The Simplified Acute Physiology Score II as a Predictor of Mortality in Patients Who Underwent Extracorporeal Membrane Oxygenation for Septic Shock

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Background. **The use of extracorporeal membrane oxygenation (ECMO) for patients with septic shock is controversial. The outcomes are favorable in children but heterogeneous in adults. The present study aimed to analyze the outcomes of adult patients who underwent ECMO for septic shock, and to determine the factors associated with prognosis.**

Methods. **We respectively reviewed the medical records of patients who underwent ECMO for septic shock between January 2007 and December 2013. Patients were divided into survivor and nonsurvivor groups based on survival to hospital discharge. The patient characteristics before and during ECMO were compared between the groups. Independent risk factors for mortality were evaluated using multivariate logistic regression, receiver-operating characteristic curves, and Kaplan-Meier analysis.**

Results. **Twenty-eight patients were treated with venoarterial (n = 21), venovenous (n = 4), or venoarteriovenous (n = 3) mode ECMO. The overall survival rate to hospital discharge was 35.7%. The Simplified Acute Physiology Score II (SAPS II) and prealbumin were predictors of survival to hospital discharge. The optimal cutoff value for SAPS II was 80 (area under the curve 0.80, $p = 0.010$). Kaplan-Meier survival curves showed that the cumulative survival rate at hospital discharge and at 54-month follow-up was significantly higher among patients with SAPS II of 80 or less compared with patients with SAPS II greater than 80 (66.7% versus 12.5% and 58.3% versus 12.5%, respectively; $p = 0.001$).**

Conclusions. **It is still difficult to conclude whether ECMO should be recommended as therapy for adult patients with septic shock. However, a SAPS II score of 80 or less may be an indicator of favorable outcomes with the use of ECMO.**

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Extracorporeal membrane oxygenation (ECMO) has been used widely to treat many diseases and has improved clinical outcomes [1–3]. However, the use of ECMO for patients with septic shock is controversial. Moreover, the outcomes may be more favorable for children [4, 5], but are heterogeneous for adults [6–9]. Hence, further clinical studies are needed to confirm whether the use of ECMO should be recommended for adult patients with septic shock. Accordingly, the present study aimed to analyze the outcomes of adult patients who underwent ECMO for septic shock, and to determine the factors associated with prognosis, focusing specifically on the Simplified Acute Physiology Score II (SAPS II) designed to measure the severity of disease for patients admitted to intensive care units.

Patients and Methods

Study Design and Population

The study was approved by the Institutional Review Board of the Chuncheon Sacred Heart Hospital. We retrospectively reviewed the ECMO database for adult patients who underwent ECMO for acute respiratory or circulatory failure between January 2007 and December 2013 at Chuncheon Sacred Heart Hospital in Korea. Among the 156 patients identified, 28 were placed on ECMO to assist with the management of septic shock with or without respiratory failure. The primary outcome assessed in this study was survival to hospital discharge. We also sought to identify predictors of mortality. According to the Third International Consensus definitions, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to

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Abbreviations and Acronyms

CPR = cardiopulmonary resuscitation
ECMO = extracorporeal membrane oxygenation
ECPR = extracorporeal cardiopulmonary resuscitation
SAPS = Simplified Acute Physiology Score
VA = venoarterial
VAV = venoarteriovenous
VIS = vasoactive inotropic score
VV = venovenous

infection, and septic shock is defined as a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality [10].

Indications for and Type of ECMO

The decision to initiate ECMO was made by our institution's critical care team. Venoarterial (VA) ECMO was indicated for acute circulatory failure with (1) systolic blood pressure less than 80 mm Hg despite adequate intravascular volume replacement and the infusion of a high-dose vasopressor (norepinephrine greater than 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$), or (2) cardiac arrest that lasted more than 10 minutes despite cardiopulmonary resuscitation (CPR). Venovenous (VV) ECMO was indicated for acute respiratory failure based on lung dysfunction, measured as a ratio of arterial oxygen tension to inspired oxygen fraction (Pao_2/Fio_2) of less than 100 on ventilation with 100% oxygen, and the infusion of a low-dose vasopressor (norepinephrine less than 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). Venoarteriovenous (VAV) ECMO was used for patients who had acute respiratory failure as a Pao_2/Fio_2 ratio of less than 100 on ventilation with 100% oxygen, and the infusion of a high-dose vasopressor (norepinephrine greater than 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

