# Hyperlactatemia Post-CABG: Case Studies in Three Patients

**Ardyan Wardhana[1*], Juni Kurniawaty[2]**

1. *Department of Clinical Medicine, Faculty of Medicine, Universitas Surabaya, Surabaya, Indonesia*
2. *Department of Anesthesiology and Intensive Therapy, School of Medicine, Faculty of Medicine Public Health and Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia*

**penulis korespondensi*

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## ABSTRACT

**Introduction:** Hyperlactatemia after CABG may signal intra- or postoperative complications by reflecting a mismatch between tissue oxygen supply and metabolic demand, with potential for organ dysfunction and worse outcomes. This case report examined contributing factors—including metabolic acidosis, postoperative metabolic stress, and inotropic agents—to guide targeted interventions and improve clinical results.

**Case Description:** Three patients underwent CABG, with the first and second remaining hemodynamically stable in the ICU on dobutamine and nitroglycerin, whereas the third required norepinephrine, epinephrine, and temporary pacing for instability. None exceeded 4 mmol/L during CPB or immediately after separation, yet all showed immediate-onset hyperlactatemia (IHL)—a phenomenon reported in 17% of cases, especially with longer CPB/cross-clamp times. All subsequently developed late-onset hyperlactatemia (LHL) at 4–12 hours: first and third patient had hyperglycemia, whereas the second reached the highest 12-hour lactate peak without hyperglycemia. LHL likely reflected type-B lactate from postoperative inflammatory/metabolic stress and insulin resistance, typically normalizing within 12–24 hours without a marked drop in base excess. Third patient's sharp 4-hour surge was plausibly epinephrine-related—more consistent with preserved metabolic reserve than with adverse prognosis.

**Conclusion:** In post-CABG patients, hyperlactatemia may arise from non-hypoxic, multifactorial mechanisms (inflammation, metabolic stress, and inotropes) and thus warrants context-aware interpretation and targeted management rather than reflexive attribution to tissue hypoxia.

**Keywords:** cardiopulmonary bypass, coronary artery bypass grafting, heart surgery, hyperlactatemia, stress hyperglycemia

# Hiperlaktatemia Post-CABG: Studi Kasus pada Tiga Pasien

**Ardyan Wardhana[1*], Juni Kurniawaty[2]**

1. *Departemen Kedokteran Klinik, Fakultas Kedokteran, Universitas Surabaya, Surabaya, Indonesia*
2. *Departemen Anestesi dan Terapi Intensif, Fakultas Kedokteran, Kesehatan Masyarakat dan Keperawatan, Universitas Gadjah Mada, Yogyakarta, Indonesia*

**corresponding author*

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***ABSTRAK***

***Pendahuluan:*** *Hiperlaktatemia setelah CABG dapat menandakan komplikasi intraoperatif maupun pascaoperatif karena mencerminkan ketidakseimbangan antara suplai oksigen jaringan dan kebutuhan metabolik, yang berpotensi menyebabkan disfungsi organ serta memperburuk luaran. Laporan kasus ini menelaah faktor-faktor yang berkontribusi—termasuk asidosis metabolik, stres metabolik pascaoperasi, dan penggunaan agen inotropik—untuk memandu intervensi yang terarah dan meningkatkan hasil klinis.*

***Deskripsi Kasus:*** *Tiga pasien menjalani CABG; pasien pertama dan kedua tetap hemodinamis stabil di ICU dengan dukungan dobutamin dan nitrogliserin, sedangkan pasien ketiga memerlukan norepinefrin, epinefrin, dan pacing sementara karena ketidakstabilan hemodinamik. Tidak ada yang melebihi 4 mmol/L selama CPB atau segera setelah lepas mesin, namun seluruhnya menunjukkan hiperlaktatemia onset segera (IHL)—fenomena yang dilaporkan pada ~17% kasus, terutama dengan durasi CPB dan waktu penjepitan aorta yang lebih lama. Seluruh pasien kemudian mengalami hiperlaktatemia onset lambat (LHL) pada 4–12 jam pascaoperasi: pasien pertama dan ketiga mengalami hiperglikemia, sedangkan pasien kedua mencapai puncak laktat tertinggi pada jam ke-12 tanpa hiperglikemia. LHL kemungkinan mencerminkan laktat tipe B akibat respons inflamasi dan stres metabolik pascaoperasi serta resistensi insulin yang meningkatkan produksi laktat dan hiperglikemia, umumnya kembali normal dalam 12–24 jam tanpa penurunan base excess yang bermakna. Lonjakan tajam laktat pada 4 jam pada pasien ketiga diduga dipicu oleh pemberian epinefrin—lebih konsisten sebagai penanda cadangan metabolik yang masih baik daripada pertanda luaran buruk.*

