Cardiovascular Topics

Effect of lactate levels on extubation time in coronary artery bypass grafting surgery

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Abstract

Aim: In current practice, fast-track protocols are gaining importance in patients undergoing cardiac surgery. For this purpose, besides different application techniques, biomarkers are frequently examined in the peri-operative period. We aimed to examine whether serum lactate levels at different peri-operative intervals had an effect on the extubation time.

Methods: The patients were analysed in two groups according to the extubation time (early < 6 hours, and late extubation > 6 hours). Individual characteristics, co-existing diseases, blood transfusion, inotropic support, intra-aortic balloon pump, cardiopulmonary bypass time, aortic cross-clamp time, and the serial measurements of serum lactate levels were recorded. Correlations of serial measurements of lactate levels and the peri-operative variables with extubation times were analysed.

Results: No significant differences were observed between the groups in terms of co-existing diseases and individual characteristics. However, cardiopulmonary bypass, aortic cross-clamp times and all lactate levels after aortic cross-clamping were found to be significantly different ($p = 0.001$). A statistically significant correlation was found between the cut-off value of 1.7 for serum lactate levels after aortic-cross clamping (L2); 1.9 for levels after aortic cross-clamp removal (L3); 2.2 for levels after cardiopumonary bypass (L4); 2.1 for levels after intensive care admission (L5); 1.7 for levels after first postoperative hour in the intensive care unit (L6), and 1.8 for the difference between pre-operative levels (L0) and the peak level of lactate in the peri-operative period (ΔL) in predicting extubation time ($p < 0.01$).

Conclusion: We concluded that cardiopulmonary bypass and aortic cross-clamp times, and intra-operative serum lactate levels were important in predicting early extubation after isolated coronary artery bypass graft surgery.

Keywords: cardiac surgery, lactate, early extubation

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Cardiac surgery practices have changed and developed over time. Studies have been conducted to reduce the extubation time by abandoning high-dose and opioid-based anaesthesia, which is performed to suppress the stress response to surgery and to provide haemodynamic stability.[1] In a study conducted with the 'fast-track protocol' in the 1990s, the extubation time was reduced from 22.1 to 15.4 hours.[2] Over time, the traditional or late extubation practice has moved toward early extubation. There have even been studies on ultra-fast-track protocols (in the operating room or within one hour).[3]

In cardiac surgery, early extubation causes a significant reduction in length of mechanical ventilation and intensive care unit (ICU) and hospital stay.[4] Also, Camp *et al.*[5] showed in a study of 2 211 patients that early extubation was associated with a reduction in cases of pneumonia and sepsis, length of stay in ICU/hospital, and re-intubation time. Borracci *et al.*[6] stated that early extubation did not adversely affect clinical results in patients over 70 years of age and at low to intermediate risk. However, Richey *et al.*[7] suggested that the early extubation protocol shortens the ventilation time, but prolongs the length of stay in the ICU. However, many studies have been conducted to examine possible factors to determine early extubation criteria.[8-10]

In current practice, techniques or protocols that shorten the duration of surgical and interventional procedures and therefore reduce the length of ICU/hospital stay and thus cost, are gaining importance. In this sense, biomarkers, especially those that can be studied routinely, constitute a serious field of study. Therefore, in our study, we determined whether lactate levels obtained by arterial blood gas analysis at different peri-operative times would predict extubation time.

Methods

After the approval of the local ethics committee (decision no: 2019/0325, date: 28/08/2019), we reviewed the files of patients who had undergone open-heart surgery between January and December 2018 at our hospital. Patients older than 18 years who had undergone isolated coronary artery surgery were included in the study. Patients who had undergone isolated valve surgery or concomitant valve surgery with coronary artery surgery and vessel surgery were excluded. Additionally, emergency surgeries, off-pump coronary artery surgery, and patients who had died were not included. At the same time, patients who developed postoperative complications (cardiac output, severe anaemia, mesenteric ischaemia, septic shock, renal failure and pancreatitis), which could have caused an increase in lactate level were also excluded.

Age, gender, body mass index (BMI), ejection fraction (EF, %), pre-operative haemoglobin (Hb) value, and the number of vessels intervened in were recorded manually from the patient files or from the electronic system. In addition, data on co-existing diseases, such as diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD) and atrial fibrillation (AF); whether blood transfusion, inotropic support and intra-aortic balloon pump (IABP) were applied; and intra-operative variables, such as cardiopulmonary bypass time (CPBT) and aortic cross-clamp time (ACCT), were recorded.

