Lactate level and unplanned readmission to the surgical intensive care unit: a retrospective cohort study

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Background: This study aimed to investigate the association between lactate levels during intensive care unit (ICU) stay and unplanned ICU readmission rates within 48 and 120 h in surgical patients.

Methods: This single-center retrospective cohort study evaluated adult patients who were discharged from the ICU between January 2012 and December 2018. The association between lactate levels (initial lactate at ICU admission, peak level during ICU stay, and last level before ICU discharge) and unplanned ICU readmission was investigated using uni- and multivariable logistic regression analyses.

Results: The cohort included 3,707 patients. The unplanned ICU readmission rate within 48 and 120 h was 2.1% (n=78 patients) and 4.5% (n=166 patients), respectively. In the multivariable model, 1 mg dL^{-1} increase in the peak lactate level during ICU stay was associated with 1.1-fold increase in unplanned ICU readmission within 48 h (odds ratio: 1.10; 95% confidence interval: 1.02 to 1.2; P=0.016). In contrast, both initial and last lactate levels during ICU stay were not significantly associated. A similar trend was observed for unplanned ICU readmission within 120 h. On receiver operating characteristic analysis, the areas under the curve (AUC) of the initial, last, and peak lactate levels were 0.61, 0.53, and 0.63, respectively.

Conclusions: The peak lactate level during ICU admission is independently associated with unplanned ICU readmission within both, 48 and 120 h among surgical ICU patients. However, the lactate level has relatively poor predictive capability for unplanned ICU readmissions, and a new model is needed to predict unplanned ICU readmissions among surgical patients.

Keywords: Critical care; hyperlactatemia; intensive care units (ICU); lactate; lactic acid

Introduction

Intensive care unit (ICU) readmission after discharge is among the key markers of quality of care and outcomes in critically ill patients (1,2). In previous studies, the ICU readmission rates ranged from 1.2% to 14.5% (3-6). ICU readmission is known to be associated with increased hospitalization and mortality rates among critically ill

patients (3,4,7-10). Therefore, reducing ICU readmission rates has considerable implications with respect to the improvement of hospital outcomes, quality of care, hospital resource utilization, and cost savings in critically ill patients (11).

The serum lactate level, which was first reported by Broder and Weil *et al.* (12,13), has been widely used as an important marker, that reflects altered tissue perfusion in

critically ill patients (14). In particular, the elevation in lactate levels directly reflects tissue hypoperfusion induced by macrocirculatory or microcirculatory dysfunction (15,16), reduced oxygen delivery (17), enhanced glycolysis (18), or metabolic blocks of pyruvate dehydrogenase (19). Thus, elevated lactate levels or lactate kinetics is known to be a predictive factor for poor outcomes in critically ill patients (20). Previous studies have reported that elevated lactate levels were associated with higher mortality among surgical ICU patients (21) and neurologic ICU patients (22). Therefore, elevated lactate levels may serve as an indicator in predicting outcomes including ICU readmission among ICU patients. However, the outcome measure of these studies mostly included mortality and not ICU readmission, and thus, the association between lactate levels in the ICU and ICU readmission rates remains unclear.

Therefore, this study aimed to investigate the association between lactate levels (initial lactate at ICU admission, peak level during ICU stay, and last level before ICU discharge) and unplanned ICU readmission rates within 48 or 120 h in surgical ICU patients. We hypothesized that increased lactate levels during the ICU stay are associated with unplanned ICU readmission rates in surgical and critically ill patients.

We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/apm-20-291).

Methods

Study design and data source

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective cohort study was conducted in a single tertiary academic hospital and was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (SNUBH) (IRB approval number: B-1904/534-103). The requirement for informed consent was waived owing to the retrospective design of this study. Data were collected from the electronic medical records of Bundang Hospital Electronic System for Total Care (BESTCare) at SNUBH (23).

Study population

We evaluated adult patients (≥18 years old) who were admitted to the ICU in the surgical department and were discharged from there between January 2012 and December 2018. For multiple ICU admissions (≥2) in one patient, only the first ICU admission during the study period was included in the analysis, given that the main endpoint of this study was unplanned ICU readmission. Patients who were transferred to another hospital directly after ICU discharge and those with incomplete or missing medical records pertaining to serum lactate levels were excluded.

Measurement of lactate level

The lactate level was commonly measured using radial or femoral arterial blood in the ICU. The initial lactate level (mg dL^{-1}) was defined as the first serum lactate level measured within 6 hours after ICU admission, regardless of whether the patient was admitted to the ICU from the emergency room, general ward, or postoperatively. The last lactate level was defined as the last measurement before ICU discharge. The maximum value of the lactate level during ICU stay was defined as the peak lactate level.

