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Original Article

Use of lactate as a marker of occult hypoperfusion and outcome following adult cardiac surgery

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Abstract

Background: Hyperlactaemia (HL) is a hypoperfusion marker associated with increased mortality. We aimed to determine whether postoperative serial arterial lactate (AL) measurements after cardiac surgery could predict mortality, atrial fibrillation, wound infection, prolonged ventilation, ICU stay duration, and renal failure.

Methods: Between September 2020 and November 2022, this prospective cohort study was conducted on 100 patients who were split into two groups: Group 1 (n= 17) had low lactate levels, and Group 2 (n= 83) had high lactate levels equivalent to or greater than 4 mmol/L.

Results: Body mass index (BMI) (26± 2.6 vs. 23.2 ±1.4, P 0.001), diabetes mellitus (59% vs. 29.4%, P = 0.026), and smoking (57.8% vs. 17.6%, P = 0.003) were all significantly higher in Group 2. Group 2 had a significantly longer cross-clamp time (77 ±22 vs. 64 26; P = 0.043). Atrial fibrillation (39.8% vs. 0%, P = 0.001), ventilation time (24 (8- 150) vs. 8 (6- 12) hours, P = 0.001), renal dysfunction (26.5% vs. 0%, P = 0.016), length of ICU stay (4 (1- 10) vs. 2 (2- 3) days, P = 0.001), and mortality (28.9% vs. 0%, P = 0.04) were all significantly higher in Group 2. Peak intraoperative lactate showed moderate significant positive correlations with BMI (r = 0.349, p < 0.001), cross-clamp (r = 0.483, P < 0.001), cardiopulmonary bypass time (r = 0.426, P < 0.001), and length of ICU stay (r = 0.468, P < 0.001).

Conclusion: Hyperlactatemia could be associated with higher postoperative morbidity and mortality. Hyperlactemia and its causes should be treated once diagnosed to improve the outcomes.

KEYWORDS
Coronary Artery Bypass Grafting; Hyperlactaemia; Cardiopulmonary bypass; Aortic cross-clamp

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Introduction

Hyperlactaemia (HL), a well-known marker of hypoperfusion, has been linked to mortality in various clinical settings. Both adult [1, 2] and pediatric [3, 4] cardiac surgery outcomes are associated with elevated blood lactate levels postoperatively. Patients undergoing cardiovascular surgery, as opposed to septic patients, typically have brief postoperative intensive care unit (ICU) and hospital lengths of stay (LOS) [5]. However, approximately 10% of these patients require long-term care due to end-organ failure [6]. Furthermore, generalized tissue hypoperfusion following cardiac surgery has been linked to a longer ICU stay [7]. Cardiopulmonary bypass (CPB), pharmacological therapy, cardioplegia, hypothermia, and tissue hypoxia are non-hypoxic causes of hyperlactatemia that are

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common during and after cardiac surgery [8]. The present study aimed to determine whether postoperative serial arterial lactate (AL) measurements after cardiac surgery could predict outcomes, including mortality, atrial fibrillation, wound infection, prolonged ventilation, ICU stay duration, and renal failure.

Patients and Methods

Design

This is a prospective cohort study of patients admitted to the Cardiac Surgery departments at Benha University and Nasser Institute hospitals for coronary artery bypass grafting (CABG), valve surgery, or both from September 2020 to November 2022. The study was carried out after the approval of the local ethical committee, and the patient's written informed consent was obtained.

Target population:

One-hundred patients were enrolled to measure lactate levels both intraoperatively and postoperatively. Participants were divided into two groups: those with low serum lactate levels (Group 1) and those with high blood lactate levels (Group 2), defined as serum lactate equal to or greater than 4 mmol/L. All intraoperative and postoperative data were collected using a standard data collection sheet. The maximum intraoperative lactate value was measured to find potential preoperative and intraoperative risk factors for HL. The postoperative morbidity and mortality related to HL were studied using the overall peak lactate levels (containing intraoperative and postoperative values). The link between HL and intraoperative and postoperative clinical characteristics and several HL risk factors were evaluated. An ordinary arterial blood gas analyzer was used to measure the blood lactate levels (GEM Premier 3000 Blood Gas Analyzer). 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 to ICU, and then 6 and 12 hours after transfer to ICU. The first sample (baseline) was obtained as soon as the catheter was placed.

We included adult patients of both genders and ages above 18 who underwent open heart surgery with a cardiopulmonary bypass and an ejection fraction greater than 40%. We excluded urgent surgery, extreme age groups, hepatic dysfunction, end-stage renal disease, off-pump surgery, and adult congenital heart disease.

Operative findings:

We gathered information on the type of operation, the length of the ischemic time, and the duration of the cardiopulmonary bypass. The on-pump procedure was performed on all patients. Every surgical procedure was carried out through a standard median sternotomy incision. The initial (baseline) sample of arterial lactate was obtained as soon as the arterial catheter was placed. Ringer's lactate, mannitol, and sodium bicarbonate solutions were combined to make a 1200 ml priming volume for the CPB circuit. The usual CPB techniques were used. Mean arterial pressure was continually monitored throughout CPB and kept between 60 and 80mmHg. During the operation, blood sugar levels were kept between 100 and 140 mg/dL. As blood sugar levels reached 180 mg/dL or above, insulin infusion began. Adrenaline was used as the first-line inotrope, with doses ranging from 0.01-0.2 mcg/kg/min. Antegrade cold blood cardioplegia and systemic hypothermia to 30-32C were administered to all patients.