The serum lactate levels at seven different times were recorded: pre-operative (L0), at the start of CPB (L1), after aortic-cross clamping (L2), after aortic cross-clamp removal (L3), after CPB (L4), at ICU admission (L5), and postoperative first hour in ICU (L6). The difference between L0 and the peak level of lactate in the peri-operative period was indicated as ΔL.

After the patients were taken to the operating room and monitored, anaesthesia induction was performed with intravenous fentanyl (1–5 µ/kg), midazolam (0.5 mg/kg), propofol (1–1.5 mg/kg), and rocuronium (0.6 mg/kg), according to haemodynamic stability. Anaesthesia was then maintained with an inhalation anaesthetic (sevoflurane, at one minimum alveolar concentration), and infusion of remifentanil (0.25 µ/kg/min). Muscle relaxation was provided with rocuronium (0.2 mg/kg) at intervals of 20–25 minutes.

Surgical procedures were started with a median sternotomy. CPB was used for all isolated coronary artery bypass grafts (CABGs). During CPB, moderate systemic hypothermia was applied. During CPB, the flow rate was maintained between 2.2 and 2.5 l/min/m^2, a perfusion pressure of 50–80 mmHg, and haematocrit between 20 and 25%.

Following the surgery, the patient was extubated, determined by decisions based on clinical appearance, laboratory tests and lung imaging. Clinically, patients had to be awake and they had to be haemodynamically stabilised, moving the limbs, and without excessive bleeding (< 50 ml/h) or neurological deficit. Pneumothorax, atelectasis and severe pleural effusion should be excluded on the chest X-ray. Arterial blood gas analysis should show pH > 7.35, PaO_2 > 70 mmHg and $PaCO_2$ < 40 mmHg.

Table 1. Comparison of individual features, co-existing diseases and peri-operative data

	Extubation time		
Variables	*< 6 hours (n = 129)*	*≥ 6 hours (n = 78)*	*p-value*
Gender: M/F, *n*	107/22	63/15	0.711[a]
Age, mean ± SD	58.81 ± 10.32	60.91 ± 10.64	0.211[c]
BMI, mean ± SD	28.70 ± 4.92	28.66 ± 4.52	0.948[d]
Vessels, *n* (%)	6 (4.7)	2 (2.6)	0.537[b]
1	55 (42.6)	27 (34.6)	
2	45 (34.9)	31 (39.7)	
3	23 (17.8)	18 (23.1)	
4	50.23 ± 9.52	48.21 ± 9.36	0.114[c]
ACCT, mean ± SD	59.11 ± 22.04	70.68 ± 24.88	0.001[c]*
CPBT, mean ± SD	96.57 ± 32.15	115.62 ± 31.23	0.001[c]*
Pre-operative Hb, mean ± SD	13.25 ± 1.76	13.53 ± 1.53	0.232[c]
DM, *n* (%)	39 (30.2)	18 (23.1)	0.264[a]
HT, *n* (%)	55 (42.6)	36 (46.2)	0.621[a]
COPD, *n* (%)	16 (12.4)	5 (6.4)	0.166[a]
Heart failure, *n* (%)	19 (14.7)	11 (14.1)	0.901[a]
Inotropes, *n* (%)	33 (25.6)	24 (30.8)	0.418[a]
IABP, *n* (%)	18 (14)	13 (16.7)	0.596[a]
AF, *n* (%)	20 (15.5)	9 (11.5)	0.426[a]
Blood transfusion, *n* (%)	75 (58.1)	39 (50)	0.264[a]

[a]Pearson's chi-squared test, [b]Fisher–Freeman–Halton test, [c]Mann–Whitney *U*-test, [d]Student's *t*-test, *$p < 0.01$.
BMI: body mass index, Hb: haemoglobin, DM: diabetes mellitus, HT: hypertension, COPD: chronic obstructive pulmonary disease, IABP: intra-aortic ballon pump, AF: atrial fibrillation, ACCT: aortic cross-clamping time, CPBT: cardiopulmonary bypass time.