Assessment of unplanned ICU readmission

Unplanned ICU readmission was defined as an unexpected second admission to the ICU, from which the patient was originally discharged during the same hospitalization. We evaluated ICU readmission within 48 and 120 h based on previous studies (5,24). We selected 48 h, as proximate readmissions may be most likely to be attributable to ICU care or triage decisions (25). In contrast, readmissions after 120 hours are more likely to be elective or caused by events occurring on the floor after discharge.

Potential covariates

Clinicodemographic data, including sex, age (years), body mass index (BMI, kg m^{-2}), socioeconomic status [e.g., type of insurance (medical aid beneficiary program or national health insurance program)], Charlson comorbidity index at ICU admission, Acute Physiology and Chronic Health Evaluation (APACHE) II score at ICU admission, characteristics of ICU stay (year of discharge, duration, ventilator care, postoperative ICU care, and admission to the cardiothoracic department), were collected. Medical aid beneficiaries include those having low incomes; the bulk of the hospital charges for these patients are paid by the government. For patients in the national health insurance

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program, the government covers approximately two-thirds of their hospital charges. The International Classification of Disease-10 (ICD-10) codes in the electronic health record system were used to calculate the Charlson comorbidity index of all patients.

Statistical analysis

Baseline characteristics have been presented as the mean value with the standard deviation (SD) for continuous variables or numbers with percentages for categorical variables. Univariable logistic regression analysis was initially conducted to investigate the individual association of all covariates with ICU readmission. Covariates with a P value of <0.2 in the univariable model were then entered into the final multivariable logistic regression model. All the results of the logistic regression model were provided as odds ratio (OR) with 95% confidence interval (CI), and the goodness of fit in each multivariable model was confirmed via the Hosmer-Lemeshow statistic test with a criterion of P>0.05. We analyzed multi-collinearity in each multivariable model with a variance inflation factor <2.0. Finally, we performed receiver operating characteristic (ROC) analysis for unplanned readmission within 48 h based on three main variables (i.e., initial lactate, last lactate, and peak lactate level during ICU stay) with two traditional scoring systems, namely, APACHE II and Charlson comorbidity index. The results of the ROC analysis were presented as the areas under the curve (AUC) with 95% CI. All analyses were performed using the R software package, version 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria), and P<0.05 was considered statistically significant.

Results

Patient characteristics

Among the 11,552 adult patients (age ≥18 years) discharged alive from the surgical ICU between January 2012 and December 2018, 7,845 were excluded due to multiple admissions (n=712), transfer to another hospital after ICU discharge (n=114), and incomplete or missing medical records of serum lactate levels at ICU admission and discharge (n=7,019). Finally, 3,707 patients were included in the analysis. The baseline patient characteristics are presented in *Table 1*. The mean (SD) initial, peak, and last lactate level (mg dL^{-1}) after ICU admission were 2.7 (5.9), 4.2 (3.4), and 1.8 (1.2), respectively. The unplanned

ICU readmission rates within 48 and 120 h were 2.1% (n=78 patients) and 4.5% (n=166 patients), respectively (*Figure 1*). The departments with the highest readmission rates were the neurosurgery department (53.6%), followed by cardiopulmonary (23.8%), general surgery (9.8%), and orthopedic surgery departments (5.6%).

Unplanned ICU readmissions and lactate level

The mean peak lactate level was 6.66 and 4.13 mg dL^{-1} in those who were and were not readmitted within 48 h, respectively, and was 5.55 and 4.11 mg dL^{-1} in those who were and were not readmitted within 120 h, respectively. The results of uni- and multivariable logistic regression analyses for unplanned ICU readmission within 48 h after ICU discharge are presented in *Table 2*. In the multivariable logistic regression model for unplanned ICU readmission within 48 h, a 1 mg dL^{-1} increase in peak lactate level during ICU stay was associated with a 1.1-fold increase in unplanned ICU readmission within 48 h (OR: 1.10; 95% CI: 1.02 to 1.2; P=0.016), but the initial and last lactate levels during ICU stay were not (P=0.336 and P=0.342, respectively). The results of uni- and multivariable logistic regression analyses for unplanned ICU readmission within 120 h after ICU discharge are presented in *Table 3*. In the multivariable logistic regression model for unplanned ICU readmission within 120 h, a 1 mg dL^{-1} increase in peak lactate level during ICU stay was associated with a 1.1-fold increase of unplanned ICU readmission within 120 h (OR: 1.10; 95% CI: 1.03 to 1.17; P=0.002). However, both initial and last lactate levels during ICU stay were not significantly associated with unplanned ICU readmission within 120 h (P=0.373 and P=0.612, respectively).

