# Outcomes of extracorporeal life support for low cardiac output syndrome after major cardiac surgery

Sung Jun Park, MD, Joon Bum Kim, MD, Sung-Ho Jung, MD, PhD, Suk Jung Choo, MD, PhD, Cheol Hyun Chung, MD, PhD, and Jae Won Lee, MD, PhD

**Objective:** Extracorporeal life support (ECLS) is a widely accepted modality for the treatment of postoperative low cardiac output syndrome (LCOS) after major cardiac surgery by providing temporary circulatory support for the stunned myocardium. We sought to identify the factors that affect outcomes of ECLS for postoperative LCOS.

**Methods:** From 2005 to 2011, of a total of 9267 adult patients underwent major cardiac surgery, 93 patients (aged, 60.6 ± 13.8 years; 47 women) underwent ECLS to treat postoperative LCOS.

**Results:** Thirty-nine (41.9%) patients were weaned off ECLS successfully, and 1 patient underwent heart transplantation. A final total of 23 patients (24.3%), including 1 heart transplantation recipient, survived until the end of the follow-up period (median, 611 days; range, 125-2247 days). On logistic regression analysis, old age ($P = .001$), a high blood lactate level before ECLS initiation ($P < .001$), cardiopulmonary bypass weaning failure after surgery ($P < .001$), and postoperative bleeding ($P = .012$) were independent factors associated with mortality. In contrast, administration of anticoagulant nafamostat mesilate ($P = .040$) was found to be associated with improved outcomes of ECLS. When the predictive value of pre-ECLS blood lactate level for mortality was assessed using the receiver operating characteristic curve, the greatest accuracy was obtained at the cutoff value of 7.9 mmol/L, with 63% sensitivity and 68% specificity.

**Conclusions:** High lactate level before ECLS is an independent predictor of mortality after ECLS, necessitating earlier ECLS implementations before profound lactic acidosis develops. Moreover, nafamostat mesilate should be considered as alternative to heparin to reduce the risk of bleeding in these high-risk patients. (J Thorac Cardiovasc Surg 2014;147:283-9)



Extracorporeal life support (ECLS) is a widely accepted modality for the treatment of postoperative low cardiac output syndrome (LCOS) after major cardiac surgery.[1-5] By providing temporary circulatory support for the stunned myocardium, ECLS allows time for cardiac recovery.[6] When the failing heart is unlikely to recover despite prolonged ECLS for more than 48 to 72 hours, either implantation of a ventricular assist device (VAD) or heart transplantation (HT) is desirable before the onset of end-organ insults.[2,7] Unfortunately, these destination therapies for irreversible cardiac insults are still practically unavailable in many developing countries because of their cost and the limited availability of donor hearts. In South Korea, for instance, the National Health Insurance Corporation has not approved the implantation of VADs because of the associated costs. Furthermore, given that the number of donor hearts is very limited in Korea, bridging to HT is rarely successful in cases of postoperative irreversible heart failure.[8] Consequently, the recovery of cardiac function by the use of ECLS may be the only option for management of postoperative LCOS after cardiac surgery in many countries under similar conditions. In these regards, there have been only a few reports related to the use of ECLS as a ''bridge-to-recovery'' for LCOS after cardiac surgery. Therefore, the present study aimed to evaluate the early outcomes of ECLS after major cardiac surgery and to determine the predictive factors of mortality.

## PATIENTS AND METHODS

### Patients

Between May 2005 and December 2011, 9267 adult patients underwent major cardiac surgery at the Asan Medical Center, Seoul, Korea. These operations included valve surgery, coronary artery bypass grafting, aortic surgery, resectioning of cardiac tumors, pericardiectomy, pulmonary thromboembolectomy, and HT. Among these patients, 103 (1.1%) required postoperative ECLS for LCOS. The exclusion of 10 patients who received ECLS preoperatively left a final cohort that comprised 93 patients and formed the subject population in this study. The breakdown of patients with different clinical situations that required ECLS were as follows: (1) 39 patients with usual postoperative LCOS that was unresponsive to inotropic drugs or intra-aortic balloon pumping (IABP), (2) 21 patients with witnessed cardiac arrest that was unresponsive to standard advanced

From the Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea.

Disclosures: Authors have nothing to disclose with regard to commercial support.

Received for publication Sept 7, 2012; revisions received Oct 9, 2012; accepted for publication Nov 6, 2012; available ahead of print Dec 7, 2012.

Address for reprints: Joon Bum Kim, MD, 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).

0022-5223/$36.00



http://dx.doi.org/10.1016/j.jtcvs.2012.11.006

**Abbreviations and Acronyms**

ACT = activated clotting time
CI = confidence interval
CPB = cardiopulmonary bypass
ELCS = extracorporeal life support
HR = hazard ratio
HT = heart transplantation
IABP = intra-aortic balloon pumping
LCOS = low cardiac output syndrome
VAD = ventricular assist device

cardiopulmonary life support, and (3) 33 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.