Statistical analysis

The Number Cruncher Statistical System (NCSS) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum and maximum) were used for evaluating the study data. The conformity of the quantitative data to the normal distribution was tested with the Shapiro–Wilk test and graphical examinations. The independent groups *t*-test was used for comparison of normally distributed quantitative variables between two groups, and the Mann–Whitney *U*-test was used for comparisons between two groups of non-normally distributed quantitative variables. Pearson's chi-squared test and the Fisher–Freeman–Halton exact test were used to compare qualitative data. Diagnostic screening tests (sensitivity, specificity, positive and negative predictive values) and receiver operating characteristic (ROC) curve analysis were used to determine the cut-off value for the parameters. Statistical significance was accepted as $p < 0.05$.

Results

Data from 207 patients who underwent isolated CABG were obtained after excluding those who had had emergency and valve surgery as seen from scanning the files. There were 170 (82.1%) males and 37 (17.9%) females. The patients' mean age was 59.60 ± 10.46 years and the mean BMI was 28.68 ± 4.76 kg/m^2. The extubation time of most of the cases (62.3%, $n = 129$) was less than six hours.

There were no statistically significant differences between the subjects' gender, age, BMI, the number of vessels worked on, EF, incidence of AF, DM, HT, COPD and heart failure (HF),

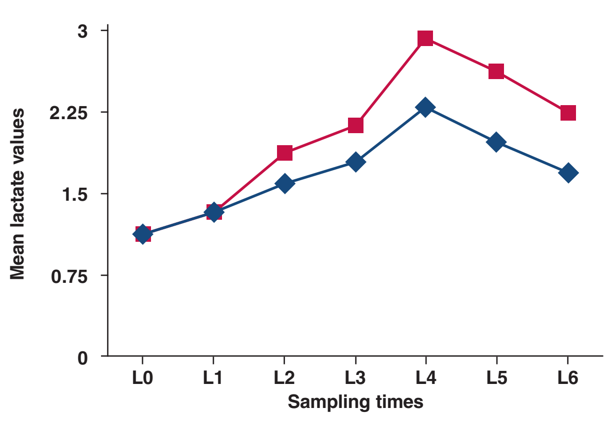

Fig. 1. Distribution of lactate measurements. Red line: extubation time ≥ 6 hours; blue line: extubation time < 6 hours.

Table 2. Comparison of serum lactate levels, mmol/l

Sampling times	Extubation time < 6 hours (n = 129)	≥ 6 hours (n = 78)	p-value
L0, mean ± SD	1.11 ± 0.32	1.12 ± 0.28	0.798[d]
median (min–max)	1.1 (0.5–1.9)	1.2 (0.6–1.7)	
L1, mean ± SD	1.32 ± 0.34	1.33 ± 0.39	0.830[c]
median (min–max)	1.3 (0.5–2.1)	1.3 (0.7–3)	
L2, mean ± SD	1.58 ± 0.53	1.87 ± 0.75	0.001[c]*
median (min–max)	1.5 (0.6–4.5)	1.9 (0.9–5.6)	
L3, mean ± SD	1.78 ± 0.55	2.11 ± 0.78	0.001[c]*
median (min–max)	1.7 (0.7–3.6)	2 (0.7–5.3)	
L4, mean ± SD	2.28 ± 0.74	2.91 ± 1.14	0.001[c]*
median (min–max)	2.1 (0.9–4.8)	2.6 (1.2–6.2)	
L5, mean ± SD	1.96 ± 0.87	2.61 ± 1.37	0.001[c]*
median (min–max)	1.7 (0.8–5.2)	2.3 (0.9–6.5)	
L6, mean ± SD	1.67 ± 0.74	2.23 ± 1.10	0.001[c]*
median (min–max)	1.5 (0.8–4.1)	2.2 (0.8–6.6)	
ΔL, mean ± SD	1.37 ± 0.69	2.39 ± 1.29	0.001[c]*
median (min–max)	1.2 (0.3–3.7)	2.2 (0.4–5.6)	

[c]Mann–Whitney *U*-test, [d]Student's *t*-test, *$p < 0.01$.