Receiver operating characteristic analysis

On ROC analysis for unplanned ICU readmissions within 48 h, the AUCs of the initial, last, and peak lactate levels during ICU stay were 0.61 (95% CI: 0.60 to 0.64), 0.53 (95% CI: 0.51 to 0.55), and 0.63 (95% CI: 0.60 to 0.65), respectively (*Table 4*). Additionally, the AUCs of the APACHE II score and Charlson comorbidity index were 0.62 (95% CI: 0.60 to 0.64) and 0.55 (95% CI: 0.53 to 0.57), respectively.

Discussion

The present study showed that in surgical ICU patients,

Table 1 Baseline characteristics of patients

Variable	Total (n=3,707), n (%)	Mean	SD
Sex: male	2,281 (61.5)		
Age, year		63.6	14.8
Body mass index, kg m^{-2}		23.9	3.7
Charlson comorbidity index		0.7	1.3
APACHE II at ICU admission		25.2	7.8
Length of ICU stay, h		83.2	456.2
Postoperative ICU admission	3,004 (81.0)		
Admission to cardiothoracic department	2,021 (54.5)		
Ventilator care	1,957 (52.8)		
Year of ICU discharge			
2012	269 (7.3)		
2013	467 (12.6)		
2014	728 (19.6)		
2015	469 (12.7)		
2016	537 (14.5)		
2017	592 (16.0)		
2018	645 (17.4)		
Initial lactate level after ICU adm, mg dL^{-1}		2.7	5.9
Peak lactate level during ICU stay, mg dL^{-1}		4.2	3.4
Last lactate level before ICU discharge, mg dL^{-1}		1.8	1.2

Presented as number (percentage) or mean value (standard deviation). SD, standard deviation; APACHE, acute physiology and chronic health evaluation; ICU, intensive care unit.
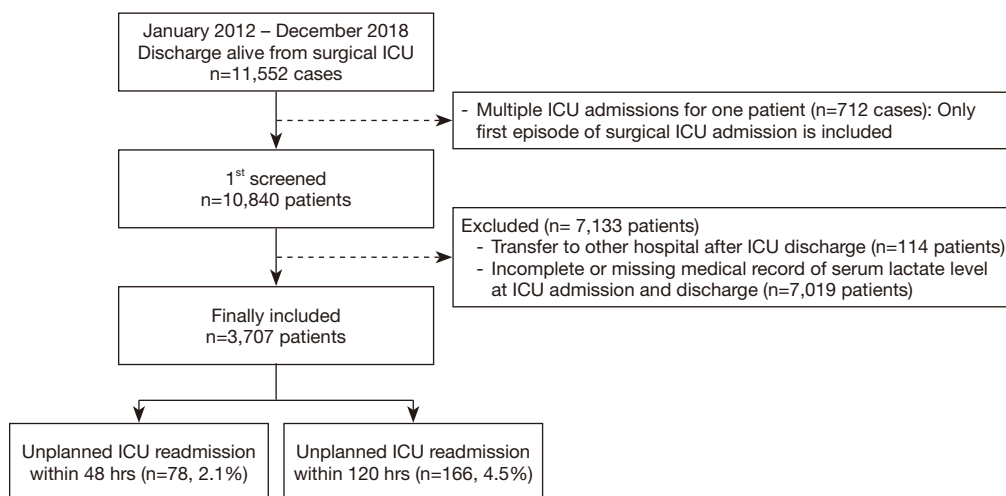

Figure 1 Patient selection flow chart.

Table 2 Uni- and multivariable logistic regression analysis for unplanned ICU readmission within 48 h after ICU discharge

