. Data collection was based on the local database and routine measurements performed during the operation. Following approval by the local ethical committee and getting informed, written consent, consecutive adult patients (age > 18 years) undergoing cardiac surgery operations were admitted to this study. No operation-based selection was applied (excluding cardiac transplantation that is not performed at our institution). The only exclusion criteria was the presence of an abnormal (> 2 mmol/l) plasma lactate value before entering CPB. Patients with off-pump coronary artery bypass were not included in the study (n = 8). Hyperlactactemia was defined as an arterial lactate concentration > 3 mmol/L.

Patients were classified according to their HL or LL status. These conditions are generally associated with emergency procedure, unstable preoperative hemodynamics, and pre or intra-operative need for inotropic support or intra-aortic balloon pump. Such patients (2.7%) were excluded from the subsequent analysis. The remaining 92 patients were analyzed according to the purposes of the study. Patients underwent CABG with 1 to 3 venous grafts and the left internal mammary artery (LIMA) was used for revascularization of the left anterior descending coronary artery (LAD).

Premedication included atropine sulphate (0.5 mg), promethazine (0.5 mg/ kg), and morphine sulfate (0.1 mg/g), remifenteil (1micro gm/kg /slowly) and midazolam intramuscularly administered one hour before the induction of anesthesia. Anesthesia was induced with an intravenous infusion of remifentanil (0.1 micro g/kg per minute) and a midazolam bolus of 0.2 mg/kg. Cisatracurium besylate (0.2 mg/kg) was subsequently administered to allow tracheal intubation. Subsequently, the anesthesia was maintained with a continuous infusion of remifentanil (dose ranging from 0.1 to 1 micro gm/kg per minute, titrated on the basis of the hemodynamic response) and midazolam (0.1 mg/kg per hour). The preoperative data collected and analyzed for demographics, lactate and pH at start of operation, intra-operative and after operation (6, 24, 48 hours), creatinine 48 hours after operation(mg/100), left ventricular ejection fraction (LVEF), inotropic drugs, duration of inotropic drug use, ICU stay and mortality.

All data are expressed as mean ± standard deviation of the mean or as absolute numbers and percentage. A p value of less than 0.05 was considered significant for all of the following statistical tests. The statistical analysis was performed using SPSS 14 software. Relationship between hospital and ICU stay with morbidity risk factors (and specially peak and mean blood lactate after operation) was tested with a linear regression. Factors significantly ($p < 0.05$) associated with each blood lactate at this preliminary step were entered into a stepwise forward multivariable linear regression analysis, with adequate corrections to avoid multi collinearity within the model. The multivariable approach was applied to assess the independent association between the variables tested and the peak blood lactate.

The patient population was arranged in order of increasing pH levels, LVEF, nitrate /heparin use, inotrups drugs and administration of intra aortic balloon were analyzed with respect to the HL incidence. The meaningful difference between lactate levels and pH in various time was determined by repeated measure ANOVA test (analysis of variance) then paired pH and lactate levels were tested by t paired. Postoperative outcome was firstly analyzed in the population during CABG by using a (t pair test for unpaired data) and was subsequently corrected for other covariates in a multivariable linear or logistic regression analysis.

RESULTS:

We identified a total of 92 ICU admissions during the 12 months. This group of patients had an overall mortality of 3.3% and average hospital stay of 8.8 days and an ICU stay of 47.27 hours. Demographic characteristics of the 92 patients included in this study are presented in table I. HL was found in 76 patients (82.6%), and 16 patients (17.4%) acquired LL during their ICU

Table 1:
Demographic and Procedure Related Data and Preoperative Medication in Patients Undergoing Coronary Artery Bypass Grafting.