***Simpulan:*** *Pada pasien pasca-CABG, hiperlaktatemia dapat timbul dari mekanisme multifaktorial non-hipoksik (inflamasi, stres metabolik, inotropik) sehingga memerlukan interpretasi kontekstual dan penatalaksanaan yang terarah, bukan serta-merta diatribusikan pada hipoksia jaringan.*

***Kata kunci:*** *coronary artery bypass grafting, hiperglikemia stres, hiperlaktatemia, mesin pintas jantung-paru, operasi jantung*

## INTRODUCTION

Hyperlactatemia is a medical condition characterized by an elevated concentration of lactate in the blood, often caused by tissue hypoperfusion or oxidative metabolic dysfunction. In the context of cardiac surgery, particularly Coronary Artery Bypass Grafting (CABG), hyperlactatemia can serve as an important indicator of intraoperative or postoperative complications.[1] Elevated lactate levels in post-CABG patients may indicate an imbalance between oxygen supply and the metabolic demands of tissues, which could lead to organ dysfunction and worsen patient outcomes.[2] A deep understanding of the mechanisms underlying hyperlactatemia in CABG patients is crucial for identifying appropriate interventions and improving clinical outcomes.

In this case report, we describe three patients who experienced hyperlactatemia with distinct characteristics after undergoing CABG surgery. This occurrence is noteworthy because of the persistent lactate elevation, despite other hemodynamic parameters appearing stable. Through this report, we aim to explore potential factors, including the effects of cardiopulmonary bypass (CPB) machines, potential metabolic acidosis, and the impact of postoperative metabolic stress. Consequently, this report seeks to provide additional insights for clinicians in understanding the dynamics of hyperlactatemia in post-CABG patients.

This report aims to explore the contributing factors to hyperlactatemia in post-CABG patients, including potential metabolic acidosis, metabolic stress, and the use of inotropic agents. Another objective of this report is to identify patterns of hyperlactatemia onset, including its bimodal distribution with early and late peaks, and their implications for patient prognosis.

## CASE DESCRIPTION

The first patient, a 65-year-old male, was admitted with unstable angina pectoris with chronic total occlusion in the left anterior descending artery (LAD) and right coronary artery (RCA). The patient had a history of hypertension but no history of diabetes mellitus. His medication history included atorvastatin 40 mg, bisoprolol 2.5 mg, candesartan 8 mg, amiodarone 200 mg, furosemide 40 mg, spironolactone 25 mg, nitroglycerine 2.5 mg, and heparinization. On physical examination, the patient was not obese with a BMI of 24.87 kg/m$^2$. Preoperative electrocardiogram (ECG) showed sinus rhythm at 56 bpm, normal axis, and QS waves in leads V1-V3. Echocardiography revealed left atrial and right ventricular dilation, globally reduced left ventricular systolic function with an ejection fraction (EF) of 46%, mild mitral regurgitation, and hypokinetic disturbances in the basal mid-anteroseptal, basal mid-inferoseptal, and basal mid-inferior segments.

The patient underwent CABG surgery with left internal mammary artery (LIMA) to LAD and saphenous vein grafts (SVG) to distal RCA. Cardiopulmonary bypass (CPB) time was 99 minutes, aortic cross-clamp time was 62 minutes, and ischemic time was 55 minutes. Post-CPB, the patient received hemodynamic support with dobutamine at 5 mcg/kg/min and nitroglycerine at 0.5 mcg/kg/min. The patient was then transferred to the ICU with relatively stable hemodynamics. Transthoracic echocardiography (TTE) showed an ejection fraction (EF) of 63%, a cardiac output (CO) of 6.75 L/min, a cardiac index (CI) of 3.86 L/min/m$^2$, and a systemic vascular resistance (SVR) of 510 dynes/cm$^5$, with hypokinesia of the anteroseptal region. The ECG revealed normal sinus rhythm at 68 bpm. The progression of arterial blood gas analysis and laboratory findings during the surgery and in the ICU was presented in Table 1.

The second patient, a 65-year-old male, was admitted with three-vessel coronary artery disease involving left main (LM) disease (Medina 1-1-1) and chronic total occlusion (CTO) in the right coronary artery (RCA). The patient had no history of diabetes mellitus or hypertension. His medication history included aspirin 80 mg, clopidogrel 75 mg, atorvastatin 20 mg, bisoprolol 2.5 mg, and nitroglycerine 2.5 mg twice daily. Physical examination revealed the patient was not obese, with a body mass index (BMI) of 21.7 kg/m$^2$. Preoperative ECG showed sinus rhythm at 82 bpm and a normal axis. TTE revealed normal heart chamber dimensions, adequate left ventricular systolic function with an EF of 55%, mild mitral regurgitation, and mild hypokinesia in the basal mid-inferoseptal and anterior regions.

