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## Research Article

# Relationship between Serum Lactate Levels and Postoperative Outcomes in Patients undergoing On-Pump Coronary Bypass Surgery - @

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## ABSTRACT

**Objective:** To evaluate the relationship between serum lactate levels and postoperative outcomes in patients who underwent on-pump Coronary Artery Bypass Grafting (CABG).

**Methods:** A prospective analysis was performed on 40 adult patients who underwent isolated first-time on-pump CABG between December 2014 and March 2015. Patients were divided into two groups according to their postoperative serum lactate levels as patients with higher levels ( $\geq 3$  mmol/ L) and lower levels ( $< 3$  mmol/ L). Patients' demographics, risk factors, intraoperative and postoperative data were recorded. Serum lactate levels and postoperative mortality and morbidity rates in each group were compared and relationship between serum lactate levels and postoperative outcomes was evaluated.

**Results:** Patients with normal serum lactate levels accounted for 82.5% ( $n = 33$ ) of study population whereas patients with high blood lactate levels comprised 17.5% ( $n = 7$ ). There were no statistically significant difference between two groups according to the preoperative patients' demographics. According to the intraoperative data; aortic cross clamp, cardiopulmonary bypass and operation time was significantly higher in high lactate group than normal lactate group. In high lactate group, incidence of decreasing in mean arterial pressure under 60 mmHg was also significantly higher (100%) when compared to normal lactate group (45.5%). Postoperative data showed that hemodynamic instability occurrence and inotrope administration rates were significantly higher in high lactate group. Postoperative complications such as neurological complications, pneumonia and severe cardiac arrhythmias were observed more frequently in high lactate group.

**Conclusion:** Our study demonstrated that the high serum lactate levels were associated with the worse postoperative outcomes following on-pump CABG.

**Keywords:** Lactate; Coronary Artery Bypass Grafting; Morbidity; Mortality

## INTRODUCTION

Industrial and technological developments in the last two centuries and economical and social adaptations in this context have given rise to important changes in the incidence of diseases that causes morbidity and mortality. When in early 20th century cardiovascular diseases accounted for only 10% of overall mortality worldwide, however in our time cardiovascular diseases are the leading cause of mortality in the middle and older age and they account for more than 30% of the worldwide deaths [1,2]. In our country, cardiovascular diseases are the most important cause of mortality with 39.8% and among this group of diseases, Coronary Artery Disease (CAD) is the primary cause of death with 38.8%. CAD prevalence is ranged between 4-5% and incidence between 0.3-0.4% in Turkey, as in many other countries which means, in our country, 230-300 thousand new coronary artery disease patients are expected to present per year [3]. Furthermore, CAD is one of the important diseases which affect the patients' survival, prognosis and quality of life. The most preferred treatment approach especially in severe CAD is Conventional Coronary Artery Bypass Grafting (CABG) surgery with Cardiopulmonary Bypass (CPB), which is still the gold standard treatment method [4]. In this method, by heart being stopped, working in a motionless, blood free area without hemodynamic dysregulation provides the surgeon with necessary comfort for enhanced anastomosis without the compulsion to perform the anastomosis rapidly. In the other hand, CPB usage and cardioplegic arrest might cause various adverse effects. Nowadays, cardiac surgery is routinely performed with lower mortality rates in many centers worldwide. Nevertheless, postoperative morbidity, with relation to various risk factors, still seems to be common and complications such as arrhythmias, ventricular dysfunction that requires inotrope support, infection, gastrointestinal dysfunction, acute lung injury and renal disorders may develop [4-6].

Various parameters are used to evaluate the morbidity and mortality risk. Serum lactate level is one of these parameters which are frequently used for this purpose [7-10]. Hyperlactatemia (HL) occurs when lactate production exceeds consumption because of conditions with tissue hypoxia (HL type A); or without tissue hypoxia

(underlying disease, drugs, toxins, congenital metabolic disorders) (HL type B). However, in most cases the cause is multifactorial [11,12]. HL after open heart surgery is a common condition and often associated with increased postoperative mortality and morbidity [10,13]. Although the cause of this situation is not clear, it is indicated that tissue hypoperfusion was the probable causative mechanism [10,14]. Hemodilution and inappropriate tissue oxygenation due to lower peripheral oxygen distribution are likely to be the prompting factors for tissue hypoxia during CPB [15,16]. Both of these factors are associated with postoperative mortality and morbidity [17]. Generally, the serum lactate levels are considered as a prognostic factor after CABG. Previous studies has indicated that there were alterations in serum lactate levels due to effect of CPB on tissue perfusion, changes in tissue metabolism and postoperative effects of surgery. In these studies, it is mentioned that HL is a well-known indicator of circulation insufficiency and could be used as a prognostic factor; however, information about the effect of HL on morbidity and mortality is limited.