Variable	Univariable model		Multivariable model	
	OR (95% CI)	P	OR (95% CI)	P
Age, year	1.02 (1.00, 1.04)	0.014	1.02 (1.00, 1.04)	0.040
Body mass index, kg m^{-2}	1.06 (1.00, 1.12)	0.061	1.06 (1.00, 1.13)	0.062
Male sex (vs. female)	0.85 (0.54, 1.34)	0.482		
Year of ICU discharge				
2012	1			
2013	1.06 (0.39, 2.89)	0.913		
2014	0.86 (0.33, 2.26)	0.759		
2015	0.96 (0.34, 2.66)	0.930		
2016	0.58 (0.19, 1.74)	0.330		
2017	0.91 (0.34, 2.44)	0.847		
2018	1.26 (0.49, 3.21)	0.630		
Duration of ICU stay, per 10 h increase	1.00 (0.99, 1.00)	0.761		
APACHE II at ICU admission, per 1 point increase	1.04 (1.01, 1.07)	0.008		
Charlson comorbidity index, per 1 point increase	1.12 (0.96, 1.30)	0.141	1.12 (0.95, 1.31)	0.181
Ventilator care during ICU stay (vs. no ventilator care)	0.37 (0.22, 0.60)	<0.001	0.27 (0.16, 0.47)	<0.001
Postoperative ICU admission	0.59 (0.36, 0.97)	0.037	0.54 (0.30, 0.97)	0.038
Admission to cardiothoracic department	1.20 (0.76, 1.90)	0.425		
Initial lactate level after ICU adm, 1 mg dL^{-1} increase	1.18 (1.11, 1.25)	<0.001	1.06 (0.95, 1.18)	0.336
Peak lactate level during ICU stay, 1 mg dL^{-1} increase	1.14 (1.09, 1.19)	<0.001	1.10 (1.02, 1.20)	0.016
Last lactate level before ICU discharge, 1 mg dL^{-1} increase	1.15 (1.01, 1.31)	0.039	1.08 (0.93, 1.25)	0.342

Covariates with P<0.2 were included in multivariable model for adjustment. Hosmer Lemeshow statistics of multivariable model: Chi-square, 10.67 (P=0.221). OR, odds ratio; CI, confidence interval; ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation.

the peak level of lactate during ICU stay was significantly associated with unplanned ICU readmission both, within 48 and 120 h, but the initial lactate level after ICU admission or last lactate level before ICU discharge was not. These results indicate that the peak lactate level during ICU admission is the most appropriate predictor of unplanned ICU readmission among surgical patients. However, our results also showed that the lactate level during ICU stay has poor predictive capability (AUC <0.7), and cannot be used alone to predict unplanned ICU readmission.

The most important finding in this study was that among the initial, peak, and last lactate levels during ICU stay, only the peak lactate level was significantly associated with unplanned ICU readmission. This finding may

reflect the characteristics of our surgical cohort. First, our cohort included 81.0% (3,004/3,707) of patients who were admitted to the surgical ICU postoperatively. A higher lactate level in the postoperative period during ICU stay could reflect postoperative complications (26,27). Further, the peak lactate level in these patients may have reflected the severity of postoperative complications. In addition, a higher peak lactate level in these patients may have also reflected surgical stress (28), which may be affected by blood loss, surgical extent, or duration of surgery. Similarly, the peak lactate level was associated with postoperative outcomes such as mortality in cardiac surgery (29) or high-risk gastrointestinal surgery (30). Therefore, it is possible that in patients postoperatively admitted to the ICU, a

Table 3 Uni- and multivariable logistic regression analysis for unplanned ICU readmission within 120 h after ICU discharge

Variable	Univariable model		Multivariable model	
	OR (95% CI)	P	OR (95% CI)	P
Age, year	1.02 (1.01, 1.03)	0.001	1.02 (1.00, 1.03)	0.011
Body mass index, kg m^{-2}	0.99 (0.95, 1.04)	0.775		
Male sex (vs. female)	1.05 (0.76, 1.45)	0.762		
Year of ICU discharge				
2012	1		1	
2013	1.78 (0.86, 3.70)	0.123	2.64 (1.17, 5.94)	0.019
2014	1.19 (0.58, 2.46)	0.637	1.98 (0.88, 4.43)	0.097
2015	0.97 (0.44, 2.16)	0.949	1.44 (0.60, 3.45)	0.413
2016	0.64 (0.28, 1.49)	0.301	0.98 (0.39, 2.46)	0.970
2017	1.24 (0.59, 2.60)	0.572	2.00 (0.87, 4.60)	0.103
2018	1.58 (0.77, 3.22)	0.211	2.59 (1.15, 5.81)	0.021
Duration of ICU stay, per 10 h increase	1.01 (1.00, 1.01)	0.441		
APACHE II at ICU admission, per 1 point increase	1.02 (1.00, 1.04)	0.151	1.02 (1.00, 1.04)	0.099
Charlson comorbidity index, per 1 point increase	1.08 (0.97, 1.21)	0.159	1.04 (0.92, 1.17)	0.535
Ventilator care during ICU stay (vs. no ventilator care)	0.42 (0.30, 0.58)	<0.001	0.34 (0.24, 0.48)	<0.001
Postoperative ICU admission	0.53 (0.37, 0.74)	<0.001	0.48 (0.33, 0.70)	<0.001
Admission to cardiothoracic department	1.09 (0.80, 1.50)	0.577		
Initial lactate level after ICU adm, 1 mg dL^{-1} increase	1.13 (1.08, 1.19)	<0.001	1.04 (0.97, 1.13)	0.373
Peak lactate level during ICU stay, 1 mg dL^{-1} increase	1.09 (1.06, 1.13)	<0.001	1.10 (1.03, 1.17)	0.002
Last lactate level before ICU discharge, 1 mg dL^{-1} increase	1.04 (0.93, 1.17)	0.481	0.97 (0.85, 1.10)	0.612