Surgical revascularization consisted of a LIMA graft to the LAD artery and a SVG to the obtuse marginal branch. The surgery involved 41 minutes of CPB, 49 minutes of aortic cross-clamping, and 35 minutes of ischemic time. Post-CPB, the patient was supported with dobutamine at 5 mcg/kg/min and nitroglycerine at 0.5 mcg/kg/min. The patient was transferred to the ICU with relatively stable hemodynamic. TTE showed an EF of 60%, CO of 4.3 L/min, CI of 2.62 L/min/$m^2$, and SVR of 967 dynes/$cm^5$, with normokinetic findings. ECG revealed normal sinus rhythm at 68 bpm. The progression of arterial blood gas analysis and laboratory findings in the operating room and ICU was summarized in Table 1.

The third patient, a 69-year-old male, was admitted with three-vessel coronary artery disease involving chronic total occlusion at the ostium of the left main coronary artery. The patient had a history of hypertension but no history of diabetes mellitus. His medication history included candesartan 8 mg, bisoprolol 2.5 mg, and nitroglycerine 2.5 mg twice daily. The physical examination revealed the patient was not obese, with a BMI of 21.5 kg/$m^2$. Preoperative ECG showed atrial fibrillation with normal ventricular rate at 80 bpm, ST elevation in leads V1-V3, and ST depression in leads V5-V6. TTE revealed concentric left ventricular hypertrophy with globally and segmentally reduced systolic function, an EF of 45%, and mild aortic stenosis.

Revascularization entailed a SVG to the LAD, left circumflex artery (LCX), and posterior descending artery (PDA) artery. CPB time was 108 minutes, aortic cross-clamp time was 91 minutes, and ischemic time was 82 minutes. Post-CPB, the patient was supported with dobutamine at 5 mcg/kg/min, norepinephrine at 0.05 mcg/kg/min, epinephrine at 0.05 mcg/kg/min, and nitroglycerine at 0.5 mcg/kg/min. The patient was then transferred to the ICU with relatively unstable hemodynamic, requiring pacing. Postoperative TTE revealed an EF of 45%, CO of 5.1 L/min, CI of 3.1 L/min/$m^2$, and SVR of 580 dynes/$cm^5$, with hypokinetic findings. ECG showed normal sinus rhythm at 68 bpm, left axis deviation, and complete left bundle branch block. In the first four hours in the ICU, the patient experienced hematuria secondary to complications from Foley catheter insertion during surgery. The progression of arterial blood gas analysis and laboratory results during surgery and in the ICU was presented in Table 1.

**Table 1.** Trends in laboratory values for the three patients

| Parameter | Pre | CPB | Post | T0 | T1 | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|---|---|---|---|
| ΔCO2 (1) | N/A | N/A | N/A | 9.0 | 5.8 | 5.4 | 3.3 | N/A | N/A |
| ΔCO2 (2) | N/A | N/A | N/A | 10.7 | 11.9 | 13.4 | 5.8 | 4.0 | N/A |
| ΔCO2 (3) | N/A | N/A | N/A | 7.7 | 4.7 | 5.2 | 7.6 | 6.8 | 1.7 |
| BE (1) | -6 | 0 | -2 | -7.2 | -6.9 | -4.80 | -1.6 | -1.9 | 0.7 |
| BE (2) | -1 | -2 | -3 | -4.32 | -6.6 | -7.15 | -4.6 | -2.4 | 0.6 |
| BE (3) | -8 | -5 | -7 | -7.69 | -15.7 | -7.90 | -3.8 | 2.92 | 2.0 |
| Lactate (1) | 0.9 | 1.2 | 1.9 | 4.9 | 8.3 | 6.9 | 4.8 | 1.9 | 2.9 |
| Lactate (2) | 2.0 | 3.1 | 3.8 | 5.1 | 6.7 | 7.4 | 8.7 | 8.6 | 6.2 |
| Lactate (3) | 1.8 | 2.5 | 3.0 | 3.6 | 14.8 | 14.8 | 8 | 2.8 | 1.9 |
| ScvO2 (1) | N/A | N/A | N/A | 80.8 | 79.7 | 86.5 | 82.8 | N/A | N/A |
| ScvO2 (2) | N/A | N/A | N/A | 84.5 | 79.4 | 75.3 | 77 | 74.5 | N/A |
| ScvO2 (3) | N/A | N/A | N/A | 92.6 | 95 | 92.1 | 82.0 | N/A | N/A |
| Glu (1) | 86 | 160 | 197 | 382 | 384 | 346 | 137 | 116 | 175 |
| Glu (2) | 85 | 94 | 127 | 119 | N/A | N/A | 150 | N/A | N/A |
| Glu (3) | 159 | 188 | 176 | 237 | 340 | 277 | 200 | 138 | 154 |