Statistical analysis

Data were reported as mean and standard deviation (or minimum-maximum), while frequency and percentage were used to describe categorical data. Continuous data were compared with the t-test or Mann-Whitney test, and categorical data with the Chi-square or Fisher exact test. Spearman correlation was used to evaluate the relation between lactate levels and different variables. Descriptive analysis was performed using SPSS v23 (IBM Corp- Armonk- NY-USA). A P-value of less than 0.05 was considered statistically significant.

Results

Baseline data:

There were no differences in age, gender, hypertension, New York Heart Association (NYHA)

Table 1: Comparison of the preoperative characteristics between patients with low vs. high lactate levels. Data are presented as mean ±SD or number (percentage)

	Peak lactate level		
	<4 (n = 17)	≥4 (n = 83)	P-value
Age (years)	51 ±15	57 ±10	0.110
Sex			
Males	9 (52.9)	56 (67.5)	0.253
Females	8 (47.1)	27 (32.5)	
BMI	23.2 ±1.4	26 ±2.6	<0.001
Diabetes mellitus	5 (29.4)	49 (59)	0.026
Hypertension	9 (52.9)	29 (34.9)	0.164
Smoking	3 (17.6)	48 (57.8)	0.003
NYHA classification			
II	15 (88.2)	62 (74.7)	0.227
III	2 (11.8)	21 (25.3)	
COPD	2 (11.8)	13 (15.7)	0.682
Cross clamp (min)	64 ±26	77 ±22	0.043
CPB time (min)	98 ±33	111 ±30	0.115
Hemoglobin on pump	8.5 ±0.9	7.8 ±1.1	0.011

BMI: Body mass index; NYHA: New York heart association; COPD: Chronic obstructive lung disease; CPB: Cardiopulmonary bypass

class, or chronic obstructive pulmonary disease (COPD) between both groups. Body mass index (BMI) (26± 2.6 vs. 23.2 ±1.4, P 0.001), diabetes mellitus (59% vs. 29.4%, P = 0.026), and smoking (57.8% vs. 17.6%, P = 0.003) were all significantly higher in Group 2. (Table 1)

Operative data:

Cross-clamp time was significantly longer in Group 2 patients (77± 22 vs. 64± 26, P = 0.043). Nevertheless, their hemoglobin was considerably lower (7.8± 1.1 vs. 8.5± 0.9, P = 0.011). Cardiopulmonary bypass (CPB) time did not differ significantly (P = 0.115). (Table 2).

Postoperative data:

Atrial fibrillation (39.8% vs. 0%, P = 0.001), ventilation time (median = 24 (8- 150) vs. 8 (6- 12) hours, P = 0.001), renal dysfunction (26.5% vs. 0%, P = 0.016), length of ICU stay (median = 4 (1- 10) vs. 2 (2- 3) days, P = 0.001), and mortality (28.9% vs. 0%, P = 0.04) were all significantly higher in Group 2 patients (Table 2).

Table 2: Comparison of the outcome according to peak lactate level. Data are presented as number (percentage) or median (min-max); RR: Risk ratio; 95% CI: 95% confidence interval

	Peak lactate level			
	<4 (n = 17)	≥4 (n = 83)	RR (95% CI)	P-value
Atrial fibrillation	0 (0)	33 (39.8)	1.340 (1.165 – 1.541)	0.001
Inotropic support	13 (76.5)	75 (90.4)	1.278 (0.849 – 1.925)	0.108
Ventilation (hrs)	8 (6 - 12)	24 (8 - 150)	-	<0.001
Renal disfunction	0 (0)	22 (26.5)	1.279 (1.137 – 1.438)	0.016
GIT bleeding	0 (0)	7 (8.4)	1.224 (1.112 – 1.347)	0.214
Infection	0 (0)	14 (16.9)	1.246 (1.122 – 1.384)	0.068
Length of ICU stay (days)	2 (2 - 3)	4 (1 - 10)	-	<0.001
Hospital stay (days)	8 (7 - 10)	9 (2 - 22)	-	0.133
Mortality	0 (0)	24 (28.9)	1.288 (1.142 – 1.453)	0.011

No significant variations were found in inotropic support duration, gastrointestinal hemorrhage, or hospital stay. Moreover, the infection rate in Group 2 was greater (16.9% vs. 0%), although the difference was not statistically significant. (P = 0.068).

Peak intraoperative lactate showed moderate significant positive correlations with BMI (r = 0.349, p < 0.001), cross-clamp (r = 0.483, P < 0.001), CPB time (r = 0.426, P < 0.001), and length of ICU stay (r = 0.468, P < 0.001). Additionally, it showed a strong significant positive correlation with ventilation hours (r = 0.809, P < 0.001). In contrast, peak intraoperative lactate revealed a moderately significant negative correlation with the lowest hemoglobin on the pump (R = -0.428, P < 0.001). No significant correlations were observed regarding age and hospital stay (Table 3).