Covariates with P<0.2 were included in multivariable model for adjustment. Hosmer Lemeshow statistics: Chi-square, 10.47 (P=0.233). OR, odds ratio; CI, confidence interval; ICU, intensive care unit; APACHE, Acute Physiology and Chronic Health Evaluation.

higher peak lactate level during ICU admission could reflect both, postoperative complications and surgical stress, and this could influence unplanned ICU readmission.

However, our results showed that ICU admission in the postoperative period or mechanical ventilator use was associated with a lower rate of unplanned readmission compared with other patients in the surgical department or with no use of mechanical ventilators. This finding may have been influenced by the characteristics of the study population. Our cohort only involved patients who were discharged from the ICU to the ward and excluded those who were severely ill or needed palliative care, and not ICU management (i.e., those who died in ICU, those who were transferred to another hospital, or those who agreed to sign a do-not-resuscitate form). Therefore, the results

on postoperative ICU admission or mechanical ventilator use in the ICU need to be interpreted carefully, because these factors were not causal factors for lowering unplanned readmission rates, but reflected the characteristics of the study population

In our cohort, 19.0% (703/3,707) of the patients were not postoperatively admitted to the ICU but were rather admitted from the emergency department or ward. While many patients who undergo elective surgery are postoperatively admitted to the ICU only for continuous monitoring (31), surgical patients who are admitted to the ICU from the emergency department or ward may have more severe illnesses such as sepsis or bleeding. In these patients, the peak lactate level may reflect the disease severity, since an elevated lactate level is a useful marker

Table 4 Receiver operating characteristics analysis for unplanned readmission within 48 h according to lactate level (mg dL^{-1})

Variable	AUC (95% CI)
Initial lactate level after ICU admission	0.61 (0.60, 0.64)
Last lactate level before ICU discharge	0.53 (0.51, 0.55)
Peak lactate level during ICU stay	0.63 (0.60, 0.65)
APACHE II	0.62 (0.60, 0.64)
Charlson comorbidity index	0.55 (0.53, 0.57)

AUC, area under the curve; ROC, receiver operating characteristics; ICU, intensive care unit; CI, confidence interval; APACHE, Acute Physiology and Chronic Health Evaluation.

for the severity of acute illness in critically ill patients (32). Therefore, the peak lactate level during ICU stay in this cohort reflects not only the severity of critical illness, but also predicts unplanned ICU readmission.

A recent study by Martin *et al.* suggested that a validated clinical nomogram, which was derived from seven physiologic and demographic variables, could predict unplanned ICU readmission within 72 h among surgical patients (33). In their study, the clinical nomogram had an AUC of 0.71 for predicting unplanned ICU readmission within 72 h, which is relatively higher than that of the peak lactate level (0.63) or initial lactate level (0.61) in our study. However, the clinical nomogram was validated using seven physiologic and demographic variables (33), and we only used one variable, that is, lactate levels. Thus, if the lactate level during ICU admission is combined with other variables for developing a new model for predicting the risk of unplanned ICU admission, this model will have more predictive power. Future studies are needed to validate a new model or scoring system for predicting unplanned ICU readmission among surgical patients.

This study has some limitations. First, because this was retrospective cohort study, there were several confounders that should be controlled. Second, the generalizability of our findings may be limited, because the study was conducted in a single center. Third, many patients (7,019 patients) were excluded because their lactate level was not measured, and this could have affected the patient characteristics. For instance, relatively healthy patients whose lactate level did not need to be assessed during ICU admission may have been excluded from the final analysis. Lastly, the timing of measurement of lactate levels differed, and this could have led to bias.

In conclusion, this study showed that in surgical ICU patients, the peak lactate level during ICU admission was independently associated with unplanned ICU readmission within both, 48 and 120 h. However, the lactate level alone has relatively poor predictive capability for unplanned ICU readmission, and thus, a new model is needed.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/apm-20-291

Data Sharing Statement: Available at http://dx.doi.org/10.21037/apm-20-291

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-20-291). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This retrospective cohort study was conducted in a single tertiary academic hospital and was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (SNUBH) (IRB approval number: B-1904/534-103). The requirement for informed consent was waived owing to the retrospective design of this study.

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