N/A: not available

ΔCO2: difference in the gradient between PCO2 in the veins and arteries, BE: base excess, Glu: glucose level, CPB: cardiopulmonary bypass, T0: measurement time upon arrival at the ICU, T1: measurement time 4 hours post-ICU admission, T2: measurement time 8-10 hours post-ICU admission, T3: measurement time 12-14 hours post-ICU admission, T4: measurement time 18-20 hours post-ICU admission, T5: measurement time 24-30 hours post-ICU admission

## DISCUSSION

Hyperlactatemia is a condition that frequently occurs in patients following cardiac surgery. An observational study reported that 81.8% of post-cardiac surgery patients experienced hyperlactatemia, defined as a lactate level exceeding 2.2 mmol/L.[3] The majority of patients (57.9%) had mild hyperlactatemia, with peak lactate levels between 2.2 and 4.4 mmol/L during their ICU stay. The remaining 23.9% were classified as severe cases, as they had peak lactate levels above 4.4 mmol/L while in the ICU. In this study, lactate levels peaked 3.36 ± 3.13 hours post-surgery, and returned to normal 7.34 ± 6.56 hours after reaching their peak. Hyperlactatemia in this study was associated with a hazard ratio of 40.96 for mortality, based on multivariate analysis.

Another study defined hyperlactatemia as a lactate level exceeding 4 mmol/L, which was observed in 59.7% of patients.[4] Lactate levels gradually increased during cardiopulmonary bypass (CPB) and continued to rise up to 0-6 hours after ICU admission, before gradually declining. Unlike the previous study, a bimodal distribution of lactate levels was not observed. Another study, which used a higher threshold of 5 mmol/L, reported a 4% incidence of hyperlactatemia post-weaning from CPB. This was associated with an increased incidence of low cardiac output syndrome and higher mortality rates compared to patients with normal lactate levels or those below 5 mmol/L.[5] In the cases presented in this report, none of the three patients experienced lactate levels exceeding 4 mmol/L during CPB or after weaning from CPB.

In the context of cardiac surgery, particularly after CPB, Type A lactic acidosis can arise as a response to tissue hypoperfusion that occurs during surgery. Through tissue dialysis studies in adult patients undergoing cardiac surgery, it was found that CPB leads to elevated lactate levels and an increased lactate-to-pyruvate ratio in both myocardial and peripheral tissues. Although calculated tissue perfusion may appear adequate, some patients still experience early lactate elevation, which is possibly linked to inflammatory responses, microcirculatory changes, and mitochondrial reactions during hypothermia and CPB.[6] Type A hyperlactatemia is predominantly detected during the rewarming phase, as this period demands significant oxygen consumption, thereby increasing the risk of dysoxia.[7]

