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Original Article

Prognostic value of peak lactate during cardiopulmonary bypass in adult cardiac surgeries: A retrospective cohort study

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Abstract

Objective: Tissue hypoperfusion during cardiopulmonary bypass (CPB) affects cardiac surgical outcomes. Lactate, an end product of anaerobic glycolysis from oxygen deficit, is a marker of tissue hypoxia. In this study, we aimed to identify the prognostic value of blood lactate level during CPB in predicting outcomes in adults undergoing cardiac surgeries. **Materials and Methods:** We retrospectively reviewed the medical records of patients who underwent cardiac surgeries with CPB from January 2015 to December 2015. Data about the characteristics of patients, preoperative status, type of surgery, and intraoperative lactate levels were collected. The outcomes were in-hospital mortality and complications. The receiver operating characteristics (ROC) curves were used to assess the ability of peak lactate level during CPB in predicting in-hospital mortality. **Results:** A total of 97 patients, including 61 who underwent emergent or urgent surgery, were enrolled. The types of surgery included coronary artery bypass grafting (CABG, n = 52), valve surgery (n = 27), combined surgery (CABG and valve surgery, n = 4), great vessel surgery (including aortic dissection, n = 9), and others (n = 5). The median CPB time was 139 min (interquartile range = 120–175). The median initial lactate and peak lactate levels during CPB were 0.9 and 4.2 mmol/L, respectively. In-hospital mortality was 14.4%, which was significantly associated with age and peak lactate level in the multivariate logistic regression model. When the peak lactate level during CPB reached 7.25 mmol/L, in-hospital mortality could be predicted with an area under the ROC curve of 0.75 (95% confidence interval: 0.59–0.90; P = 0.003), with a sensitivity of 57% and specificity of 93%. **Conclusion:** Hyperlactatemia during CPB was associated with increased in-hospital mortality. Thus, early detection of such conditions and aggressive postoperative care are important.

Keywords: *Cardiopulmonary bypass, In-hospital mortality, Lactate*

Introduction

Cardiopulmonary bypass (CPB) provides adequate systemic oxygenation and perfusion during cardiac operation through the adjustment of flow rate, temperature, oxygen concentration, and hemoglobin level [1]. Intraoperative events, including surgical techniques, methods used in myocardial protection, and CPB, can affect surgical outcomes. Altered mental status and decreased urine output are signs of tissue hypoperfusion; however, an adequate and timely assessment of such signs cannot be carried out during cardiac operation. Cerebral oximetry is the continuous monitoring of brain oxygenation concentration in the frontal cortex, which is a sentinel index for perfusion in other vital organs. However, such a procedure is not performed in each hospital [2]. Central venous oxygen saturation ($ScvO_2$) is no longer a resuscitation goal in the new surviving sepsis campaign guidelines, and it also has a limited role in patients under general anesthesia [3]. Other markers of local perfusions, such as tissue oxygen saturation and subcutaneous partial oxygen pressure, require individual monitors and electrodes [4]. Therefore, a parameter that is easier to use and more accessible, such as blood lactate level, is helpful.

Lactate is an end product of anaerobic glycolysis from oxygen deficit and tissue hypoperfusion. It is an obtainable surrogate marker of tissue hypoxia and disease severity and is considered an index marker of circulatory shock [5,6]. Moreover, an elevated lactate level is observed during cardiac

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operation with CPB in a bimodal distribution. Type A hyperlactatemia can occur during or soon after the initiation of CPB tissue due to hypoperfusion. Meanwhile, type B hyperlactatemia can be observed 4–14 h after surgery when a patient is admitted to an intensive care unit (ICU) under adequate oxygen delivery owing to increased substrate utilization [7-9]. A higher lactate level during CPB reflects inadequate tissue perfusion, which may be associated with poor surgical outcomes. Demers *et al*. have found an increased risk of postoperative morbidity and mortality in patients with higher peak lactate value during CPB [10]. In our study, we aimed to identify the prognostic value of blood lactate level during CPB in postoperative surgical outcomes in consecutive daily practices.

