Survival Predictors in Acute Respiratory Distress Syndrome With Extracorporeal Membrane Oxygenation

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Background. Extracorporeal membrane oxygenation (ECMO) can be used as a salvage therapy, but the effectiveness is controversial. The aim of this study was to investigate the predictors of mortality and the influence of organ dysfunction scores in severe acute respiratory distress syndrome (ARDS) patients treated with ECMO.

Methods. The records of adult severe ARDS patients receiving ECMO support from May 2006 to December 2011 at Chang Gung Memorial Hospital were retrospectively analyzed.

Results. The records of 65 patients with severe ARDS who received venovenous ECMO were analyzed. The hospital survival rate was 47.7%. Survivors were younger than nonsurvivors (41.4 ± 15.4 versus 54.1 ± 16.9 years, respectively; $p = 0.002$) and had shorter duration of mechanical ventilation before ECMO (52.7 ± 51.1 versus 112.1 ± 101.0 hours, respectively; $p = 0.01$). Before ECMO, Acute Physiology and Chronic Health Evaluation II, Sequential Organ Failure Assessment, and Multiple Organ Dysfunction scores were significantly lower for survivors than for nonsurvivors. Mortality rate increased with rising predictive score. During 7 days of ECMO use, organ dysfunction scores were significantly lower for survivors than nonsurvivors.

Conclusions. Severe ARDS patients who are younger, have shorter duration of mechanical ventilation, and lower organ dysfunction scores before ECMO initiation have more favorable survival outcome. Early application of ECMO, especially if predictive score is below 2, may improve survival. Organ dysfunction scores before and during ECMO support are correlated with survival.

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Acute respiratory distress syndrome (ARDS) may lead to life-threatening refractory hypoxemia, and is associated with significant mortality. Mild, moderate, and severe ARDS by the Berlin definition are associated with mortality rates of 27%, 32%, and 45%, respectively [1]. The severity of hypoxemia is not prognostic of poor outcomes [2]. Multiple organ failure is the major cause of mortality among ARDS patients, and fewer than 20% die of refractory hypoxemia [3, 4].

For the management of ARDS, a lung-protective ventilation strategy with lower tidal volume remains the cornerstone of treatment, and the ARDS Network trial has shown significant survival improvement, more ventilator-free days, and more days without organ failure [5]. Although many alternative treatments have been investigated for ARDS, such as recruitment maneuvers, high-frequency oscillatory ventilation, inhaled nitric oxide, and extracorporeal membrane oxygenation (ECMO), their impact on mortality is undetermined [2, 6], except for early application of prolonged prone position [7].

Although ECMO can be used as a salvage therapy for severe ARDS refractory to mechanical ventilation (MV), its role has not been definitively established [2]. Transferring severe ARDS patients to centers with an ECMO-based management protocol is associated with significant survival benefit [8]. The survival rate of severe ARDS patients supported with ECMO was approximately 50% in a multicenter database [6]. For influenza A (H1N1)–induced ARDS treated with ECMO, the survival rate was reported to range from 64% to 79% [4, 9, 10]. With ECMO, a "lung rest" strategy may be used to further lower the delivered tidal volume and airway pressure to minimize ventilator-associated lung injury (VALI), which may improve outcomes [2, 6, 11].

The precise indications for ECMO for severe ARDS patients are controversial, and the factors predictive of outcome are not well established. The effect on other organs of a lung rest strategy using ECMO has also not been addressed. The aim of this study was to investigate the

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Abbreviations and Acronyms

APACHE	= Acute Physiology and Chronic Health Evaluation
ARDS	= acute respiratory distress syndrome
AUC	= area under the curve
CI	= confidence interval
ECMO	= extracorporeal membrane oxygenation
MOD	= Multiple Organ Dysfunction
MV	= mechanical ventilation
SOFA	= Sequential Organ Failure Assessment
VALI	= ventilator-associated lung injury

predictors of mortality and the influence of organ dysfunction scores for severe ARDS patients treated with ECMO.

