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Maximum and minimum lactate levels within 24 hours after veno-arterial extracorporeal membrane oxygenation induction are risk factors for intensive care unit mortality: a retrospective observational study

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Introduction: Lactate level and clearance were hypothesized to be potential prognostic factors for mortality in patients with refractory cardiogenic shock who underwent veno-arterial (VA) extracorporeal membrane oxygenation (ECMO). This study aimed to determine the prognosis of VA-ECMO patients and whether the lactate level at intensive care unit (ICU) admission (La) and at 24 h after VA-ECMO induction (L24), minimum (L24min) or maximum (L24max) lactate level within 24 h after VA-ECMO induction, and/or maximum lactate level after ICU admission (Lmax) could predict ICU mortality in VA-ECMO patients.
Materials and Methods: This retrospective observational study included consecutive patients who underwent VA-ECMO for severe cardiogenic shock and admitted to the ICU in a hospital from April 2009 to March 2017. Risk factors for ICU mortality with respect to lactate levels after VA-ECMO induction were determined through multiple logistic regression analysis.
Results: VA-ECMO induction was performed in 67 adult patients, of whom 23 (34.3%) survived to ICU discharge. La, L24min, L24max, and Lmax were risk factors for ICU mortality in VA-ECMO patients after adjustment for the Acute Physiology and Chronic Health Evaluation II score and use of continuous renal replacement therapy and refractory ventricular arrhythmia after VA-ECMO induction, which were confounding factors in univariate analysis (La: odds ratio [OR], 1.44; 95% confidence interval [CI], 1.13-2.05; L24min: OR, 1.20; 95% CI, 1.01-2.56; L24max: OR, 1.44; 95% CI, 1.11-2.02; Lmax: OR, 1.52; 95% CI, 1.14-2.21).
Conclusion: Lactate levels can be a therapeutic target and indicator of the need for improved patient management after VA-ECMO induction.

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Key words: intensive care unit mortality, lactate level, veno-arterial extracorporeal membrane oxygenation

Introduction

According to the 2012 Extracorporeal Life Support Organization (ELSO) registry report, the use of respiratory and cardiac extracorporeal membrane oxygenation (ECMO) had dramatically increased from 1996 to 2012.[1] The H1N1 influenza pandemic in 2009 resulted in the rapid increase in the number of respiratory ECMO–supported patients worldwide. The report also indicated high survival proportions of respiratory ECMO–supported patients (neonate: 75%; pediatric: 56%; adult: 55%) but relatively low survival proportion of cardiac (neonate: 40%; pediatric: 49%; adult: 39%) and extracorporeal cardiopulmonary resuscitation (E-CPR) (neonate: 39%; pediatric: 40%; adult: 27%) patients,[1] which needs to be improved. Recent studies have reported on predictive scores for prognosticating respiratory or cardiac

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ECMO patients.[2-7] Each study's predictive score has excellent discrimination for patient mortality, with areas under the receiver operating curve (AUCs) of 0.74,[2] 0.9,[3] 0.77,[4] 0.84,[5] 0.89,[6] and 0.85.[7] These risk models include various patient backgrounds and laboratory data in the ECMO cannulation or pre-ECMO support phase, indicating that precise evaluation of patients' characteristics and general condition is required when deciding on veno-arterial (VA) ECMO induction. However, in the clinical setting, the decision to induce VA-ECMO must be quick and is usually based on insufficient patient data. In such situations, we need to evaluate the general condition of patients using laboratory data after VA-ECMO induction to improve their low survival probability. Parameters that provide the most accurate prognostic information must be determined. In E-CPR cases, the patients' circulation must be restored as rapidly as possible, and the oxygen supply should be adequate to meet the demand of ischemic tissues during severe circulatory failure. Lactate levels are generally monitored to detect tissue hypoxia and hypoperfusion in the intensive care unit (ICU). Lactate values and clearance within 24 h after medical intervention have been elucidated as powerful predictors of mortality in patients with septic shock.[8,9] Similarly, in recent years, lactate levels at a specific time, lactate clearance after VA-ECMO induction,[10] and maximum lactate level for the first 24 h during VA-ECMO support[11] in patients with refractory cardiogenic shock have been elucidated as risk factors for 30-day mortality after VA-ECMO induction. Thus, lactate levels after VA-ECMO induction appear to have a potential therapeutic target value after VA-ECMO induction; nonetheless, its clinical value has not been fully examined.