Materials and methods

Inclusion criteria of enrolled cases

We retrospectively reviewed the medical records of adult patients who underwent cardiac surgery with CPB from January 2015 to December 2015. The exclusion criterion was patients who underwent cardiac surgery without CPB.

Variables of interest and outcomes

Data about the baseline characteristics of the participants, including age, gender, body mass index (BMI), comorbidities, left ventricular ejection fraction (LVEF, %), European system for cardiac operative risk evaluation II (EuroSCORE II) score, preoperative hematocrit level, and serum creatinine levels, were obtained. The types of surgery were coronary artery bypass grafting (CABG), valve surgery, combined surgery (CABG and valve surgery), great vessel surgery (including aortic dissection), and other surgeries. The urgency of surgery was classified as elective, urgent, and emergent. An emergent operation was performed before the beginning of the next working day after making the decision to operate. Urgent surgery was defined as surgery performed in the same admission due to medical conditions that could not be treated without a definitive procedure. Meanwhile, elective surgery was defined as a scheduled operation. The definitions of urgency were based on the EuroSCORE II.

The intraoperative variables included CPB time, aortic cross-clamp time, initial lactate level at the beginning of the operation, and peak lactate level during CPB. The primary outcome was in-hospital mortality. The secondary outcomes were the length of ICU and hospital stay and postoperative complications, which include cardiac (the use of intra-aortic balloon pump or extracorporeal membrane oxygenation), neurologic (focal brain lesion, convulsion, or encephalopathy), pulmonary (mechanical ventilation more than 48 h, re-intubation, or acute respiratory distress), digestive (gastrointestinal tract bleeding, hepatic dysfunction, and abdominal compartment syndrome), and renal complications (acute kidney injury requiring renal replacement therapy).

Cardiopulmonary bypass

All patients were managed with the same CPB technique. After systemic heparinization, arterial and venous cannulations were performed centrally or peripherally. We used 1.5 L of Ringer's solution (sodium chloride: 8.6 g/L, potassium chloride: 0.3 g/L, and calcium chloride: 0.33 g/L) to prime the circuit, which is a lactate-free crystalloid solution. The flow rate was maintained at 2.4 L/min/m^2 at 37°C and 2.2 L/min/m^2 at 32°C. During CPB, the mean systemic arterial pressure was continuously monitored and maintained at no <50 mmHg. Hematocrit was kept higher than 20%. The systemic oxygen saturation was monitored and maintained at no <95%. We regularly assessed for arterial blood gas and lactate level at the beginning of CPB and every 30 min during CPB using GEM® Premier 3000. We used Medtronic BioTrend to monitor $ScvO_2$ and kept it around 65%–75% by adjusting the oxygenator. Moreover, the blood glucose level of each patient was evaluated, and insulin was administered to control blood glucose level if hyperglycemia (>200 mg/dL) was noted. According to this policy, we developed our goal-directed perfusion to optimize hemodynamics, flow, hematocrit, and oxygen demand.

Statistical analysis

The results were expressed as medians with interquartile ranges (IQR) due to the small sample size without normal distribution. The relationships between in-hospital mortality and potential risk factors identified via a univariate analysis were assessed using Chi-square test, Fisher's exact test, or Mann–Whitney U-test. The receiver operating characteristics (ROC) curves were constructed, and the area under curve (AUC) was established to assess the ability of peak lactate level during CPB in predicting in-hospital mortality. Thus, the cutoff value for peak lactate level was determined with the ROC curves using the Youden index. Furthermore, a multiple logistic regression analysis was performed to estimate the independent predictive factors for in-hospital mortality, and the odds ratio (OR) was presented. This model included the risk factors first identified through univariate analysis ($P < 0.1$). $P < 0.05$ was considered statistically significant in the multivariate logistic regression model. Statistical analyses were performed using the Statistical Package for the Social Sciences software version 21 (IBM Corp, Armonk, NY).

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Local Ethics Committee of the institute (Number: IRB 106-95-B). Informed written consent was waived because the study was a retrospective data analysis.