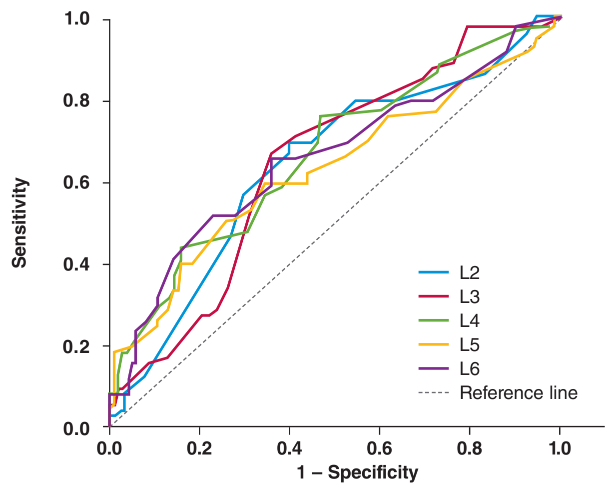

Fig. 2. ROC curve for lactate levels.

use of inotropic drugs or IABP, and blood transfusion status according to extubation times ($p > 0.05$) (Table 1). However, it was observed that ACCT, CPBT and ΔL values were significantly different between the two groups ($p = 0.001$; $p < 0.01$), but pre-operative Hb values did not differ ($p > 0.05$) (Table 1).

The distribution of peri-operative serum lactate levels is presented in Fig. 1. Mean lactate levels were observed to peak in L4. The lactate values of L2, L3, L4, L5 and L6 were found to be statistically significantly higher in cases where extubation time was longer than six hours ($p = 0.001$; $p < 0.01$). However, L0 and L1 lactate values did not differ significantly ($p > 0.05$) (Table 2).

In predicting extubation time, a statistically significant correlation was found between the cut-off value of 1.7 for L2; 1.9 for L3; 2.2 for L4; 2.1 for L5; 1.7 for L6 and 1.8 for ΔL ($p < 0.01$) (Table 3). ROC curve graphs of lactate levels and ΔL values are presented in Figs 2 and 3. The area under the curve of ΔL levels was more acceptable than the others (0.742).

Discussion

In this research, we examined the distribution of serum lactate levels in samples taken at different peri-operative times and their relationship with early extubation in patients undergoing isolated CABG surgery. It was observed that serum lactate levels reached peak levels after the ACC was removed. We concluded that lactate values from the onset of CPB to the postoperative period, as well as the difference between pre-operative and maximum lactate values (ΔL), measured in the peri-operative period, were high in late-extubated patients. However, among the variables we examined, only the duration of CPB and ACCT was longer in patients who were extubated late.

Mechanical ventilation duration exceeding 24 hours after cardiac surgery is defined as prolonged ventilation and is seen in approximately 10% of patients.[11,12] Prolonged mechanical ventilation increases the length of stay in the ICU and the cost of treatment. Therefore, prolonged mechanical ventilation is considered to be as serious a complication as stroke and acute renal failure.[13]

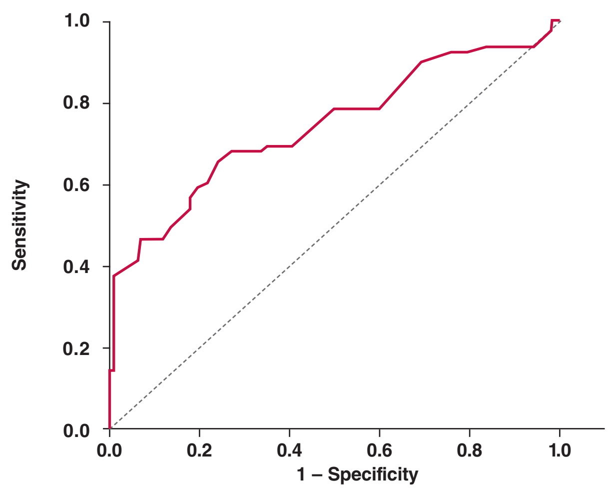

Fig. 3. ROC curve for ΔL.

Table 3. Diagnostic scans and ROC curve analyses for lactate levels in predicting extubation time

	Diagnostic scan					ROC curve		
Sampling times	Cut-off value	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area	95% CI	p-value
L2	≥ 1.7	69.23	60.47	51.40	76.50	0.641	0.563–0.720	0.001*
L3	≥ 1.9	66.67	64.34	53.10	76.10	0.648	0.572–0.724	0.001*
L4	≥ 2.2	75.64	53.49	49.60	78.40	0.667	0.590–0.743	0.001*
L5	≥ 2.1	58.97	65.89	51.10	72.60	0.629	0.547–0.711	0.002*
L6	≥ 1.7	58.97	64.34	50.00	72.20	0.657	0.578–0.737	0.001*
ΔL	≥ 1.8	65.38	75.97	62.20	78.40	0.742	0.668–0.816	0.001*

