Blood lactate level during extracorporeal life support as a surrogate marker for survival

Sung Jun Park, MD,[a] Sang-pil Kim, MD, PhD,[b] Joon Bum Kim, MD, PhD,[a] Sung-Ho Jung, MD, PhD,[a] Suk Jung Choo, MD, PhD,[a] Cheol Hyun Chung, MD, PhD,[a] and Jae Won Lee, MD, PhD[a]

Objective: The establishment of reliable markers to monitor adequate tissue perfusion during extracorporeal life support is clinically important to improve outcomes.

Methods: We evaluated 115 consecutive adult patients (aged 61.7 ± 13.4 years, 59 female patients) undergoing extracorporeal life support to manage low cardiac output syndrome after major cardiac surgery. The blood lactate levels serially measured during extracorporeal life support (at 6, 12, and 24 hours) were analyzed.

Results: Forty-seven patients (40.8%) were weaned off extracorporeal life support successfully, and 32 patients (27.8%) survived to discharge. On logistic regression analysis, a high blood lactate level before extracorporeal life support (relative risk [RR], 1.19; 95% confidence interval [CI], 1.06-1.34) and cardiopulmonary bypass weaning failure after surgery (RR, 4.39; 95% CI, 1.44-13.35) emerged as baseline risk factors of mortality. After adjustment with these factors, blood lactate levels at 6 hours (RR, 1.24; 95% CI, 1.06-1.46), 12 hours (RR, 1.35; 95% CI, 1.10-1.67), and 24 hours (RR, 1.46; 95% CI, 1.10-1.93) were predictive of mortality. When the predictive values of serial blood lactate levels for mortality were assessed using the receiver operating characteristic method, the greatest accuracy was obtained at cutoff values of 7.05 mmol/L at 6 hours (sensitivity, 75.5%; specificity, 75.0%), 4.95 mmol/L at 12 hours (sensitivity, 70.4%; specificity, 76%), and 4.15 mmol/L at 24 hours (sensitivity, 62%; specificity, 93.1%).

Conclusions: Blood lactate measurement can be used as a reliable tool for monitoring adequate tissue perfusion during extracorporeal life support and was strongly predictive of mortality. Therefore, in patients without adequate decrement in lactate levels during extracorporeal life support, potential factors responsible for inadequate perfusion should be identified and corrected. (J Thorac Cardiovasc Surg 2014;148:714-20)

With the technologic advancement of extracorporeal life support (ECLS) and improvement in its management strategies, the use of ECLS has been generalized in clinical practice over the past decade. ECLS can provide total circulatory support with fully oxygenated blood so that systemic tissue perfusion is satisfied in patients with severe respiratory or circulatory failure. Nevertheless, achieving adequate tissue perfusion can be disturbed by unexpected clinical situations, such as device-related problems, cannulation-related complications, and hemorrhagic events. These situations may lead to tissue hypoperfusion and consequent end-organ damage, ultimately hampering the outcomes of ECLS.[1,2] In these regards, early detection of suboptimal tissue perfusion despite the ECLS implementation will be clinically important to identify correctable factors of hypoperfusion and thereby to improve the outcomes. Nonetheless, the reliable monitoring markers of adequate tissue perfusion during ECLS have not been established to date.

High lactate level is known to be an independent predictor of low cardiac output syndrome and major complications after cardiac surgery.[3,4] Blood lactate level can be promptly measured in intensive care unit (ICU) settings from simple arterial blood gas analysis (ABGA) samplings. In this study, we hypothesized that arterial blood lactate level during ECLS can be used as a reliable predictive marker of mortality. Therefore, we sought to evaluate the role of serially measured arterial lactate level during ECLS as a monitoring tool for tissue perfusion in the setting of post-cardiac surgery ECLS.

METHODS

Patients

Between May 2005 and December 2012, 10,197 adult patients underwent major cardiac surgery at the Asan Medical Center, Seoul, Korea. These surgeries included valve surgery, coronary artery bypass grafting, aortic surgery, resection of cardiac tumors, pericardiectomy, pulmonary thromboembolectomy, and heart transplantation. Of these patients, 125 were supported with venoarterial-type ECLS for low cardiac output

From the Department of Thoracic and Cardiovascular Surgery,[a] Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; and Department of Thoracic and Cardiovascular Surgery,[b] Pusan National University Hospital, Busan, Korea.

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Drs Park and Kim contributed equally as first authors in this article.

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Address for reprints: Joon Bum Kim, MD, PhD, Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, 388-1 Pungnap-dong Songpa-gu, Seoul 138-736, South Korea (E-mail: jbkim1975@amc.seoul.kr).

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Abbreviations and Acronyms

ABGA = arterial blood gas analysis
CI = confidence interval
CPB = cardiopulmonary bypass
ECLS = extracorporeal life support
ICU = intensive care unit
ROC = receiver operating characteristic
RR = relative risk

syndrome after major cardiac surgery at the Asan Medical Center, Seoul, Korea. After exclusion of 10 patients who underwent preoperative ECLS, 115 patients were included in this study. Clinical situations that required postoperative ECLS were as follows: (1) 48 patients with usual postoperative low cardiac output syndrome that was unresponsive to inotropics or intra-aortic balloon pumping, (2) 27 patients with witnessed cardiac arrest that was unresponsive to standard advanced cardiopulmonary life support, and (3) 40 patients with postoperative cardiopulmonary bypass (CPB) weaning failure.