In this study, the relationship serum of lactate levels with morbidity and mortality was evaluated by comparing serial serum lactate levels, which we obtained from patients who underwent on-pump CABG, with a number of various parameters.

## MATERIALS AND METHODS

### Study design and patient selection

Data of patients who underwent isolated first-time on-pump CABG in our institution were collected prospectively between December 2014 and March 2015, after obtaining approval of institutional ethics committee. Informed consent forms were obtained from all of patients before the operation. A total of 40 on-pump CABG patients were included in the study consecutively. In this study, the cut-off value of HL was accepted as 3 mmol/ L [18,19]. Patients were divided into two groups according to the serum lactate levels as patients with normal lactate levels ( $< 3$  mmol/ L) and higher lactate levels ( $\geq 3$  mmol/ L). Demographic data, risk factors, CPB and cross clamp time, occurrence of hemodynamic instability during CPB and need for vasopressors, use of inotropes for longer than three

hours, postoperative hemodynamic data, neurological, infectious and renal complications, mechanical ventilation and postoperative hospitalization duration of the patients in clinic and intensive care unit were recorded. Serum lactate levels and postoperative mortality and morbidity rates in each group were compared and the relationship between serum lactate levels and postoperative outcomes was evaluated. Patients with following conditions were excluded from the study: preoperatively detected abnormal arterial lactate levels, coexisting malignancy, history of chronic inflammatory disease or presence of active infection, presence of liver failure, patients who underwent additional surgical procedure and patients who were operated using different surgical techniques other than conventional on-pump CABG procedure.

### Surgical technique

Median sternotomy was performed to all patients that were implemented CABG with CPB. Heparin was given at the dose of 350 IU/kg and as ACT > 450 sec. LITA and other grafts were prepared by standard technique. After purse strings which were put into ascending aorta and right atrial appendage for standard CPB, arterial cannula and two-stage venous cannula was used. With the roller pump, approximately 60-80 mmHg tension arterial was tried to provide with the flow of 1.8-2.2 L/mn/m<sup>2</sup>. While we supplant cardiopulmonary bypass, aortic cross clamp was put and diastolic arrest was provided by crystalloid cardioplegia. Firstly, distal anastomoses in company with cardiopulmonary bypass and with aortic cross clamp in the situation that heart is in diastolic arrest was carried out, and then proximal anastomoses was performed with side clamp that was put into ascending aorta. After cardiopulmonary bypass was ended and cannulae were removed, heparin was neutralized with protamine.

### Statistical analysis

Statistical analysis of data was performed using the Statistical Package for the Social Sciences (SPSS) statistical package program (version 18.0, SPSS, Chicago, Illinois, USA). Shapiro-Wilk test was performed in order to assess whether the data showed a normal distribution or not. Mean  $\pm$  standard deviation values were given for the variables that showed normal distribution whereas median (minimum-maximum) values were given for inconsistent variables. Categorical variables were given with n values and percentages and Pearson chi-squared test and Fisher's exact test were performed for comparison. Independent-Samples T Test was performed for comparison of two groups for variables that are consistent with normal distribution whereas Mann-Whitney U test was used for inconsistent variables. p values lower than 0.05 was considered as statistically significant.

## RESULTS

The mean age of patients was  $60.9 \pm 9.5$  years (range: 39-82), and 36 (90%) of them were male. Patients with normal lactate levels accounted for 82.5% (n = 33) of all patients whereas 17.5% (n = 7) of the patients had high lactate levels. No significant difference between two groups was found according to the preoperative baseline characteristics of patients ( $p > 0.05$ ) (Table 1).