Variable	Number(percentage) Or Mean ± Standard Deviation
Age(year)	60.33 ± 9.07
Gender (female / male)	23/ 44(34.3 % / 65.7 %)
Body mass index(BMI)	26.44 ± 4.19
Intra Aortic Balloon	4 (4.4 %)
Diabetes on medication	33(35.9 %)
Previous MI	29 (32 %)
Neurological Dysfunction	1 (1.1 %)
Nitrates Heparin(No. of patients)	14 (15.2 %)
Duration of inotropic drug use(hours)	36.69 ± 13.41
Inotropic drugs	16 (17.4 %)
Neurological Dysfunction	1 (1.1 %)
New Onset Stroke	1 (1.1 %)
ICU stay(hours)	47.27 ± 14.38
Hospital stay (days)	8.88 ± 2.66
Max lactate after operation	4.57 ± 1.81
Mean lactate after operation	3.08 ± 1.01
HL/LL	76(82.6) / 16 (17.4)
Mortality	3 (3.3)

stay. We compared peak, mean of lactate levels by time and duration of hospital stay. Then compared lactate and PH level in various time. We found positive effect of time on lactate and pH levels. Postoperative lactate concentration and other metabolic parameters are presented in table 2. Evolution of lactate concentrations, pH values, and base excess during the first 24 postoperative hours are illustrated in figure 1. On day one HL and LL patients had comparable lactate concentrations, which remained significantly higher than those of HL patients.

Table 2:
Preoperative,Intraoperative and Postoperative Metabolic Data on Patients Under Going Coronary Artery Bypass Grafting

Variable	Mean ± Standard Deviation
Creatinine 48 hours after operation	1.22 ± 0.33
pH at start of operation	7.41 ± 0.05
Intra operative pH	7.45 ± 0.05
pH 6 hours after operation	7.40 ± 0.06
pH 24 hours after operation	7.42 ± 0.05
pH 48 hours after operation	7.44 ± 0.04
Lactate at start of operation(mol/lit)	1.60 ± 0.75
Intra operative lactate	3.30 ± 1.17
Lactate 6 hour after operation	3.83 ± 2.03
Lactate 24 hours after operation	3.16 ± 1.6
Lactate 48 hours after operation	2.02 ± 0.92

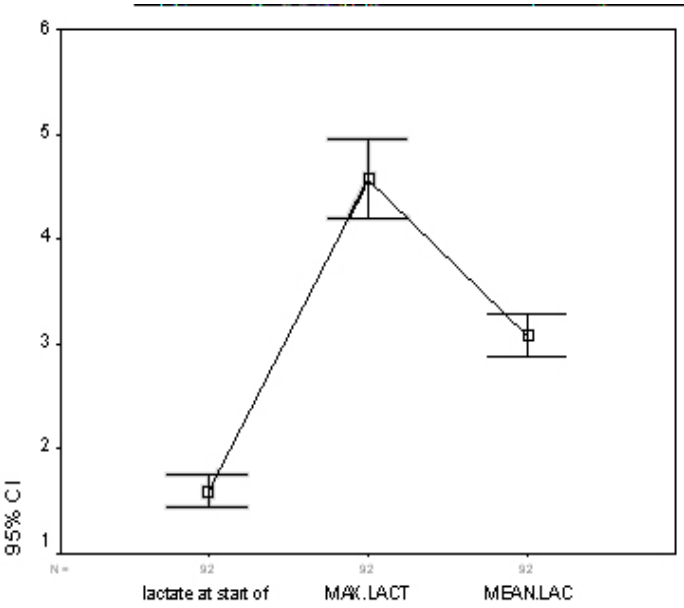

Figure 1: Lactate concentration: start, max and mean

Table 3:
The Association Between Risk Factors of Lactate Level and The Duration of Hospital Stay