This study aimed to investigate the survival proportion of VA-ECMO–supported adult patients in our hospital and to determine whether the lactate level at admission to ICU (La) and 24 h after VA-ECMO induction (L24), the minimum (L24min) or maximum (L24max) lactate level within 24 h after VA-ECMO induction, and/or the maximum lactate level after ICU admission (Lmax) could predict ICU mortality in VA-ECMO patients.

Materials and Methods

This retrospective observational study was conducted at an eight-bed general ICU of Nagasaki University Hospital. Study approval was granted by the Ethics Committee of Nagasaki University Hospital (no. 16020814), and the requirement for acquisition of written informed consent from patients was waived owing to the retrospective nature of the study.

Consecutive adult (>18 years) patients with refractory cardiogenic shock who underwent urgent VA-ECMO in our hospital and were subsequently admitted to our ICU from April 2009 to March 2017 were included in this study. At least two physicians, including an intensive care physician, cardiovascular medicine physician, cardiothoracic surgeon, anesthesiologist, and/or emergency medical physician, were involved in the decision making for VA-ECMO induction. The indications for VA-ECMO were refractory cardiogenic shock even after volume administration, vasoconstrictor and inotropic support, sustained life-threatening ventricular arrhythmia, and cardiopulmonary arrest even after standard advanced cardiovascular life support. All patients underwent ECMO inflow circuit cannulation at the femoral artery and outflow cannulation at the femoral vein. In principle, anticoagulation was achieved with the use of unfractionated heparin, and we adjusted the heparin dose from 200 to 1200 units/h to maintain an activated clotting time of >200 s. Patients who (1) underwent VA-ECMO due to low-output syndrome after cardiac surgery, (2) received transient support during and after lung transplantation operation, (3) already underwent VA-ECMO support prior to arrival to our hospital (i.e., at another hospital), (4) were treated using a left ventricular assist device, (5) underwent surgical operation after VA-ECMO induction, (6) underwent VA-ECMO after admission to our ICU following trauma and massive bleeding, and (7) had missing demographic data were excluded from this study.

We collected patients' data from electronic medical records. Collected data included patients' demographics and Acute Physiology and Chronic Health Evaluation (APACHE) II score, length of ICU stay, duration of VA-ECMO support, success rate of ECMO weaning, use of intra-aortic balloon pumping support, use of continuous renal replacement therapy (CRRT), ICU mortality, bleeding complications after VA-ECMO induction, primary diagnosis for VA-ECMO indication, catecholamine index at VA-ECMO induction and maximum catecholamine index after VA-ECMO induction, arterial blood gas analysis, La, L24min, L24max, L24, Lmax, history of out-of-hospital cardiac arrest, and call for medical emergency team in hospital. Finally, we calculated the maximum lactate clearance within 24 h after VA-ECMO induction (L24maxC) as the difference between La and L24min or as the percent decrease in lactate from La to L24min—that is, (La – L24min)/La.

Statistical analysis

Continuous variables were expressed as median plus interquartile range (IQR), and categorical variables were ex-

pressed as frequency plus percentage. We divided the study population into two groups: survivors and nonsurvivors. In the first step of the univariate analysis, differences in each variable between survivors and nonsurvivors were statistically analyzed using Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables. In the second step, we used simple and multiple logistic regression analyses to determine which lactate levels (La, L24min, L24max, L24, or Lmax) and L24maxC are the risk factors for ICU mortality in VA-ECMO patients. For the potential confounding factors in the multiple logistic regression analyses, variables with $p<0.2$ in the univariate analysis were selected. In this study, we excluded age from potential confounders because APACHE II includes the age score. Furthermore, as there was no observation on which survivors had refractory ventricular arrhythmia after VA-ECMO induction, the estimate calculated with a general logistic regression model becomes unstable in such a case. Thus, we used Firth's modified logistic regression model.[12] Additionally, if the lactate level was statistically significant, we analyzed the receiver operating characteristic curve to determine the optimal cutoff level and calculated each AUC, sensitivity, and specificity to discriminate ICU mortality. All tests were two-sided, and $p<0.05$ was considered statistically significant. All statistical analyses were performed using JMP Pro 14 (SAS Institute Inc., Cary, NC, USA).