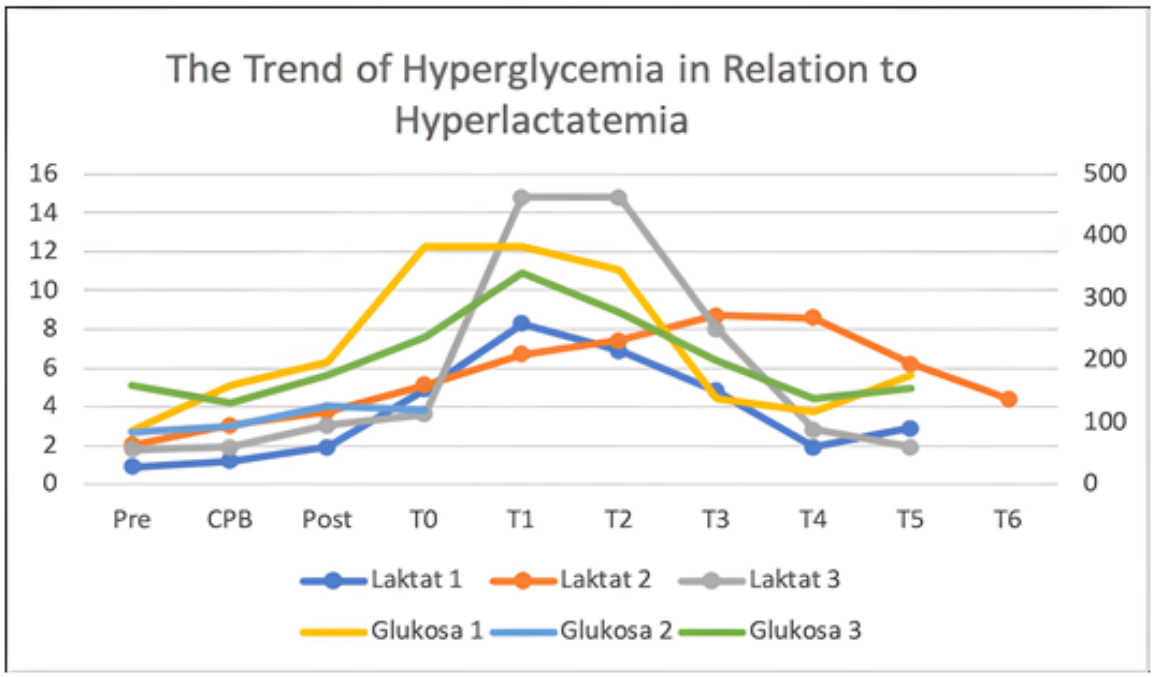


**Figure 1.** Trends of glucose and lactate levels post CABG in three patients

All three patients experienced hyperlactatemia upon initial ICU admission, with lactate levels exceeding 3 mmol/L as shown in Figure 1. Lactate levels upon ICU admission serve as a better predictor of mortality than lactate levels during the ICU stay. A prospective observational study by Maillet et al. reported that lactate levels exceeding 3 mmol/L at the time of ICU admission were associated with increased mortality.[8] Furthermore, early ICU admission hyperlactatemia is an independent risk factor for poor outcomes in adult post-cardiac surgery patients.[1] Another study found similar results, where patients with hyperlactatemia at ICU admission had worse outcomes, including higher mortality, increased use of ECMO, and longer hospital stays compared to those without early ICU hyperlactatemia.[9] The elevated lactate levels upon ICU admission reflect intraoperative events, including the use of CPB, the success of revascularization, the efficacy of myocardial protection, and hemodynamic management.

Hyperlactatemia exhibits a bimodal distribution during cardiac surgery and post-operative care in the ICU. Therefore, hyperlactatemia in cardiac surgery is classified into two types: Immediate-Onset Hyperlactatemia (IHL) and Late-Onset Hyperlactatemia (LHL). The peak increase in lactate levels upon ICU admission is observed in IHL, while the peak for LHL occurs 4 to 24 hours after ICU admission. IHL occurs during or immediately after CPB in patients undergoing on-pump cardiac surgery and often persists until the patient arrives in the ICU. The peak of IHL occurred 3 hours post-ICU admission and decreased by the fifth hour, while LHL peaked at the seventh hour post-ICU admission.[9] Using a definition of hyperlactatemia as lactate levels >3 mmol/L, the incidence of hyperlactatemia within the first hour of ICU admission was reported to be 17%.[9]

Patients with IHL had longer CPB durations (150 ± 56 vs. 181 ± 54 minutes, $p < 0.001$) and aortic cross-clamp times (120 ± 44 vs. 144 ± 49, $p < 0.001$) compared to those without hyperlactatemia.[9] In another study, patients with IHL had significantly longer CPB times (92.40 ± 26.0 vs. 83.96 ± 28.18 minutes; $p = 0.003$) and aortic cross-clamp times (55.8 ± 18.2 vs. 48.4 ± 19.8 minutes; $p = 0.007$) compared to patients without elevated lactate levels.[4] A retrospective study reported that patients with elevated lactate levels at the time of ICU admission had longer CPB and aortic cross-clamp times compared to patients who experienced lactate elevation 4-8 hours post-surgery and those with normolactatemia.[8]

CPB duration and aortic cross-clamp time are key factors predicting the occurrence of IHL. These variables often reflect more complex or complicated cardiac procedures. Univariate analysis revealed that more complex procedures, such as multi-vessel CABG and dual valve surgery, were strongly associated with an increased risk of IHL.[9] The longer the CPB and aortic cross-clamp times, the greater the likelihood of systemic hypoperfusion to the organs, promoting anaerobic metabolism and increased lactate production due to more active glycolysis. Additionally, the IHL group experienced more frequent hypotension and required greater vasopressor support compared to the LHL group, potentially reflecting intraoperative hemodynamic instability and difficulties weaning from CPB.

Several factors contribute to IHL, including tissue hypoxia, impaired oxygen uptake due to capillary sludging caused by non-pulsatile flow, increased endogenous and exogenous catecholamines, systemic inflammation, and microvascular thrombosis. Furthermore, prolonged CPB duration, hemodilution, low CPB flow rate, and low oxygen delivery are all CPB management factors contributing to lactate elevation.