The study was approved by the institutional ethics committee/review board of the University of Ulsan, and the requirement for informed patient consent was waived in view of the retrospective nature of the study.

Extracorporeal Life Support Devices and Management

Venoarterial ECLS was implemented at the common femoral artery and vein or internal jugular vein using the Seldinger technique in all 115 patients. The ECLS system consisted of a centrifugal pump, a hollow fiber membrane oxygenator with an integral heat exchanger, and a heparin-bound circuit. Three types of ECLS system were used: the Capiox Emergent Bypass System (Terumo Corp, Tokyo, Japan) was used for 94 patients (81.7%), the PLS System (Maquet, Hirrlingen, Germany) was used for 14 patients (12.2%), and the Bio-Console 560 System (Medtronic, Inc, Minneapolis, Minn) was used for 7 patients (6.1%).

Blood lactate level measurement was performed routinely every 2 to 3 hours from simple ABGA samples. The ABGA samples were analyzed by GEM Premier 3000 (Instrumentation Laboratory, Lexington, Mass).

An intravenous heparin bolus of 100 U/kg was administered to achieve a celite activated clotting time (measured using a Hemochron 401 machine, Soma Technology, Bloomfield, Conn) of 300 seconds before cannulation of arterial and venous catheter. After the initiation of ECLS, the activated clotting time was maintained within a range of 180 to 200 seconds. From 2010, nafamostat mesilate (Futhan; Torii Pharmaceutical, Tokyo, Japan), a synthetic serine protease inhibitor, was adopted to use as an alternative anticoagulant to heparin for patients with a high risk of bleeding. For these patients, a half-dose of heparin was administered before cannulation, and activated clotting time was maintained within 160 to 180 seconds after the administration of a starting dose of 0.75 mg/kg nafamostat mesilate. The patients (n = 5) with severe coagulopathy in the immediate postoperative period were not administered heparin or nafamostat mesilate until the bleeding was controlled. The details of coagulation strategy during ECLS and ECLS weaning protocol have been described.[5]

We tried to maintain the ECLS blood flow greater than the cardiac index of 2.4 L/min/m^2. To maintain the mean arterial pressure of 60 to 70 mm Hg, vasopressors such as norepinephrine or vasopressin were administered as needed. Red blood cells and platelets were transfused to maintain the hematocrit of 30% to 35% and platelet count greater than $100 \times 10^3/mm^3$ for patients with a high bleeding risk. An antegrade perfusion catheter for distal limb perfusion was routinely placed distal to the arterial cannulation site, except in the case of the failure to implant the catheter because of technical difficulties.

Statistical Analysis

Categoric variables are presented as frequencies and percentages, and were compared using the Chi-square test or Fisher exact test. Continuous variables are expressed as mean ± standard deviation and were compared using the Student unpaired *t* test. To determine the baseline risk factors for mortality, logistic regression models were used. At the first stage of the analyses, baseline characteristics of patients and variables related to ECLS were considered in the logistic regression model. Variables with a *P* value of .20 or less in univariable analyses were candidates for the multivariable models. Multivariable analyses involved a backward elimination technique, and only variables with a *P* value of .10 or less were used in the final model. To evaluate the impact of post-ECLS lactate level on death, further multivariable analyses were conducted that involved serial post-ECLS lactate levels at each point and significant variables affecting mortality in the second stage of the analyses. Results were expressed as a relative risk (RR) with 95% confidence intervals (CIs). The predictive value of post-ECLS lactate level for mortality was evaluated by analyzing areas under receiver operating characteristic (ROC) curves, with their 95% CI. The optimal cutoff value corresponded to the value with the greatest accuracy. Survival was estimated by the Kaplan–Meier method and compared by the log-rank test. All reported *P* values are 2-sided. Statistical analyses were performed with SPSS 18.0 for Windows Software (IBM, Armonk, NY).

RESULTS

The baseline characteristics and clinical data related to ECLS of the patients are shown in Tables 1 and 2, respectively. The patients who died in-hospital required a longer CPB time during surgery and were more likely to undergo ECLS at the end of the operation because of CPB weaning failure than those who survived to discharge, whereas there were no significant differences between the 2 groups in other baseline profiles. The levels of arterial blood lactate before and after the initiation of ECLS were significantly higher in patients who died in-hospital compared with those in the group of survivors to discharge.

Sixty-three patients (54.8%) experienced at least 1 complication during ECLS. Table 3 provides the details of complications that occurred during ECLS. The serial blood lactate levels at 6 hours (9.73 ± 4.48 vs 7.01 ± 4.39; $P = .007$), 12 hours (8.10 ± 4.76 vs 5.14 ± 3.74; $P = .003$), and 24 hours (6.48 ± 4.98 vs 4.00 ± 2.92; $P = .008$) after ECLS initiation were significantly higher in the patients who had at least 1 complication (n = 63) than the patients without complications (n = 52). The incidence rates of overall complications were significantly higher in patients who died in-hospital than those who survived to discharge ($P = .003$).

The overall outcomes of ECLS are summarized in Figure 1. Two patients underwent successful heart transplantation and survived to discharge. Forty-seven patients (40.8%) were weaned off ECLS successfully; however, 17 patients died after successful weaning from ECLS in-hospital. The cause of death after successful weaning was multiple organ failure in 6 patients, profound cardiac failure in 3 patients, sepsis in 2 patients, pan-peritonitis in 2 patients, aortic rupture in 2 patients,

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