Results

In this study, VA-ECMO was performed on 120 adult patients, of whom 67 adult patients (44 men and 23 women) with a median age of 62 (range: 47-71) years were included in this study (Figure 1). Of these patients, 23 (34.3%) survived to ICU discharge (Table 1). Patients' survival proportion in each primary diagnosis was 63.6% for myocarditis, 61.5% for pulmonary artery embolization, 33.3% for life-threatening arrhythmia, 26.1% for cardiogenic shock due to acute coronary syndrome, and 0% for cardiac failure and pulmonary hypertension (Table 1).

In the univariate analysis, the APACHE II score, length of ICU stay (Table 1), La, L24min, L24max, L24, Lmax, use of CRRT, and frequency of refractory ventricular arrhythmia after VA-ECMO induction (Table 2) were higher in nonsur-

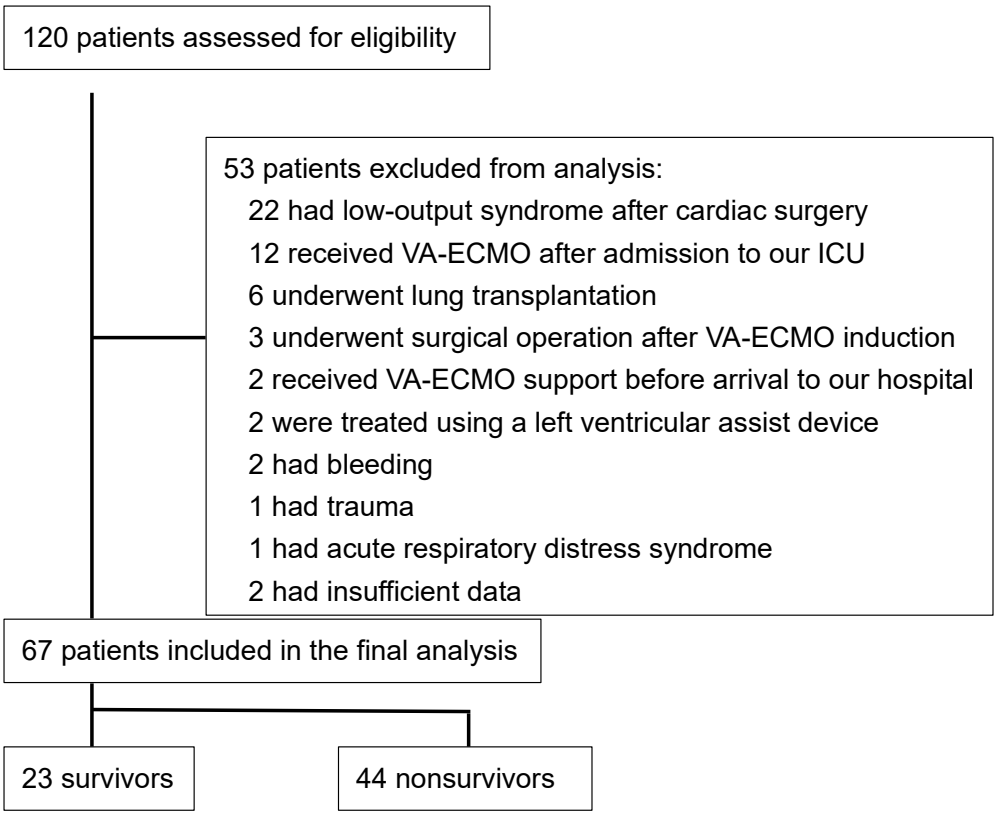

Figure 1. Study flowchart

vivors than in survivors. The proportion of successful VA-ECMO weaning was higher in survivors than in nonsurvivors (Table 2). The L24maxC (mmol/L or %) was not significantly different between survivors and nonsurvivors (Table 2). Multiple logistic regression analysis revealed that La, L24min, L24max, and Lmax were risk factors for ICU mortality in VA-ECMO–supported patients after adjustment for APACHE II score, use of CRRT, and refractory ventricular arrhythmia after VA-ECMO induction, which were determined as confounding factors in the univariate analysis. The unadjusted and adjusted odds ratios (ORs) and 95% confidence interval (CI) are presented in Table 3.