When the intraoperative data of patients were assessed, no significant difference was found between two group regarding use of Internal Thoracic Artery (ITA), number of distal anastomoses or use of blood products during operation ( $p > 0.05$ ). When compared to normal lactate group, cross clamp, CPB and operation time was significantly longer in high lactate group ( $p < 0.05$ ). Moreover, in

high lactate group, incidence of decreasing in mean arterial pressure under 60 mmHg during CPB was also significantly higher (100%) when compared to normal lactate group (45.5%) ( $p < 0.05$ ). Use of inotropic agents during operation were significantly higher in high lactate group when compared with normal lactate group ( $p < 0.05$ ). Intraoperative data of patients were listed in (Table 2).

When the postoperative data of patients were assessed, presence of postoperative hemodynamic instability and inotrope administration occurred in high lactate group with a significantly higher rate when compared to normal lactate group ( $p < 0.01$ ). Mechanical ventilation duration was obviously higher in high lactate group ( $p < 0.05$ ). Need for Intra-Aortic Balloon Pump (IABP) counter pulsation, re-intubation, use of blood products, occurrence of postoperative hyperglycemia (blood glucose level >160 mg/ dL), reoperation and mortality were higher in high lactate group, although it was not statistically significant ( $p > 0.05$ ). Considering complications developed postoperatively; in high lactate group, neurological complications and pneumonia were significantly more frequent than normal lactate group ( $p < 0.05$ ). There was no significant difference between two groups considering other respiratory complications, infections, urinary system and gastrointestinal complications ( $p > 0.05$ ). Postoperative Atrial Fibrillation (POAF) was observed in 6 patients (15%). There was no significant difference between two groups about POAF occurrence ( $p > 0.05$ ); whereas severe arrhythmias such as Ventricular Fibrillation (VF) / Atrioventricular (AV) block were seen significantly more frequent in high lactate group ( $p < 0.05$ ). In high lactate group, hospitalization durations in clinic and intensive care unit were longer compared to normal lactate group; however, it was not statistically significant yet close to significance ( $p > 0.05$ ). Postoperative data of the patients were listed in (Table 3).

**Table 1:** Demographics and preoperative patient characteristics.

	Normal lactate group (n = 33)	High lactate group (n = 7)	P value
<b>Sex</b>			0.552
Female	3 (9.1%)	1 (14.3%)	
Male	30 (90.9%)	6 (85.7%)	
<b>Age (years)</b>	$60.5 \pm 9.2$	$62.4 \pm 11.3$	0.647
<b>Active smokers</b>	20 (60.6%)	4 (57.1%)	1.000
<b>Active alcohol consumption</b>	2 (6.1%)	1 (14.3%)	0.448
<b>Diabetes Mellitus</b>	15 (45.5%)	1 (14.3%)	0.066
<b>Hypertension</b>	21 (63.6%)	7 (100%)	0.081
<b>Dyslipidaemia</b>	16 (48.5%)	3 (42.9%)	1.000
<b>Obesity</b>	10 (30.3%)	1 (14.3%)	0.650
<b>BMI (kg/m<sup>2</sup>)</b>	$27.8 \pm 4.5$	$27.3 \pm 3.2$	0.972
<b>COPD</b>	3 (9.1%)	2 (28.6%)	0.204
<b>Chronic renal insufficiency</b>	6 (18.2%)	2 (28.6%)	0.366
<b>Carotid artery disease</b>	2 (6.1%)	2 (28.6%)	0.134
<b>PVD</b>	2 (6.1%)	0 (0%)	1.000
<b>LMCA stenosis</b>	8 (24.2%)	3 (42.9%)	0.369
<b>Previous CVA</b>	3 (9.1%)	2 (28.6%)	0.204
<b>Previous PCI</b>	7 (21.2%)	2 (28.6%)	0.645
<b>LVEF &gt; %50</b>	22 (66.7%)	5 (71.4%)	0.811
<b>EuroSCORE</b>	$2.8 \pm 1.7$	$3.5 \pm 2.1$	0.126

BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease; CVA: Cerebrovascular Accident; EuroSCORE: European System for Cardiac Operative Risk Evaluation; LMCA: Left Main Coronary Artery; LVEF: Left Ventricular Ejection Fraction; PCI: Percutaneous Coronary Intervention; PVD: Peripheral Vascular Disease