Results

Characteristics of the patients

During the study, we performed 103 cardiac operations, and patients who underwent cardiac surgery without CPB (n = 6) were excluded. A total of 97 patients with a median age of 64 years were enrolled in the study (IQR = 55–74), and the male-to-female ratio was 2:1. The median preoperative left ventricular ejection fraction was 66% (IQR = 54–74), and the median EuroSCORE II score was 2.2 (IQR = 1.3–4.7). Other baseline characteristics, including BMI, comorbidities, preoperative hematocrit levels, and serum creatinine levels, are listed in Table 1. The type and urgency of surgery are listed in Table 2. In terms of the types of surgery, most patients underwent CABG (53.6%) and valve surgery (27.8%). Meanwhile, in terms of urgency, 36 (37.1%), 46 (47.4%), and 15 (15.5%)

patients underwent elective, urgent, and emergency surgeries, respectively. Great vessel surgery for aortic dissection accounted for 53.3% of all emergent surgeries. Other surgeries included left atrial mass excision, pulmonary endarterectomy, removal of a pacemaker, and repair of the ventricular septal defect.

Outcome analysis

The in-hospital mortality was 14.4%, and the causes of death were cardiogenic shock in 57% and septic shock in 43%. Excluding in-hospital mortality cases, the median length of ICU stay was 5 days (IQR = 4–7.5), and that of hospital stay was 19 days (IQR = 13–29). The primary outcome and detailed complications are listed in Table 3.

The median CPB time was 139 min (IQR = 120–175). The median lactate level at the beginning of surgery and the peak lactate during CPB was 0.9 (IQR = 0.6–1.6) and 4.2 mmol/L (IQR = 3.1–6.0), respectively. A significantly higher peak lactate level during CPB in nonsurvivors was noted [Table 2].

Risk factors of mortality

Age, EuroSCORE II score, type of surgery, CPB time, and peak lactate level were significant variables between survivors and nonsurvivors. The factors associated with in-hospital mortality included age, great vessel surgery, CPB time, and peak lactate level in the univariate analysis. In the multivariate logistic analysis, older age (OR: 1.2; 95% confidence interval [CI]: 1.0–1.3; $P = 0.02$) and peak lactate level (OR: 1.6; 95% CI: 1.1–2.4; $P = 0.03$) were significant predictors of in-hospital mortality [Table 4].

Predictive value of peak lactate

The AUC of ROC was 0.75 (95% CI: 0.59–0.90; $P = 0.003$) [Figure 1]. We further calculated the best cutoff value that can be used to predict in-hospital mortality. A peak lactate level of 7.25 mmol/L during operation could predict in-hospital mortality with a remarkable specificity of 93% and positive likelihood ratio of 8.14. The comparisons of baseline characteristics, intraoperative parameters and postoperative outcomes between patients with peak lactate level ≥ 7.25 and < 7.25 mmol/L were listed in appendix [Appendix Tables 1-3].

Table 1: Demographic data of all patients and differences between survivors and nonsurvivors

	All patients (*n*=97), *n* (%)	Survivors (*n*=83), *n* (%)	Non-survivors (*n*=14), *n* (%)	*P**
Gender				
Male/female, *n* (ratio)	64/33 (66/34)	57/26 (69/31)	7/7 (50/50)	0.175
Age, median (IQR)	64 (55-74)	62 (55-71)	74 (63-77)	0.019
BMI, median (IQR)	25.1 (23-28.5)	25.2 (22.6-28.6)	24.5 (23.8-28.5)	0.879
Prior cardiac operation, number (ratio)	10 (10.3)	9 (10.8)	1 (7.1)	0.675
LVEF (%), median (IQR)	66 (54-74)	66 (56-75)	54 (37-75)	0.349
EuroSCORE II, median (IQR)	2.3 (1.3-4.7)	2.0 (1.2-4.0)	5.6 (2.9-14.5)	0.003
Co-morbidity, *n* (ratio)				
DM	39 (40.2)	34 (41.0)	5 (35.7)	0.712
HTN	67 (69.1)	56 (67.5)	11 (78.6)	0.408
Cirrhosis	2 (2.1)	2 (2.4)	0 (0)	0.559
ESRD	4 (4.1)	4 (4.8)	0 (0)	0.404
Old CVA	6 (6.2)	5 (6.0)	1 (7.1)	0.873
Preoperation hematocrit, median (IQR)	36 (30.8-41.1)	36 (30.8-41.0)	36.9 (31.1-42.4)	0.674
Preoperation creatinine, median (IQR)	1.1 (0.8-1.5)	1.1 (0.8-1.5)	1.3 (0.8-2.2)	0.413