The negative outcomes of prolonged ventilation increase the need for early extubation protocols. Studies have shown that early extubation does not increase postoperative morbidity and mortality rates, even in high-risk patients.[14] In addition, early extubation did not increase the risk of postoperative re-intubation.[15] However, Richey *et al.*[7] observed that the early extubation protocol shortened the ventilation time in cardiac surgery, but extended the length of stay in the ICU. In this study, the length of hospital stay did not affect other primary and secondary outcomes, such as 30-day mortality rate, and incidence of re-intubation, postoperative stroke and renal failure. However, in this study, an early extubation protocol did not significantly reduce the rate of patients extubated after 12 hours.

In current studies, the variables affecting early extubation have been examined and various findings have been obtained. Nguyen *et al.*[8] stated that male patients and those who had isolated valve surgery with a BMI > 30 kg/m^2 could be extubated earlier. Aksoy *et al.*[10] observed that the duration of ventilation was prolonged in female patients with long CPB duration and high leukocyte and lactate values. Although the female gender was observed as a risk factor in both studies, the findings obtained in terms of age and BMI are inconsistent.

In another study examining risk factors, age, BMI, COPD, DM, albumin level, isolated aortic valve replacement, and multiple surgeries affected extubation time.[9] In this study, Subramaniam *et al.*,[9] contrary to Nguyen *et al.*,[8] stated that female gender was not a risk factor. Additionally, an increase in BMI (> 30 kg/m^2) facilitated early extubation for Nguyen *et al.*,[8] while Subramaniam *et al.*[9] argued that an increase in BMI made early extubation difficult.

In our study, age, gender, BMI and presence of co-morbidities did not differ between the groups. Among the intra-operative variables, as in the study by Aksoy *et al.*,[10] we observed longer CPB duration in those who were extubated late. Another similarity is that Aksoy *et al.*[10] showed that increased lactate levels cause delayed extubation. However, these researchers did not specify the lactate sampling times. In our study, a significant increase was observed in all serial serum lactate measurements (except L0 and L1) of patients who were extubated late.

Studies have shown that serum lactate levels are an independent risk factor in predicting morbidity and mortality in cardiac surgery. Hajjar *et al.*[16] concluded that 10% of the patients they examined developed major complications and that lactate, age and left ventricular ejection fraction < 40% were the main predictors. Similarly, Duval *et al.*[17] observed that an increase in intra-operative lactate level was important for determining morbidity. However, they concluded that only difference in lactate level (ΔL) > 1 mmol/l for 30-day mortality was an independent factor.

Reviewing 779 elective cardiac surgeries, Govender *et al.*[18] showed that increased intra-operative lactate level was associated with mortality, ICU length of stay, and the risk of developing postoperative renal failure. Michaud *et al.*[13] reported that a serum lactate level of > 4 mmol/l at admission to the ICU prolonged the mechanical ventilation time.

The increase in lactate levels during cardiac surgery has been associated with various factors. In a retrospective study of 917 patients who had undergone mitral valve surgery, Evans *et al.*[19] determined that factors that increased the lactate level at admission to the ICU were gender (male patient), long duration of CPB and blood transfusion. However, in patients with a successful fast-track management protocol, lactate levels were observed to decrease significantly at admission to the recovery unit.[20] In the same study, the baseline excess simultaneously decreased significantly.

In our study, the serum lactate levels increased significantly less in patients who were extubated early. Prolongation of CPB duration and ACCT were the main reasons for the increase in serum lactate levels in both groups. However, we observed that lactate levels were at lower threshold values, such as 1.7–2.2 mmol/l in patients with a long intubation time, unlike in the study by Michaud *et al.*[13]

Limitations

Our research has several limitations. First, our research was designed retrospectively. Second, only patients who had undergone isolated CABG surgery were included in the study. Third, the study period covered patients for one year. The last limitation was that pre- and post-extubation blood gas analysis was not included. The main reason for this was the difficulty in standardisation of timing of samples taken before and after extubation. These four limiting factors led to the small number of patients included in the study.

Conclusion

We conclude that intra-operative serial serum lactate levels, particularly ΔL, are important in predicting early extubation after isolated CABG surgery. Extended CPB and ACCT can prolong the mechanical ventilation time.

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