All three patients experienced a subsequent increase in lactate levels between 4 to 12 hours postoperatively. Lactate levels in all three patients rose 4 hours post-surgery and then gradually decreased. However, the progression of other related parameters exhibited different characteristics across the patients. Patient 1 showed a peak in lactate levels at 4 hours postoperatively, accompanied by a trend of declining base deficit and increasing blood glucose levels. Patient 2 experienced the highest lactate peak at 12 hours post-surgery, along with a concurrent increase in base deficit but without elevated glucose levels. Patient 3 demonstrated a pattern similar to Patient 1 but with a significantly higher spike in lactate levels at the 4-hour post-surgery mark.

All three patients had postoperative ALT and AST levels within the normal range, suggesting that liver impairment was not contributing to lactate clearance issues. The gradual rise in lactate starting 4 hours post-surgery and its subsequent decline beginning around 12 hours indicates an additional source of lactate beyond Immediate-Onset Hyperlactatemia (IHL).

This delayed increase in lactate levels several hours post-surgery is termed Late-Onset Hyperlactatemia (LHL), which peaks 4-14 hours post-surgery and returns to normal within 12-24 hours. One of its characteristics is that LHL tends not to significantly affect the strong ion difference or base excess unless lactate levels become severely elevated. This was demonstrated in Patient 1, where LHL's contribution to IHL did not exacerbate the acidosis condition.

Using the definition of hyperlactatemia as lactate levels > 3 mmol/L, the incidence of hyperlactatemia beyond the first hour of ICU admission was reported to be 70.8%.[9] This type of hyperlactatemia is due to the increase in Type B lactate, often accompanied by hyperglycemia. It is not associated with anaerobic conditions caused by reduced oxygen supply to tissues. This was demonstrated in a study by Hosein, which measured changes in lactate levels every 30 minutes for 12 hours post-Fontan surgery and correlated them with changes in the lactate-pyruvate ratio and cardiac index measured using PiCCO.[10] The results showed that the rise in lactate levels was not accompanied by an increase in the lactate-pyruvate ratio or a decrease in the cardiac index. A study in pediatric patients undergoing cardiac surgery reported that hyperlactatemia occurring 4 hours after ICU admission did not correlate with a reduction in oxygen supply.[11]

Systemic inflammatory responses triggered by oxidative stress can occur due to hemolysis, ischemia, reperfusion injury, and neutrophil activation during CPB.[12] This inflammatory response, leading to mitochondrial dysfunction, coupled with the stress response from surgery that accelerates glycolysis, increases lactate production several hours after surgery.

The most plausible explanation for Type B hyperlactatemia occurring without tissue hypoxia is "accelerated glycolysis," where increased glucose uptake by peripheral tissues due to the stress response leads to elevated pyruvate production, which is subsequently converted into lactate. In this context, the increased production of pyruvate from accelerated glycolysis results in higher lactate production via a simple mass effect on the lactate-pyruvate equilibrium. Meanwhile, the elevated pyruvate production is also associated with increased pyruvate oxidation through the citric acid cycle, meaning aerobic respiration remains active in cases of Type B hyperlactatemia.[13] Type B hyperlactatemia is also associated with insulin resistance that occurs post-surgery, which further elevates lactate levels by inhibiting pyruvate dehydrogenase.[14] This is evidenced by the fact that hyperglycemia is more common in LHL than in IHL.[8]

The third patient exhibited a significant spike in lactate levels, resulting in severe metabolic acidosis 4 hours post-surgery, even though the patient's lactate levels at ICU admission were the lowest among the three patients. The addition of epinephrine at ICU admission to stabilize hemodynamics may have contributed to this lactate surge. The use of epinephrine has been associated with immediate-onset hyperlactatemia (IHL) (OR, 6.0; 95% CI, 2.2 to 16.4).[8]

In septic shock population, Levy et al. found that epinephrine caused an increase in plasma lactate levels without altering the lactate-to-pyruvate ratio.[15] In contrast, norepinephrine did not cause an increase in plasma lactate levels. Epinephrine increases lactate production by stimulating β2-adrenergic receptors. Adrenergic stimulation by epinephrine increases the production of cAMP, which in turn stimulates glycogenolysis, gluconeogenesis, lipolysis, and enhances Na+-K+-ATPase activity, thereby providing more substrates for glycolysis and exacerbating the accelerated glycolysis condition.[16]

However, the increase in lactate levels and hyperglycemia caused by epinephrine administration a few hours after ICU admission is not necessarily associated with poor outcomes. In an observational study on sepsis cases, Wutrich et al. reported that survivors of shock experienced a lactate spike 4 hours after epinephrine administration, similar to the case

shown in the figure below.[17] Survivors showed an initial increase in lactate, followed by a decline back to normal levels within 24 hours. Therefore, the ability to produce lactate and hyperglycemia after epinephrine stimulation is associated with a good prognosis, as it indicates that the patient has sufficient metabolic reserves and that aerobic glycolysis can be reactivated.