*Comparison between survivors and nonsurvivors. LVEF: Left ventricular ejection fraction, EuroSCORE II: European system for cardiac operative risk evaluation II, DM: Diabetes mellitus, HTN: Hypertension, ESRD: End-stage renal disease, CVA: Cardiovascular accident, BMI: Body mass index, IQR: Interquartile ranges

Table 2: Details of cardiac operations and intraoperative parameters

	All patients (*n*=97), *n* (%)	Survivors (*n*=83), *n* (%)	Nonsurvivors (*n*=14), *n* (%)	*P**
Surgical type				0.015
CABG	52 (53.6)	48 (57.8)	4 (28.6)	
Valve surgery	27 (27.8)	24 (28.9)	3 (21.4)	
CABG + valve	4 (4.1)	3 (3.6)	1 (7.1)	
Great vessel/dissection	9 (9.3)	5 (6)	4 (28.6)	
Others, *n* (ratio)	5 (5.2)	3 (3.6)	2 (14.3)	
Priority of surgery, *n* (ratio)				
Elective	36 (37.1)	33 (39.8)	3 (21.4)	0.09
Urgency	46 (47.4)	39 (47)	7 (50)	
Emergency	15 (15.5)	11 (13.3)	4 (28.6)	
CPB time (*n*=96), median (IQR)	139 (120-175)	137 (121-163)	219 (118-310)	0.025
Cross-clamp time (*n*=94), median (IQR)	82 (66-103)	78 (65-100)	91 (70-190)	0.093
Lactate before operation, median (IQR)	0.9 (0.6-1.6)	0.9 (0.6-1.5)	0.9 (0.7-1.8)	0.54
Peak lactate during operation, median (IQR)	4.2 (3.1-6.0)	4.2 (2.9-5.6)	7.6 (3.6-11.1)	0.003

*Comparison between survivors and nonsurvivors. CABG: Coronary artery bypass grafting, CPB: Cardiopulmonary bypass, IQR: Interquartile ranges

Table 3: Primary and secondary outcomes

	All patients (*n*=97), *n* (%)	Survivors (*n*=83), *n* (%)	Nonsurvivors (*n*=14), *n* (%)	*P**
In-hospital mortality, *n* (ratio)	14 (14.4)	-	-	
Length of hospital stay, median (IQR)	19 (13-29)	20 (14-31)	9.5 (3-16)	0.001
Length of ICU stay, median (IQR)	5 (4-7.5)	5 (4-7)	3 (2-9)	0.206
Complications				
Low cardiac output	12 (12.3)	4 (4.8)	8 (57.0)	0.000
ECMO	6 (6.2)	2 (2.4)	4 (28.6)	0.000
IABP	10 (10.3)	5 (6)	5 (35.7)	0.001
AKI requiring dialysis	24 (24.7)	11 (13.3)	13 (92.9)	0.000
ARDS	3 (3.1)	0 (0)	3 (21.4)	0.000
Rebleeding	9 (9.3)	6 (7.2)	3 (21.4)	0.092
Liver failure, *n* (ratio)	8 (8.2)	1 (1.2)	7 (50)	0.000

*Comparison between survivors and nonsurvivors. ECMO: Extracorporeal membrane oxygenation, IABP: Intra-aortic balloon pump, AKI: Acute kidney injury, ARDS: Acute respiratory distress syndrome, ICU: Intensive care unit

Table 4: Predictive factors for in-hospital mortality by logistic regression model