**Table 2:** Intraoperative data of patients.

	Normal lactate group (n = 33)	High lactate group (n = 7)	P value
Use of ITA	32 (97%)	5 (71.4%)	0.074
No of distal anastomoses	3 (2:5)	3 (3:4)	0.076
Aortic cross-clamp time (min)	52.9 ± 15.5	72.3 ± 26.6	0.043
CPB time (min)	92.6 ± 28.6	130.9 ± 45.2	0.006
Operation time (min)	253.5 ± 53.5	308.6 ± 55.4	0.030
MAP <60mmHg	15 (45.5%)	7 (100%)	0.011
Use of inotropic agents	7 (21.2%)	5 (71.4%)	0.017
Use of blood products	14 (42.4%)	3 (42.9%)	1.000

CPB: Cardiopulmonary Bypass, ITA: Internal Thoracic Artery; MAP: Mean Arterial Pressure

**Table 3:** Postoperative data of patients.

	Normal lactate group (n = 33)	High lactate group (n = 7)	P value
Hemodynamic instability	1 (3%)	5 (71.4%)	<b>0.001</b>
Use of inotropic agents	3 (9.1%)	5 (71.4%)	<b>0.002</b>
Need for IABP	0 (0%)	1 (14.3%)	0.175
MV time (h)	8 (3:93)	22 (7:102)	<b>0.014</b>
Re-intubation	1 (3%)	1 (14.3%)	0.323
Use of blood products	17 (51.5%)	5 (71.4%)	0.427
Presence of hyperglycemia	21 (63.6%)	5 (71.4%)	1.000
Neurological complications	0 (0%)	2 (28.6%)	<b>0.027</b>
Pneumonia	2 (6.1%)	3 (42.9%)	<b>0.030</b>
Pneumothorax	1 (3%)	0 (0%)	1.000
Pleural effusion	17 (51.5%)	3 (42.9%)	1.000
Sternal dehiscence	1 (3%)	0 (0%)	1.000
Wound infections	4 (12.1%)	0 (0%)	1.000
Renal dysfunction	5 (15.2%)	3 (42.9%)	0.128
GIS complications	2 (6.1%)	1 (14.3%)	0.448
POAF	6 (18.2%)	0 (0%)	0.289
Severe arrhythmias	0 (0%)	2 (28.6%)	<b>0.027</b>
Reexploration	1 (3%)	1 (14.3%)	0.323
ICU stay (h)	40 (19:163)	49 (24:238)	0.135
Hospital stay (days)	7.0 ± 2.4	10.3 ± 6.6	0.055
Mortality	0 (0%)	1 (14.3%)	0.175

GIS: Gastrointestinal System, IABP: Intra-Aortic Balloon Pump, ICU: Intensive Care Unit, MV: Mechanical Ventilation, POAF: Postoperative Atrial Fibrillation

## DISCUSSION

In recent years, the great increase in the incidence of CAD caused an increase in need for myocardial revascularization which is a remarkable treatment modality for this clinical condition. Myocardial revascularization is the gold standard in case medical treatment is inadequate. The effect of CABG on reducing angina and increasing the expected life span was proved in many studies. Moreover, acceptable mortality and morbidity rates of CABG makes this approach the most favorable, gold standard method. Conventional on-pump CABG has been the preferred treatment method for multiple vessel disease for over 40 years [4]. Although CABG is safe and effective, CPB and cardioplegic arrest may cause some adverse effects. As a result of rapid

developments in the technology and our knowledge, cardiac surgery is performed with lower preoperative morbidity and mortality in most cardiac surgery centers. However, postoperative morbidity, mostly interrelated with various risk factors, is still frequently encountered, causing increased hospitalization durations in clinics or intensive care units, medical expenses, workload of medical staff, which creates problems for both patient and health system [20].

Various parameters are used for estimating the risk of postoperative mortality and morbidity. Serum lactate level is a widely used parameter since it is inexpensive and provides results rapidly. Many researchers have investigated the correlation between Hyperlactatemia (HL) and morbidity and mortality [7-10,18]. Elevated blood lactate level is a metabolic disorder that is seen quite frequent in intensive care units after cardiac surgery and its pathophysiology remains unclear [13,14]. Hyperlactatemia may be caused by tissue hypoxia (type A HL) as well as it may present without tissue hypoxia (type B HL). Especially after cardiac surgery type B hyperlactatemia is common in early postoperative period. It is reported in different studies that postoperative hyperlactatemia occurrence rate is ranged between 10-20% [10,17]. In our study, this rate is similar to prior studies with a rate of 17.5% postoperative high lactate levels.