## ECLS Devices

In all 93 patients, venoarterial ECLS was administered via peripheral cannulation involving the common femoral artery and vein or internal jugular vein. 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 emergency bypass system (Terumo, Tokyo, Japan) was used for 80 (86%) patients, the PLS system (Maquet, Hirrlingen, Germany) for 6 (6.5%), and the Bio-Console 560 system (Medtronic, Minneapolis, MN) for 7 (7.5%) patients.

## Anticoagulation

Before cannulation, an intravenous heparin bolus of 100 U/kg was administered to achieve a celite activated clotting time (ACT) (measured using a Hemochron 401 machine; Soma Technology, Bloomfield, Conn) of 300 seconds, except in patients with a high risk of bleeding or in patients who were actively bleeding. The latter 2 classes of patients received a half dose of heparin. After the patients were connected to the ECLS circuit, the ACT was normally maintained within a range of 180 to 200 seconds. However, when hemorrhage had occurred or was anticipated, an attempt was made to ensure a lower ACT of 160 to 180 seconds. During the weaning process, an ACT of less than 200 seconds was achieved by significantly reducing the pump flow rate. Whenever CPB weaning failed after surgery, ECLS was performed. Heparin was then replaced by protamine sulfate, which was administered at a dose 25% lower than normally used.

In 2010, we began to use nafamostat mesilate (Futhan; Torii Pharmaceutical, Tokyo, Japan), a synthetic serine protease inhibitor, as an alternative anticoagulant to heparin for actively bleeding patients immediately after surgery. For these patients, a half dose of heparin was administered before cannulation, and ACT was maintained within 160 to 180 seconds after the administration of a starting dose of 0.75 mg/kg nafamostat mesilate. The maintenance dose of nafamostat mesilate was adjusted between 0.5 mg/kg and 1 mg/kg according to hourly measurements of ACT.

## ECLS Management

The ECLS blood flow was maintained at a cardiac index of at least 2.4 $L \cdot min^{-1} \cdot m^{-2}$. The mean arterial blood pressure was targeted at 60 to 70 mm Hg. To maintain the appropriate mean arterial pressure, we administered vasopressors as needed, rather than inotropic agents. The patients' hematocrit values were maintained at 30% to 35%, and platelets were transfused when the platelet count was less than $100 \times 10^3/mm^3$ for high bleeding risk patients and $50 \times 10^3/mm^3$ otherwise. An antegrade perfusion catheter was routinely placed distal to the arterial cannulation site for distal limb perfusion, except in instances in which this placement failed owing to technical difficulties. If signs of ischemia in the distal limbs developed, we changed the arterial cannulation to the opposite side of the femoral artery.

Successful weaning was defined as the separation from ECLS without mortality over a 24-hour period without resumption of ECLS.[9] Generally, the weaning process started with the prospect of the recovery of cardiac function when echocardiography showed adequate ventricular filling and an ejection fraction of greater than 30% to 35% at ECLS flow of a cardiac index of $1.0\,L \cdot min^{-1} \cdot m^{-2}$. As ECLS weaning proceeded, the ECLS flow was gradually reduced to 0.5 L/min. If the hemodynamic parameters remain stable for 30 minutes at the ECLS flow of 0.5 L/min, ECLS was removed from the bedside.

## Statistical Analysis

Categorical variables are presented as frequencies and percentages and were compared using the $\chi^2$ test or Fisher's exact test. Continuous variables are expressed as mean $\pm$ standard deviation and were compared using the Student unpaired *t* test. For multivariable analyses of mortality data, a logistic regression model was used. Variables with a $P$ value $\leq .20$ in univariable analyses were candidates for the multivariable models. Multivariable analyses involved a backward elimination technique, and only variables with a $P$ value $\leq .10$ were used in the final model. Results were expressed as a hazard ratio (HR) with 95% confidence intervals (CIs). The predictive value of pre-ECLS lactate level for mortality was evaluated by analyzing areas under receiver operating characteristic curves, with their 95% CIs. The optimal cutoff value corresponded to the value with the greatest accuracy. All reported $P$ values are 2-sided. Statistical analyses were performed with SPSS 18.0 for Windows Software (SPSS Inc, Chicago, Ill).

# RESULTS

The baseline characteristics of the patients are listed in Table 1. The patients who died were older and required a longer CPB time during surgery than those who survived. The preoperative echocardiographic data, however, showed no significant differences between the 2 groups.

Table 2 compares the variables related to ECLS management and complications in patients according to their final vital status. The levels of serum lactate level before ECLS were significantly higher in patients who died than in those in the group of survivors. Twenty-one (22.6%) patients were supported with an IABP before ECLS was begun. For 33 (35.4%) patients, ECLS commenced in the operating room, immediately after the main cardiac procedure, and as a result of CPB weaning failure. For the remaining 60 patients, ECLS commenced in the intensive care unit owing to delayed circulatory collapse after cardiac surgery. Among these 60 patients, 21 patients had cardiac arrest while ECLS was being instituted, and the median arrest time before the initiation of ECLS was 31 minutes (range, 3-142 minutes). Including these 21 patients, the median time interval from the end of the operation to the initiation of ECLS in the intensive care unit was 13.5 hours (range, 0.6-702.1 hours).

## Overall Outcomes

Details of complications that arose during ECLS are provided in Table 2. Twenty-five (26.9%) patients required