	Univariate		Multivariate	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	1.1 (1.0-1.1)	0.02	1.2 (1.0-1.3)	0.017
EuroSCORE II	1.0 (0.98-1.1)	0.21	-	
Surgical type				
CABG	Reference	-	Reference	-
Valve surgery	1.5 (0.3-7.2)	0.61	0.6 (0.1-6.3)	0.68
CABG + valve	4.0 (0.3-47.9)	0.27	2.4 (0.1-70.4)	0.61
Dissection	9.6 (1.8-50.7)	0.008	0.8 (0.0-25.8)	0.88
Others	8.0 (1.0-62.7)	0.05	12.8 (0.6-267.6)	0.10
CPB time	1.011 (1.004-1.018)	0.002	1.0 (1.0-1.0)	0.36
Peak lactate	1.5 (1.2-1.8)	0.000	1.6 (1.1-2.4)	0.027

EuroSCORE II: European system for cardiac operative risk evaluation II, CABG: Coronary artery bypass grafting, CPB: Cardiopulmonary bypass, OR: Odds ratio, CI: Confidence interval

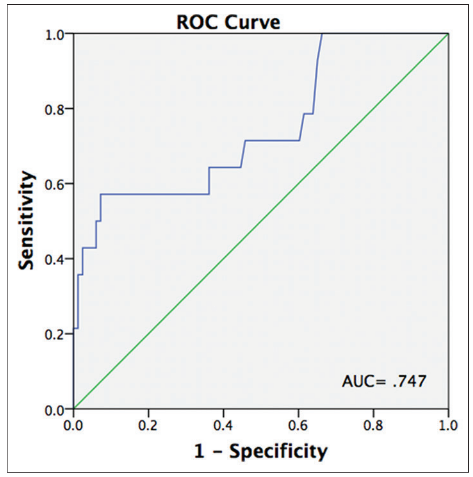

Figure 1: Receiver operating characteristics curve presents the ability of peak lactate level during cardiopulmonary bypass in predicting in-hospital mortality after cardiac operations. When the cut-off value was 7.25 mmol/L, a sensitivity of 57.1% and a specificity of 92.8% were obtained. AUC: Area under the curve; CI: Confidence interval

Discussion

The duration of CPB was significantly associated with increased morbidity. Several risk factors associated with worse outcomes after cardiac operation were identified, which included increased age, lower LVEF, higher EuroSCORE score, emergent surgery, elevated preoperative serum creatinine level, and combined cardiac procedures [11-13]. However, the perioperative events regarding surgical technique, myocardial protection, and CPB were less discussed. In this study, only age and peak lactate level predicted in-hospital mortality in adults who underwent cardiac surgery. Based on a literature review, age is considered a primary factor in most outcome-based studies. In this study, peak lactate level had a higher impact on postoperative outcome; thus, we further highlighted the importance of serum lactate level during CPB.

The mechanisms underlying hyperlactatemia were increased production and decreased clearance of lactate [14]. Tissue hypoperfusion, the release of catecholamine from gluconeogenesis and glycolysis, systemic inflammation reaction, and lactate load from blood transfusion all contributed to lactate production. Hypothermia attenuated pyruvate metabolism, the variable hepatic or renal function, and anesthetics also affected lactate clearance [15]. It is reasonable that the sum of lactate production and clearance indicates an outcome parameter of CPB.

Demers *et al*. have recognized that a peak blood lactate level higher than 4.0 mmol/L during CPB was strongly associated with postoperative mortality and morbidities, including systemic organ dysfunction and longer length of ICU and hospital stay [10]. In their study, patients with preoperative lactate level higher than 2.5 mmol/L were excluded, and the surgical procedures were mainly elective operation, including CABG (79.2%) and valve surgery (16.9%). We included all cardiac operations with CPB, which made the result more applicable to real-world practice. Using peak lactate level during surgery had a significant benefit in predicting in-hospital mortality using an AUC of 0.75. The cutoff value for peak lactate level during CPB in predicting in-hospital mortality was 7.25 mmol/L, with a sensitivity of 57% and specificity of 93%. From a clinical viewpoint, to prevent in-hospital mortality, patients whose peak lactate level is higher than 7.25 mmol/L during CPB require aggressive treatment. The cutoff values for peak lactate level obtained in this study are valuable to surgeons, anesthesiologists, and perfusionists for the reassessment of the quality of surgery, adequacy of hemodynamic status, and prevention of organ dysfunction.