The first and third patients experienced elevated blood glucose levels starting 4 hours after ICU admission, with levels returning to normal by the 12-hour mark as shown in Figure 1. In contrast, the second patient did not experience hyperglycemia despite having hyperlactatemia. The spontaneous resolution of hyperglycemia after the acute phase of illness subsides is referred to as stress hyperglycemia. Stress hyperglycemia is common in critically ill patients and appears to be a marker of disease severity.

Hyperglycemia is reported to occur in 60% of cardiac surgery patients.[18] Glucose levels can also predict lactate levels, as both are involved in glucose metabolism, where one can act as a precursor to the other. The elevation of both glucose and lactate is also a common stress response to cardiac surgery, which is why they often appear together. The co-occurrence of hyperglycemia and hyperlactatemia in cardiac surgery is reported in approximately 15.5% of patients.[19] Patients who experience both hyperlactatemia and hyperglycemia tend to have worse outcomes compared to those who experience only one of these conditions. A study by He et al. reported that hyperlactatemia accompanied by intraoperative hyperglycemia during cardiac surgery significantly increases the risk of developing postoperative acute kidney injury (OR 3.69, 95% CI, 2.68–5.13).[19]

Stress-induced hyperglycemia is mediated by the hypothalamic-pituitary-adrenal axis and the sympathoadrenal system. The physiological role of stress hyperglycemia appears to be an adaptive response aimed at providing energy sources for essential tissues, such as the brain and immune cells, during periods of significant stress. Therefore, hyperglycemia can be protective by enabling cells to survive ischemic or hypoxic challenges. However, severe hyperglycemia can alter plasma osmolarity, leading to fluid shifts and osmotic diuresis. Current guidelines for critical illness still recommend glycemic control with a target blood glucose level below 180 mg/dL. A study by Palermo et al. reported no benefit in correcting hyperglycemia in combination with hyperlactatemia in the pediatric population undergoing cardiac surgery.[14] The group of patients receiving insulin therapy showed no significant difference in the time required for lactate normalization (12.8 hours [IQR 10.8–15.2] vs 14.1 hours [IQR 10.4–16.9], P = 0.44) or in the length of hospital stay. However, the small sample size (78 vs. 54 patients) warrants caution in interpreting the results of this study.

The third patient in this case series experienced hyperlactatemia without hyperglycemia. The elevated lactate levels persisted for more than 24 hours in the ICU, peaking between 12 and 16 hours of ICU care. The occurrence of hyperlactatemia without hyperglycemia during ICU care suggests the possibility of type A lactic acidosis. Patients with hyperlactatemia and normoglycemia at 4- and 12-hours post-ICU admission tended to have higher oxygen extraction, along with an elevated lactate/pyruvate ratio, indicating that lactate production might be due to tissue hypoxia.[11]

## CONCLUSION

The three cases demonstrate that hyperlactatemia in post-cardiac surgery patients can be caused by a combination of factors, such as hypoperfusion, inflammatory responses, and the effects of medications like epinephrine. Although high lactate levels are often associated with poor prognosis, elevated lactate does not always indicate tissue hypoxia. Therefore, it is crucial to conduct a comprehensive evaluation of the contributing factors in each case to determine the appropriate management strategies, ultimately aiming to improve clinical outcomes in post-cardiac surgery patients.

## CONFLICT OF INTEREST

The authors declare no conflict of interest in relation to this study.

## REFERENCES

1. Hajjar LA, Almeida JP, Fukushima JT, Rhodes A, Vincent JL, Osawa EA, et al. High lactate levels are predictors of major complications