Demers, et al. [10] indicated that many various preoperative factors and comorbidity contribute to hyperlactatemia developed during CPB. They described age, congestive heart failure, low left ventricle ejection fraction, hypertension, Diabetes Mellitus (DM), revision surgery and emergency intervene as risk factors for hyperlactatemia. In our study, unlike the findings of Demers' study; variables such as age, hypertension, DM and low left ventricle ejection fraction were not shown to be risk factors. Similarly, in our study, nor Chronic Obstructive Pulmonary Disease (COPD) neither chronic renal failure was considered to be as an risk factor. Ranucci, et al. [17] indicated that the relation between CPB time and pike lactate level was not linear and the cut-off value for CPB time was 96 minutes. Our findings support this statement with a mean CPB time of 131 minutes in high lactate group and 92 minutes with normal lactate group. Totaro, et al. [19] defined lactic acidosis prompted by  $\beta$ 2 agonist administration and high dose epinephrine. Lactic acidosis is also seen in severe hyperadrenergic state of pheochromocytoma and acute asthma [21]. Similarly to study of Totaro, et al. in our study, an increased need for vasopressor administration and hemodynamic instability occurred in high lactate group in intraoperative and postoperative period and dysregulation between O<sub>2</sub> presentation and consumption in these patients.

Ranucci, et al. [17] reported a cut-off value of 160 mg/ dL for pike blood glucose level. We also determined the cut off value as 160 mg/ dL in our study and found that hyperglycemia occurred more frequently in high lactate group although, it was not statistically significant. There are number of factors that elevate blood glucose levels postoperatively and during CPB. Especially contribution of factors such as inflammatory response to surgical stress and extracorporeal circulation, growth hormone, ACTH, epinephrine discharge, insulin resistance leads to elevated blood glucose levels [22]. In our study, when the demographics of patients were evaluated, although there were more diabetic patients in normal lactate group, interestingly, more hyperglycemia occurrence was detected in high lactate group, which was attributed to inflammatory response secondary to surgical trauma. Lactate levels that are obtained in intensive care unit was interrelated with cross clamp, CPB and operation time, high alveolar-



arterial oxygen gradient ( $p(A-a)O_2$ ) and mechanical ventilation duration [18,23]. Siegel, et al. [23] reported that mechanical ventilation duration and hospitalization duration in intensive care unit is prolonged in patients with high perioperative lactate levels. Our findings support findings of Siegel et al. as our study has shown that in high lactate group, mechanical ventilation duration was significantly prolonged compared to normal lactate group.

Despite the fact that lactate concentration is a good indicator of severeness of disease in intensive care patients, its prognostic value after cardiac surgery has not been proved. Moderate hyperlactatemia is generally considered to be benign [14,19]. Shemi, et al. [18] suggested that, serum lactate levels that are higher than 6 mmol/ L might be a useful indicator for mortality and required a thorough evaluation to find the cause of the problem and sustain survival. In our study, lactate levels that are higher than 3 mmol/ L in intensive care unit are considered to be an indicator for poor prognosis. These patients showed more hemodynamic instability, neurological complications, pneumonia and severe arrhythmias in follow-up period. Moreover, these patients were extubated far more lately and hospitalized in clinic and intensive care unit for longer periods.

## LIMITATIONS OF THE STUDY

There were several limitations in the interpretation of the results of our study. The major limitations of this study were evaluated data were limited, lack of the mid and long-term outcomes of patients, irregular distribution of patients between groups and relatively small number of patients in the study groups. A larger sample could have increased the statistical power of our research.

## CONCLUSION

It was demonstrated that assessing the serum lactate levels in postoperative period is easy, inexpensive and clinically very useful. It is very important to sustain hemodynamic stabilization, to keep the mean arterial pressure above 60 mmHg and to avoid severe hypothermia and hemodilution during CPB for preventing hyperlactatemia, which is an indicator for poor prognosis. Protecting heart during CPB well until finishing CPB may be easier, in this way, prolonged cross clamp and bypass durations could be prevented. Postoperative hyperglycemia must be managed well. Follow-up with serial lactate levels may allow defining the patients with high risk of mortality and morbidity, thus taking necessary precautions.

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