Maintaining sufficient oxygen delivery is the critical determinant to satisfy metabolic needs during CPB [16]. We followed the policy of goal-directed perfusion to maintain adequate tissue perfusion during CPB. Potential interventions that optimize tissue perfusion include manipulation of perfusion pressure and flow rates, duration of hypothermia, and ultrafiltration during rewarming. When the oxygen delivery (DO_2) was <260 mL/min/m^2, an increase in lactate level was noted [7]. Goal-directed perfusion was achieved by augmenting pump flow (target DO_2: 270 mL/min/m^2), increasing hemoglobin level, decreasing temperature, and correcting base deficit. The protocol of goal-directed perfusion was followed in each patient. Unfortunately, to date, intraoperative inotropic agents, anesthesia adjustments, ventilator settings, and corresponding CPB flow are limited, which may also result in bias.

Furthermore, serum lactate clearance is valuable in patients with hyperlactatemia during CPB. The change in lactate level after weaning from CPB in the operation room was also associated with the duration of ICU stay and severe adverse events [17]. Hajjar *et al*. have measured lactate level 6 h after admission to the ICU and found that increased lactate level is an independent risk factor of worse outcomes [18]. Increased intraoperative peak lactate level and failed clearance of lactate could be important signs that intensive postoperative care is required. Monitoring lactate level in the ICU at least 6–12 h could be a cause of concern in patient care; currently, it became our routine in ICU care. Although our protocol for lactate measurement may differ from that of other hospitals, the peak lactate level during CPB is still relevant and valuable.

The current study had several limitations. It had potential systemic bias because it is a retrospective single-center study with a small sample size. The median EuroSCORE II score in predicting 30-day mortality after surgery was 2.2%. However, the actual mean in-hospital mortality reached 14.4%, which could be partly explained by the small population in our study. Any events could be over-emphasized. In addition, the underestimation of the risk of in-hospital mortality using the Euroscore II in high-risk patients was mentioned in the literature [19]. A higher mortality after surgery in an emergent aortic dissection cohort could not be identified based on the EuroSCORE II score.

Conclusion

Hyperlactatemia during CPB was associated with postoperative morbidity and mortality. In our study, the use of peak lactate level during CPB in predicting in-hospital mortality would be a cause of concern regarding aggressive intervention in adults undergoing cardiac surgery. Further studies about postoperative lactate clearance and treatment outcomes must be conducted.

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Conflicts of interest

There are no conflicts of interest.

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Appendix

Appendix Table 1: Differences of demographic data between patients with peak lactate level ≥7.25 and <7.25 (mmol/L)

	All patients (*n*=97), *n* (%)	Peak lactate ≥7.25 (*n*=14), *n* (%)	Peak lactate <7.25 (*n*=83), *n* (%)	*P**
Gender				
Male/female, *n* (ratio)	64/33 (66/34)	9/5 (64/36)	55/28 (66/34)	0.887
Age, median (IQR)	64 (55-74)	65 (58-71)	63 (55-75)	0.745
BMI, median (IQR)	25.1 (23-28.5)	24.4 (23.4-27.0)	25.2 (22.8-29.0)	0.714
Prior cardiac operation, *n* (ratio)	10 (10.3)	2 (14.3)	8 (9.6)	0.601
LVEF (%), median (IQR)	66 (54-74)	56 (41-77)	66 (55-74)	0.294
EuroSCORE II, median (IQR)	2.3 (1.3-4.7)	6.3 (2.9-12.5)	1.9 (1.3-3.9)	0.159
Co-morbidity, *n* (ratio)				
DM	39 (40.2)	4 (29)	35 (42.2)	0.333
HTN	67 (69.1)	10 (71)	57 (68.7)	0.839
Cirrhosis	2 (2.1)	0 (0)	2 (2.4)	0.562
ESRD	4 (4.1)	0 (0)	4 (4.8)	0.407
Old CVA	6 (6.2)	1 (7)	5 (6)	0.874
Preoperation hematocrit, median (IQR)	36 (30.8-41.1)	35.4 (31.5-40.0)	36.2 (30.8-41.8)	0.942
Preoperation creatinine, median (IQR)	1.1 (0.8-1.5)	1.3 (1.0-2.1)	1.1 (0.8-1.5)	0.743