Table 3: Correlation between peak intraoperative lactate and other parameters

	Peak intraoperative lactate	
	r	P
Age (years)	0.156	0.122
Body mass index	.349	<.001
Cross clamp (min)	.483	<.001
Cardiopulmonary bypass time (min)	.426	<.001
Lowest Hb on pump	-.428	<.001
Ventilation (hrs)	.809	<.001
Length of ICU stay (days)	.468	<.001
Hospital stay (days)	-0.062	0.539

r: Correlation coefficient

Discussion

Hyperlactaemia is a frequent metabolic anomaly after heart surgery that may be linked to increased mortality. Hajjar and colleagues [9] found no statistically significant difference between patients with high intraoperative lactate levels and those with lower lactate levels in terms of demographic data such as age, gender, hypertension, NYHA, and COPD. In this study, there was a significant difference between the two groups in terms of intraoperative parameters like cross-clamp time; it was higher in the patients with high intraoperative lactate levels than in the other group. This result is consistent with Maillet Ranucci and coworkers' findings [10]. Rashkin and associates found that higher blood lactate levels six hours after surgery and immediately following surgery strongly indicated significant cardiac morbidity like atrial fibrillation [11].

Patients with peak lactate levels greater than or equal to 4mmol/L had longer postoperative ventilation hours. This result contrasts with the findings of Basran and colleagues [12], who found no statistically significant difference between both groups regarding ventilation hours. In their study, extubation of patients was done on an elective basis, but in our study, we had clear criteria for extubation; one of them was decreasing at arterial lactate level, which is usually associated with improvement in perfusion, and this takes time, so patients with intraoperative hyperlactatemia had a long time of postoperative ventilation and this coincides with Mirmohammad-Sadeghi and associates' study [13].

Another study done by Rashkin and coworkers [11] found that diabetes mellitus has no statistically significant difference in both groups regarding lactate, which can be explained by the fact that in our study, we did not follow a strict program of preoperative control of hyperglycemia, which resulted in some of our patients being poorly controlled and had hyperlactatemia. Patients with a peak intraoperative lactate level of 4 or higher have a higher incidence of renal dysfunction, and this difference is statistically significant when compared to the other group. These findings are consistent with the findings of multiple studies as such patients are exposed to longer periods of hypoperfusion that affect their kidney function. Furthermore, patients with peak lactate levels greater than or equal to 4 mmol/L have a significantly longer ICU stay as hyperlactatemia is associated with some of the morbidities that need longer duration to be managed at ICU as, which is consistent with the findings of Provenchere et al. [14].

Infection was also higher in the high lactate group, but only marginally so; this finding did not entirely agree with Ranucci et al. [2]. This finding could be explained by our study's strict infection control program and prophylactic antibiotic regimen. When comparing the two groups in terms of intraoperative lactate level, we looked at a study by Demers et al. [15] on 400 patients who underwent various types of open-heart surgery. This study found an increased incidence of postoperative gastrointestinal bleeding in patients with high lactate levels, but this differs from our study because hepatic patients were excluded.

Regarding inotropic support postoperatively, there was no significant difference between the two groups, similar to Demer et al.'s findings [15]. Rashkin and colleagues [11] discovered that patients with high lactate require more inotropic support than other groups; this differs from our study. We could explain this as we excluded patients with poor ejection fraction. Unlike other studies, the length of hospital stay shows no statistically significant difference between the two groups, which could be explained by the fact that our study was conducted during the Corona epidemic when many patients were discharged on demand despite the need to continue treatment at hospital.

While Provenchere and colleagues found a substantial difference in individuals with elevated lactate levels, we did not employ an aortic balloon because we excluded patients with poor ejection fraction from the start. We observed a significant rise in lactate levels during and after rewarming. This may be because oxygen demands rise during reperfusion. Several researchers claim that the distribution of serum lactate was not bimodal. According to Maillet et al. [1] and Stammers et al. [16], complicated operations such as aortic root replacement and intracardiac repairs were linked to increased serum lactate levels. However, we were unable to demonstrate a statistical correlation between surgical complexity and HL because of the limited sample size. We could not study the relationship between preoperative anemia and creatinine with HL because patients with severe preoperative anemia and serum creatinine levels greater than 2 mg/dL were excluded. Patients with high lactate have a significantly higher mortality rate than the other group (28.9% vs. 0%, P=0.011), which is consistent with the findings of Rashkin et al. [11].

Study limitations

Our study has limitations, including a small sample size and a short postoperative follow-up period. Another limitation is the heterogeneity of cases and the single-center experience.

Conclusion

Peak intraoperative blood lactate levels of 4 mmol/L or higher have been associated with a higher risk of perioperative morbidity and mortality. Hyperlactemia and its causes should be treated once diagnosed to improve the outcomes.

Conflict of interest: Authors declare no conflict of interest.

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