La (>5.6 mmol/L), L24min (>1.9 mmol/L), L24max (>6.5 mmol/L), and Lmax (>5.6 mmol/L) showed high discriminatory power for ICU mortality—that is, AUCs were 0.83, 0.85, 0.87, and 0.90, respectively (Table 4).

Table 1. Patient characteristics

Characteristics	**Survivors (n=23)**	**Nonsurvivors (n=44)**	**p values**
Age (years)	60 [44-66]	65 [52-72]	0.14
Body weight (kg)	57.4 [51.7-70.0]	59.0 [51.8-64.5]	0.54
Height (cm)	160.0 [155.0-173.0]	162.0 [155.8-169.6]	0.92
Body mass index (kg/m^2)	23.1 [20.7-25.5]	22.5 [20.3-23.7]	0.41
Sex (male/female)	13/10	31/13	0.29
APACHE II score	15 [12-23]	28 [21-35]	<0.0001
Length of ICU stay	11 [9-16]	6 [2-12]	0.013

Primary diagnosis	**Survivors (n=23)**	**Nonsurvivors (n=44)**	**Survival proportion (%)**
Myocarditis	7 (29.1)	4 (8.9)	63.6
Pulmonary embolization	8 (33.3)	5 (11.1)	61.5
Arrhythmia	1 (4.2)	2 (4.4)	33.3
Acute coronary syndrome	6 (25.0)	17 (37.8)	26.1
Cardiac failure	0 (0)	6 (13.3)	0
Pulmonary hypertension	0 (0)	3 (6.7)	0
Others	1 (4.1)	7 (15.6)	12.5

Data are expressed as median [interquartile range] for continuous variables and n (%, according to the survivor and nonsurvivor groups) for primary diagnosis.
Significant differences ($p<0.05$) between the two groups were analyzed using the Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables.
APACHE II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit

Table 2. Patient data after VA-ECMO induction in the univariate analysis

Characteristics	Survivors (n=23)	Nonsurvivors (n=44)	p values
Catecholamine index at VA-ECMO induction	18 [6-25]	16 [5-40]	0.62
Maximum catecholamine index after ICU admission	34 [18-48]	48 [24-60]	0.056
La (mmol/L)	2.9 [1.8-4.7]	8.7 [4.5-13.6]	0.0003
Lmax (mmol/L)	3.6 [2.2-4.8]	10.4 [6.7-17.0]	<0.0001
L24min (mmol/L)	1.0 [0.7-1.5]	2.3 [1.5-8.1]	<0.0001
L24max (mmol/L)	3.2 [1.8-4.8]	9.6 [6.6-17.0]	<0.0001
L24 (mmol/L)	1.1 [0.7-2.6]	2.9 [1.6-5.0]	0.0005
L24maxC (mmol/L)	1.7 [0.6-3.1]	3.4 [0.4-7.4]	0.19
L24maxC (%)	62.1 [37.3-74.5]	54.4 [6.1-72.5]	0.27
VA-ECMO duration (days)	4.0 [3.0-7.0]	3.5 [1.0-8.0]	0.48
VA-ECMO weaning (+/−)	23/0	18/26	<0.0001
Lower extremity ischemia (+/−)	3/20	9/35	0.45
Bleeding complication after VA-ECMO induction (+/−)	13/10	27/17	0.70
IABP (+/−)	14/9	26/18	0.89
CRRT (+/−)	3/20	18/26	0.026
Infectious complication during ICU admission (+/−)	9/14	17/27	1.00
Refractory ventricular arrhythmia after VA-ECMO induction (+/−)	0/23	9/35	0.023
Out-of-hospital cardiac arrest (+/−)	5/18	8/36	0.75
Call for medical emergency team in hospital (+/−)	3/20	11/33	0.35

Data are expressed as median [interquartile range] for continuous variables and n (%, according to the survivor and nonsurvivor groups) for categorical variables.