*Comparison between patients with peak lactate level ≥ 7.25 and < 7.25 mmol/L. LVEF: Left ventricular ejection fraction, EuroSCORE II: European system for cardiac operative risk evaluation II, DM: Diabetes mellitus, HTN: Hypertension, ESRD: End-stage renal disease, CVA: Cardiovascular accident, BMI: Body mass index, IQR: Interquartile ranges

Appendix Table 2: Difference of intraoperative parameters between patients with peak lactate level ≥7.25 and <7.25 (mmol/L)

	All patients (*n*=97), *n* (%)	Peak lactate ≥7.25 (*n*=14), *n* (%)	Peak lactate <7.25 (*n*=83) , *n* (%)	*P**
Surgical type, *n* (ratio)				0.000
CABG	52 (53.6)	2 (14.3)	50 (60.2)	
Valve surgery	27 (27.8)	2 (14.3)	25 (30.1)	
CABG + valve	4 (4.1)	2 (14.3)	2 (2.4)	
Great vessel/dissection	9 (9.3)	7 (50.0)	2 (2.4)	
Others	5 (5.2)	1 (7.1)	4 (4.8)	
Priority of surgery, *n* (ratio)				0.011
Elective	36 (37.1)	4 (28.6)	32 (38.6)	
Urgency	46 (47.4)	3 (21.4)	43 (51.8)	
Emergency	15 (15.5)	7 (50.0)	8 (9.6)	
CPB time (*n*=96), median (IQR)	139 (120-175)	230 (175-356)	131 (119-156)	0.003
Cross-clamp time (*n*=94), median (IQR)	82 (66-103)	112 (84-232)	77 (65-97)	0.032
Lactate before operation, median (IQR)	0.9 (0.6-1.6)	1.8 (0.9-3.3)	0.9 (0.6-1.3)	0.062
Peak lactate during operation, median (IQR)	4.2 (3.1-6.0)	9.3 (8.1-12.5)	4.1 (2.9-5.0)	0.000

*Comparison between patients with peak lactate level ≥ 7.25 and < 7.25 mmol/L. CABG: Coronary artery bypass grafting, CPB: Cardiopulmonary bypass, IQR: Interquartile ranges

Appendix Table 3: Differences of outcomes between patients with peak lactate level ≥7.25 and <7.25 (mmol/L)

	All patients (*n*=97), *n* (%)	Peak lactate ≥7.25 (*n*=14), *n* (%)	Peak lactate <7.25 (*n*=83), *n* (%)	*P**
In-hospital mortality, *n* (ratio)	14 (14.4)	8 (57)	6 (7.2)	0.003
Length of hospital stay, median (IQR)	19 (13-29)	15 (3-35)	19 (14-27)	0.702
Length of ICU stay, median (IQR)	5 (4-7.5)	8 (3-13)	5 (4-7)	0.174
Complications				
Low cardiac output	12 (12.3)	5 (35.7)	7 (8.4)	0.066
ECMO	6 (6.2)	4 (28.6)	2 (2.4)	0.058
IABP	10 (10.3)	2 (14.3)	8 (9.6)	0.601
AKI requiring dialysis	24 (24.7)	9 (64.3)	15 (18.1)	0.004
ARDS	3 (3.1)	2 (14.3)	1 (1.2)	0.203
Rebleeding	9 (9.3)	4 (28.6)	5 (6.0)	0.100
Liver failure, *n* (ratio)	8 (8.2)	3 (21.4)	5 (6.0)	0.208

*Comparison between patients with peak lactate level ≥ 7.25 and < 7.25 mmol/L. ECMO: Extracorporeal membrane oxygenation, IABP: Intra-aortic balloon pump, AKI: Acute kidney injury, ARDS: Acute respiratory distress syndrome, IQR: Interquartile ranges, ICU: Intensive care unit