Generally, there was no limitation of ECMO use based on age. Being on a ventilator for more than 7 days, advanced multiorgan failure, and a long duration of septic shock were relative contraindications for ECMO. Patients were excluded if they had any of the following: ongoing intracranial hemorrhage; terminal malignancy; diseases including end-stage renal disease undergoing hemodialysis, liver cirrhosis Child stage greater than B, and terminal congestive heart failure; immune compromise; or loss of independence in activities of daily living. In terms of extracorporeal cardiopulmonary resuscitation (ECPR), indications for ECMO were receipt of bystander CPR, a witnessed collapse, interval from call to emergency medical service arrival less than 10 minutes, interval from call to emergency room less than 40 minutes, and age less than 70 years.

Management

We initially tried crystalloid fluid loading (30 mL/kg intravenously over 30 minutes), according to the 2008 and 2012 early goal-directed therapy guidelines [11]. Then, we used a Swan-Ganz catheter to evaluate diastolic pulmonary artery pressure, instead of a central venous pressure catheter. We challenged with volume loading until the diastolic pulmonary artery pressure reached 20 to 25 mm Hg, aiming for a mean blood pressure of 65 mm Hg. If the diastolic pulmonary artery pressure exceeded 20 to 25 mm Hg, we started low-dose norepinephrine (0.02 to 0.04 $\mu g \cdot kg^{-1} \cdot min^{-1}$). We routinely inserted the ECMO cannulas in the cardiac catheterization room, using angiography for safety. Numerous technical errors can occur when using the blind approach for insertion, even if using ultrasonography, because of going in the wrong direction, kinking of the guidewire, and tortuous vessels. We tried to use the smallest cannulas possible (21F for drainage and 17F for infusion in VA ECMO). Limb ischemia, therefore, rarely occurred. Cardiac distension is known as a complication; we rarely had severe cardiac distension that required cardiac venting owing to appropriate volume regulation combined with use of a vasopressor. We used the right femoral vein for the drainage cannula, and the left femoral vein and right femoral artery for the infusion cannulas in VAV mode.

Data Collection

Baseline clinical characteristics, before and during ECMO data, and complications were recorded. "Total arrest" was a composite of cardiac arrest occurring before ECMO insertion and ECPR (cardiac arrest occurring during EMCO insertion). Blood product transfusion (units per day) was calculated by total units during ECMO support divided by ECMO day. Pre-ECMO variables, including sepsis-related organ failure assessment score and SAPS II, were measured and calculated by collecting data regarding the worst variables within the 24 hours immediately before insertion of ECMO.

The vasoactive inotropic score (VIS) was calculated using the following equation: VIS = inotropic score (IS) + (10 × milrinone dose [$\mu g \cdot kg^{-1} \cdot min^{-1}$]) + (10,000 × vasopressin dose [$\mu g \cdot kg^{-1} \cdot min^{-1}$]) + (100 × norepinephrine dose [$\mu g \cdot kg^{-1} \cdot min^{-1}$]), where IS = dopamine dose ($\mu g \cdot kg^{-1} \cdot min^{-1}$) + dobutamine dose ($\mu g \cdot kg^{-1} \cdot min^{-1}$) + (100 × epinephrine dose [$\mu g \cdot kg^{-1} \cdot min^{-1}$]) [12]. Results of post-ECMO arterial blood gas analyses were obtained immediately after ECMO. Post-ECMO VIS was calculated 6 hours after ECMO implementation, and urine output was measured within 24 hours.

Statistical Analysis

The normality of data distributions was evaluated using the Kolmogorov-Smirnov test to select appropriate parametric and nonparametric statistical methods. Categoric variables were analyzed using the χ^2 test or Fisher's exact test. Continuous variables were expressed as median (25th to 75th percentile) and analyzed using the Mann-Whitney *U* test. Independent risk factors associated with mortality in patients who underwent ECMO for septic shock were evaluated using a