Patients and Methods

Patients

This was a retrospective study of severe ARDS patients who underwent ECMO in the medical and surgical intensive care units at a tertiary care referral center, Chang Gung Memorial Hospital, between May 2006 and December 2011. All patients had severe ARDS defined according to the Berlin definition with acute onset within 1 week, bilateral lung opacities on chest radiograph, no evidence of cardiac failure–related hydrostatic edema by echocardiography, and PaO_2 to fraction of inspired oxygen (FiO_2) ratio less than 100 mm Hg, with positive end-expiratory pressure (PEEP) 5 cm H_2O or greater [1]. Exclusion criteria were (1) age less than 18 years; (2) receiving venoarterial ECMO for intractable shock or heart failure; and (3) having significant underlying comorbidities or severe multiple organ failure refractory to treatment. Written informed consent for clinical procedures was obtained from a patient's closest relative, and the local Institutional Review Board for Human Research approved this study (CGMH IRB no.102-1729B).

ECMO Circuit Management

The indications for ECMO support were severe hypoxemia (PaO_2:FiO_2 ratio less than 60 mm Hg) and already receiving aggressive MV support (PEEP more than 10 cm H_2O or plateau airway pressure more than 35 cm H_2O), and were consistent with national guidelines according to extracorporeal life support organization, which suggested ECMO is indicated when risk of mortality is 80% or greater identified by PaO_2:FiO_2 ratio less than 80 mm Hg or FiO_2 more than 0.9 and Murray score 3 to 4 (www.elsonet.org). The ECMO circuit consisted of a centrifugal pump and hollow-fiber microporous membrane oxygenator with heparin-bound Carmeda BioActive Surface (Carmeda, a subsidiary of WL Gore & Assoc, Flagstaff, AZ) using Capiox emergent bypass system (Terumo, Tokyo, Japan). We used two wire-wound polyurethane vascular cannulae (DLP Medtronic, Minneapolis, MN [inflow, 19F to 23F, and outflow, 17F to 21F]), and the femoral-jugular venovenous ECMO was established through percutaneous cannulation. The ECMO gas flow rate was set high initially (10 L/min, pure oxygen), and the blood pump speed was gradually increased to achieve optimal oxygen saturation (90% or more).

Modest volume replacement was necessary initially to improve unsteady ECMO blood flow and oxygenation. After optimizing the ECMO, it was critical to remove the excessive extravascular lung water with diuretics or continuous renal replacement therapy to improve lung function and pulmonary compliance. The hourly fluid balance goal was set at approximately −100 mL/h and modulated according to dry weight to achieve negative fluid balance, and the function of nonpulmonary organs was closely monitored. In our practice, the criteria for weaning from ECMO were resolving lung infiltration, lung compliance greater than 20 cm H_2O, PaO_2 greater than 60 mm Hg and $PaCO_2$ less than 45 mm Hg under FiO_2 0.4, PEEP 6 to 8 cm H_2O or less, and peak airway pressure of 30 cm H_2O or less.

Measurements

Demographic, clinical, and physiologic data were collected retrospectively. Organ dysfunction scores, including Sequential Organ Failure Assessment (SOFA) score and Multiple Organ Dysfunction (MOD) score, were recorded. Ventilation and oxygenation variables were recorded 6, 24, and 48 hours after ECMO support.

Statistical Analysis

Continuous variables are presented as mean ± SD. Student's *t* test was used to compare continuous variables between survivors and nonsurvivors. Calibration was assessed using Hosmer-Lemeshow goodness-of-fit test (C statistic). Generalized estimating equations were used to compare serial changes of the organ dysfunction scores. The χ^2 test for trends was applied to assess categoric data associated with predictive scores. Cutoff points were calculated by obtaining the best Youden index (sensitivity + specificity − 1). All statistical analyses were performed with SPSS 18.0 statistical software (SPSS, Chicago, IL). A p value less than 0.05 was considered significant.

Results

Patient Characteristics

In all, 81 patients with severe ARDS who received ECMO during the study period were included in the study. After excluding 16 patients (2 patients aged less than 18 years and 14 patients receiving venoarterial ECMO for intractable shock or heart failure), 65 patients were in the final analysis. Of those, 37 patients were successfully weaned from ECMO, and 31 patients survived; 28 patients could not be weaned from ECMO and did not survive (Fig 1). A summary of the demographic data and clinical