Variable	Hospital Stay	
HL (6 hours after operation)	0.26	0.011
Nitrate, heparin	0.37	0.001
Inotrups drugs	-0.31	0.006
Intra aortic ballon-none	-0.28	0.011
R Square = 39 %		
H L, LL	-0.24	0.016
Nitrate heparin	0.32	0.002
Intraaortic balloon none	-0.31	0.003
New onset stroke	0.21	0.037
Neurologic dysfunction	0.21	0.037
Inotrups drugs	-0.29	0.005
R Square = 47 %		
Mean lactate after operation	0.29	0.007
Nitrate heparin	0.30	0.004
Intraaortic balloon-none	-0.27	0.012
Inotrups drugs	-0.33	0.003
R Square = 39 %		
Max lactate after operation	0.30	0.004
Nitrate heparin	0.33	0.001
Intra aortic balloon	-0.31	0.005
Inotrups drugs	-0.30	0.006
Nitrate heparin	0.33	0.001
R Square = 40 %		
Nitrate heparin	0.33	0.000
Creatinine 48 hours after operation	0.31	0.001
Duration of inotropic drug (use /in hours)	0.24	0.010
R Square = 31 %		

DISCUSSION:

The main findings of this study are that lactate level in 6 hours after CABG (coronary artery bypass graft surgery) is more likely related to prolonged ICU and hospital stay and it could be used as a marker of a worse postoperative outcome in terms of morbidity. The rate of patients demonstrating HL 6 hours after CABG was relatively high. The overall incidence of HL was 76% which is higher than otherstudies. [5] Other observations suggest that HL occurs frequently after normothermic cardiac surgery.[13] Various preoperative factors 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 by Demers and coworkers, [5] who reported an HL incidence of 18%.[14] Some of these factors were confirmed in our study however, our study population had a significantly shorter CPB duration and a lower degree of hemodilution during CPB. Given that both these factors seem to favor the onset of HL, the lower HL rate in our population is reasonably explained.The role of CPB duration in the determinationof HL during CPB

has been highlighted by other authors.

We couldn't determine the association between CPB duration and peak blood lactate level. A threshold of 3 mmol/L at ICU admission enable us to identify patients with a poorer outcome and a higher risk of mortality.[13] Pertinently, development of HL (lactate> 3 mmol/L) during the ICU stay was not associated with a poorer outcome. HL observed in our study was mostly the consequence of excess lactate production as previously described. After cardiac surgery increased intracellular concentrations of the free fatty acids inhibit conversion of pyruvate to acetyl-coenzyme A, leading to increased lactic acid production. Moreover, stimulation of adrenergic receptors raises the plasma glucose concentration, thereby increasing the substrate for glucolysis. Post-operative mild increase of lactate concentration on ICU admission (<3 mmol/L) was able to identify patients early with a poorer outcome: higher morbidity and ICU mortality rates. However, patients who subsequently acquired HL in the ICU had higher morbidity and ICU mortality comparable to that of patients with LL.

We prospectively tested a mildly elevated lactate level (3 mmol/L), which is 50% higher than the upper normal limit in our laboratory. Analysis of ROC curves of lactate concentration to predict ICU mortality showed that this arbitrary value was the best compromise of sensitivity and specificity. A higher value (eg, 5 mmol/L) would have slightly increased the specificity but at the expense of a sharp loss of sensitivity. [13] Lactate concentration was measured, also influenced prediction of ICU mortality. Detection of HL was the best predictor of hospital mortality as compared to later determinations. Some of our results might contribute to modifying the management of cardiac surgery.

CONCLUSIONS:

HL is frequent after cardiac surgery. Based on our analyses, postoperative measurement of lactate levels appears to be clinically useful. A threshold of 3 mmol/L at ICU admission was able to identify a subpopulation of patients at higher postoperative risk. Sequential determinations identified patients at higher risk for major complications and thus the need for closer surveillance of their therapeutic responses and metabolic consequences. Further studies are needed to determine whether correction of some risk factors could control or prevent this metabolic disturbance and thereby improve prognosis.

ACKNOWLEDGEMENT:

The present study has been funded by Delasa Heart Center and special acknowledge to Sina Heart Hospital for continues support throughout our study.

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