after cardiac surgery. J Thorac Cardiovasc Surg. 2013 Aug;146(2):455-60. doi: 10.1016/j.jtcvs.2013.02.003.
2. Toraman F, Evrenkaya S, Yuce M, Aksoy N, Karabulut H, Bozkulak Y, et al. Lactic acidosis after cardiac surgery is associated with adverse outcome. Heart Surg Forum. 2004 Apr 1;7(2):E155-9. doi: 10.1532/HSF98.20041002.
3. Kogan A, Preisman S, Bar A, Sternik L, Lavee J, Malachy A, et al. The impact of hyperlactatemia on postoperative outcome after adult cardiac surgery. J Anesth. 2012 Apr;26(2):174-8. doi: 10.1007/s00540-011-1287-0.
4. Naik R, George G, Karuppiah S, Philip MA. Hyperlactatemia in patients undergoing adult cardiac surgery under cardiopulmonary bypass: Causative factors and its effect on surgical outcome. Ann Card Anaesth. 2016 Oct-Dec;19(4):668-675. doi: 10.4103/0971-9784.191579.
5. Seghrouchni A, Atmani N, Moutakiallah Y, Belmekki A, El Bekkali Y, Houssa MA. Does severe hyperlactatemia during cardiopulmonary bypass predict a worse outcome? Ann Med Surg (Lond). 2021 Dec 21;73:103198. doi: 10.1016/j.amsu.2021.103198.
6. Stephens EH, Epting CL, Backer CL, Wald EL. Hyperlactatemia: An Update on Postoperative Lactate. World J Pediatr Congenit Heart Surg. 2020 May;11(3):316-324. doi: 10.1177/2150135120903977.
7. Ranucci M, Isgrò G, Carlucci C, De La Torre T, Enginoli S, Frigiola A; Surgical and Clinical Outcome REsearch Group. Central venous oxygen saturation and blood lactate levels during cardiopulmonary bypass are associated with outcome after pediatric cardiac surgery. Crit Care. 2010;14(4):R149. doi: 10.1186/cc9217.
8. Maillet JM, Le Besnerais P, Cantoni M, Nataf P, Ruffenach A, Lessana A, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest. 2003 May;123(5):1361-6. doi: 10.1378/chest.123.5.1361.
9. Algarni KD. The effect of hyperlactatemia timing on the outcomes after cardiac surgery. Cardiothorac Surg 2020; 28: 18. doi:10.1186/s43057-020-00029-w.
10. Hosein RB, Morris KP, Brawn WJ, Barron DJ. Use of tissue microdialysis to investigate hyperlactataemia following paediatric cardiac surgery. Interact Cardiovasc Thorac Surg. 2008 May;7(3):384-8; discussion 388. doi: 10.1510/icvts.2007.166264.
11. Klee P, Rimensberger PC, Karam O. Association Between Lactates, Blood Glucose, and Systemic Oxygen Delivery in Children After Cardiopulmonary Bypass. Front Pediatr. 2020 Jun 23;8:332. doi: 10.3389/fped.2020.00332.
12. Zakkar M, Guida G, Suleiman MS, Angelini GD. Cardiopulmonary bypass and oxidative stress. Oxid Med Cell Longev. 2015;2015:189863. doi: 10.1155/2015/189863.
13. Minton J, Sidebotham DA. Hyperlactatemia and Cardiac Surgery. J Extra Corpor Technol 2017; 49: 7–15. Available from: https://pubmed.ncbi.nlm.nih.gov/28298660/
14. Palermo RA, Palac HL, Wald EL, Wainwright MS, Costello JM, Eltayeb OM, et al. Metabolic Uncoupling Following Cardiopulmonary Bypass. Congenit Heart Dis. 2015 Nov-Dec;10(6):E250-7. doi: 10.1111/chd.12285.
15. Levy B, Perez P, Perny J, Thivilier C, Gerard A. Comparison of norepinephrine-dobutamine to epinephrine for hemodynamics, lactate metabolism, and organ function variables in cardiogenic shock. A prospective, randomized pilot study. Crit Care Med. 2011 Mar;39(3):450-5. doi: 10.1097/CCM.0b013e3181ffe0eb.
16. Garcia-Alvarez M, Marik P, Bellomo R. Stress hyperlactataemia: present understanding and controversy. Lancet Diabetes Endocrinol. 2014 Apr;2(4):339-47. doi: 10.1016/S2213-8587(13)70154-2.
17. Wutrich Y, Barraud D, Conrad M, Cravoisy-Popovic A, Nace L, Bollaert PE, et al. Early increase in arterial lactate concentration under epinephrine infusion is associated with a better prognosis during shock. Shock. 2010 Jul;34(1):4-9. doi: 10.1097/SHK.0b013e3181ce2d23.
18. Matsumoto S, Omiya H, Fujinaka W, Morimatsu H. Association between intraoperative hyperglycemia and

postoperative end-organ dysfunctions after cardiac surgery: a retrospective observational study. J Anesth. 2022 Apr;36(2):174-84. doi: 10.1007/s00540-021-03024-5.

19. He Q, Tan Z, Chen D, Cai S, Zhou L. Association between intraoperative hyperglycemia/hyperlactatemia and acute kidney injury following on-pump cardiac surgery: a retrospective cohort study. Front Cardiovasc Med. 2023 Dec 8;10:1218127. doi: 10.3389/fcvm.2023.1218127.