Significant differences ($p<0.05$) between the two groups were analyzed using Mann-Whitney U test for continuous variables and Fisher's exact test for categorical variables.

La, lactate level at ICU admission; Lmax, maximum lactate level after ICU admission; L24min, minimum lactate level within 24 h after VA-ECMO induction; L24max, maximum lactate level within 24 h after VA-ECMO induction; L24, lactate level at 24 h after VA-ECMO induction; L24maxC, maximum lactate clearance within 24 h after VA-ECMO induction; CRRT, continuous renal replacement therapy; IABP, intra-aortic balloon pumping; ICU, intensive care unit; VA-ECMO, veno-arterial extracorporeal membrane oxygenation

Table 3. Risk factors for ICU mortality in VA-ECMO patients using logistic regression analyses

Variables	Unadjusted ORs		Adjusted ORs	
	Estimate (95% CI)	p values	Estimate (95% CI)	p values
La (mmol/L)	1.49 (1.18-1.88)	0.0007	1.44 (1.13-2.05)	0.0004
Lmax (mmol/L)	1.73 (1.29-2.32)	0.0002	1.52 (1.14-2.21)	<0.0001
L24min (mmol/L)	2.31 (1.17-4.57)	0.0157	1.20 (1.01-2.56)	0.0203
L24max (mmol/L)	1.54 (1.21-1.95)	0.0003	1.44 (1.11-2.02)	0.0002
L24 (mmol/L)	1.86 (1.13-3.07)	0.0144	1.09 (0.92-2.50)	0.2407

Significant differences ($p<0.05$) between the two groups were analyzed using simple and multiple logistic regression analyses with Firth correction after adjustment for APACHE II score, CRRT, and refractory ventricular arrhythmia after VA-ECMO induction.

APACHE II, Acute Physiology and Chronic Health Evaluation II; CI, confidence interval; CRRT, continuous renal replacement therapy; OR, odds ratio; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; La, lactate level at ICU admission; Lmax, maximum lactate level after ICU admission; L24min, minimum lactate level within 24 h after VA-ECMO induction; L24max, maximum lactate level within 24 h after VA-ECMO induction; L24, lactate level at 24 h after VA-ECMO induction

Table 4. AUC for each lactate level

Variables	Cutoff values	AUC	Sensitivity (%)	Specificity (%)
La (mmol/L)	5.6	0.83	65.9	91.3
Lmax (mmol/L)	5.6	0.90	86.4	83.6
L24min (mmol/L)	1.9	0.85	65.9	91.3
L24max (mmol/L)	6.5	0.87	77.8	87.5
L24 (mmol/L)	1.2	0.79	97.0	52.6

AUC, area under the curve; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; La, lactate level at ICU admission; Lmax, maximum lactate level after ICU admission; L24min, minimum lactate level within 24 h after VA-ECMO induction; L24max, maximum lactate level within 24 h after VA-ECMO induction; L24, lactate level at 24 h after VA-ECMO induction

Discussion

Our study revealed that La, L24min, L24max, and Lmax were risk factors for ICU mortality in VA-ECMO–supported patients (Table 3). The ICU mortality in VA-ECMO–supported patients was 65.7%. Our study also showed different survival proportions (63.6% for myocarditis, 61.5% for pulmonary artery embolization, and 26.1% for cardiogenic shock due to acute coronary syndrome) (Table 1).

Recent trend in VA-ECMO–supported patients

The results were similar with the previous report that the survival proportion of cardiac ECMO–supported adult patients was different between diagnoses (66% for myocarditis, 35% for cardiogenic shock, and 46% for cardiomyopathy).[1] These results suggested that we need to be cautious with the patient's primary diagnosis when deciding for cardiac ECMO or E-CPR indication. In addition, we have to pay attention to recent trends in VA-ECMO–supported patients' characteristics. The ELSO registry data showed that the number of elderly patients aged 70 years or older who underwent VA-ECMO increased almost threefold from 2005-2010 to 2011-2015,[13] whereas the number increased twofold in younger patients. According to Salna et al.,[14] VA-ECMO patients aged 72 years or older had a 2.5-fold increased OR with respect to hospital mortality. Elderly patients had a higher rate of complications (e.g., multiple-organ failure, hyperbilirubinemia, cannula site bleeding, disseminated intravascular coagulation, renal failure) than younger patients.[13] Some of these patients' characteristics (older age) and complications (elevated bilirubin, creatinine levels) prior to VA-ECMO induction were included in predictive mortality risk models.[3-5] Another multicenter cohort study of E-CPR patients[15] showed that there was more than a tenfold increase in the number of E-CPR patients from 2003 to 2014 (35 to 400 per year). There was also a trend for increased age and chronic disease complication in these patients, and the survival proportion (28-30%) did not improve despite advances in ECMO care during the study period, suggesting that we need to consider the appropriate indication or contraindication based on precise evaluation of patients' characteristics prior to VA-ECMO induction.

Clinical value of lactate levels and lactate clearance

In the clinical setting, the decision to induce VA-ECMO must be quick and is usually based on insufficient patient data. In such situations, we need to evaluate the general condition of patients using laboratory data after VA-ECMO induction to improve their low survival probability. Lactate levels are generally monitored to detect tissue hypoxia and hypoperfusion in the ICU, and its level and clearance were reported as prognostic factors for adverse outcome and mortality in critically ill patients.[8,9,16-19] Recently, lactate values and clearance after VA-ECMO induction have been reported as prognostic factors in VA-ECMO patients. Rigamonti et al.11 showed that the peak lactate level during the first 24 h after VA-ECMO induction was a prognostic predictor of 30-day mortality (adjusted OR: 1.22; 95% CI: 1.04-1.44; p=0.016) in cardiogenic shock or cardiac arrest patients. Our study also showed that L24max (adjusted OR: 1.44; 95% CI: 1.11-2.02; p=0.0002) and L24min (adjusted OR: 1.20; 95% CI: 1.01-2.56; p=0.02) were risk factors for ICU mortality (Table 3). Notably, almost all survivors had L24min (median: 1.0 mmol/L; IQR: 0.7-1.5) in the normal physiologic range, whereas that of nonsurvivors (median: 2.3 mmol/L; IQR: 1.5-8.1) did not decrease within normal physiologic range (Table 2). Rigamonti et al.11 also showed that the minimum lactate level almost decreased within normal range (median: 1.3 mmol/L; IQR: 0.8-1.7 mmol/L) within 24 h after VA-ECMO induction in acute coronary syndrome survivors. These data suggested that the fluctuations in lactate values within 24 h after VA-ECMO induction affected their prognosis, and normalization of hyperlactatemia or lactic acidosis within 24 h after VA-ECMO induction may be the therapeutic target to improve the low survival proportion in cardiac ECMO or E-CPR cases.

A previous report[20] stated that lactate clearance (AUC: 0.66; cutoff: 68.7%; p=0.004) at 24 h after VA-ECMO induction was predictive of 30-day mortality. Nevertheless, another report[10] showed no significant difference in lactate clearance at 24 h after VA-ECMO induction between survivors and nonsurvivors. The latter study also suggested that the lactate clearance at 6 h after VA-ECMO induction was a risk factor for 30-day mortality. These study populations had quite a high mean lactate level prior to VA-ECMO induction (survivors/nonsurvivors: 12.1/11.3 mmol/L[10], 7.6/12.3 mmol/L[20]). Although we could not show data on the precise lactate level at VA-ECMO induction in our study, the mean La was 2.9 mmol/L in survivors, which was quite lower than 8.7 mmol/L in nonsurvivors. It was possible that VA-ECMO improved the lactate level in survivors more than in nonsurvivors until ICU admission after VA-ECMO induction. Assuming that this was true, the lactate clearance at an earlier phase than 24 h, such as at 6 h after VA-ECMO induction as mentioned previously,[10] could also be a powerful predictor of ICU mortality in our study. Recently, Wengenmayer et

al.[21] suggested the use of the PREDICT VA-ECMO score, a new predictive risk model for hospital mortality in cardiogenic shock patients, which included lactate value, pH, and standard bicarbonate at 1, 6, and 12 h after VA-ECMO induction. The AUC values of the 6- and 12-h PREDICT VA-ECMO score were 0.82 and 0.84, respectively, which were significantly higher than those of the APACHE II score (0.66) and Sequential Organ Failure Assessment (0.73). Li et al.[22] also showed that lactate clearance levels at 6 h (-2.64 mmol/L in survivors, -0.12 mmol/L in nonsurvivors; adjusted OR: 0.5; 95% CI: 0.3-0.9, C statistic=0.68; p=0.02) and at 12 h (-6.6 mmol/L in survivors, -2.8 mmol/L in nonsurvivors, adjusted OR: 0.1; 95% CI: 0.02-0.3, C statistic=0.72; p<0.001) after VA-ECMO induction in postcardiotomy patients were risk factors for hospital mortality. It means that uncured lactic acidosis even at an earlier phase than 24 h after VA-ECMO induction was a powerful predictor of mortality, so we have to take into consideration both the lactate level and clearance even during the early phase after VA-ECMO induction.

Monitoring of peripheral tissue oxygenation and perfusion

More effective medical interventions are needed if hyperlactatemia is prolonged or worsened even immediately after VA-ECMO induction, which is indicative of remaining hypoxia or hypoperfusion in peripheral tissues. Monitoring of peripheral tissue oxygenation and perfusion has been initiated. Wong et al.[23] reported that near-infrared spectroscopy could detect cerebral ischemia and peripheral vascular event. A decrease in cerebral oximetry values requires medical interventions such as methods to increase blood pressure, oxygenation, and ECMO flow, and 80% of these patients' underlying ischemia was corrected. Kara et al.[24] reported the usefulness of sublingual microcirculatory measurements in VA-ECMO–supported patients. Although there was no significant difference in the global circulation parameter between survivors and nonsurvivors, microcirculation parameters in large and small vessels were significantly different between the two groups. The perfused vessel density of the sublingual microcirculation at the VA-ECMO cannulation could predict ICU mortality. Similarly, Yeh et al.[25] showed the usefulness of microcirculation parameters in cardiac VA-ECMO cases in predicting 28-day mortality. Evaluation of microcirculation in septic shock patients has garnered much attention.[26] Both stabilization of global microcirculation parameters such as blood pressure and resuscitation-of-microcirculation–guided therapy have been advocated. Clinicians who are involved in VA-ECMO management may need to familiarize this monitoring field to improve the survival proportion of the VA-ECMO–supported patients.

Our study has some limitations. First, this is a small, retrospective, observational study. Second, the patients' primary diagnosis was heterogeneous. Each disease has a different pathophysiology and mortality rate. Further large cohort studies are required to detect the risk factors for each disease cohort (i.e., cardiac failure, acute myocardial infarction, acute respiratory failure, post-cardiac surgery, and cardiopulmonary arrest). Third, there were no data on CPR duration, time from the onset of cardiopulmonary arrest or cardiogenic shock to VA-ECMO induction, or initial VA-ECMO flow. These variables may affect the patient's prognosis.[27] Fourth, lactate levels could not be monitored continuously as with heart rate and pulse oximetry; hence, precise evaluation of lactate level fluctuations in each patient was difficult. There is no monitoring device for serial calculation of lactate levels at present. Thus, more careful monitoring of the lactate levels (e.g., one or more times per hour during the early phase after VA-ECMO induction) is needed to clarify the precise significance of lactate level fluctuations in the patient's prognosis. The development of microcirculation-monitoring devices combined with evaluation of lactate level fluctuations will result in improvement in medical care and mortality in VA-ECMO patients.

In conclusion, the ICU mortality in cardiac or respiratory failure patients who underwent VA-ECMO was 65.2%. La (>4.9 mmol/L), L24min (>1.9 mmol/L), L24max (>6.5 mmol/L), and Lmax (>5.6 mmol/L) were risk factors for ICU mortality in VA-ECMO patients. Lactate levels can be a potential therapeutic target and indicator of the need for improvement in patient management after VA-ECMO induction.

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Competing interests

T.H. received lecture fees from Ono Pharmaceutical Co., Ltd. The rest of the authors declare that they have no competing interests.

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