

Extra-corporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome: A Single Center Experience

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Background: Acute respiratory distress syndrome (ARDS) is associated with high morbidity and mortality rate. We report our treatment results with extracorporeal membrane oxygenation for severe ARDS patients.

Patients and Methods: From December 2001 through July 2005, there were 10 patients receiving treatment of extracorporeal membrane oxygenation (ECMO) for ARDS and/or septic shock in our hospital. There were six male and four female patients. The median age at the time of ECMO support was 4.3 years old (range: 2.1-71). Venous-arterial-ECMO was used for the patients with severe desaturation and persistent hypotension, and venovenous-ECMO was used for the patients with severe desaturation but preserved cardiac function.

Results: Five patients (50%) survived the ECMO. The ECMO survival rate was 20% (1/5) between 2001 and 2002, and was 80% (4/5) between 2003 and 2005. The median ECMO supporting time was 89 hours. The cause of mortality was hypoxic encephalopathy in 2 patients, intra-cranial hemorrhage in 1 patient, deteriorated pulmonary function in 1 patient and uncontrolled sepsis in 1 patient. All the survived patients were discharged from the hospital.

Conclusion: ECMO can rescue more patients with severe ARDS, even in the condition of septic shock. Improved results were reported in the literature, and our series also shows similar trend. For those patients with severe ARDS whose conditions cannot be improved or even deteriorate under conventional therapy, ECMO can provide a chance of survival.

Key Words: Acute respiratory distress syndrome • Extracorporeal membrane oxygenation • Septic shock

INTRODUCTION

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are associated with high morbidity and mortality rate.¹ Conventional therapies² include intubation and mechanical ventilation, permis-

sive hypercapnia, prone position, chest care, avoidance of fluid overload and so on. However, clinical conditions still deteriorate in severe patients. In such circumstance, extracorporeal membrane oxygenation (ECMO) can provide a chance of survival.^{3,4}

PATIENTS AND METHODS

Patients

From December 2001 through July 2005, there were 10 patients who received treatment of extracorporeal membrane oxygenation (ECMO) for ARDS and/or septic shock in our hospital (Table 1). There were six male and four female patients. The median age at the time of ECMO support was 4.3 years old (range: 2.1-71). Six

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Table 1. Clinical summary of ECMO patients

| No. | Age (years) | Gender | BW (kg) | Diagnosis | AaDO ₂ | OI | ECMO mode | ECMO flow (mL/kg) | ECMO time (hours) | Outcome |
|-----|-------------|--------|---------|-------------------------|-------------------|------|-----------|-------------------|-------------------|----------|
| 1 | 2.6 | F | 14 | Pneumonia | 643 | 27.4 | VV | 100 | 192 | Died |
| 2 | 5.5 | M | 24 | Pneumonia, Septic shock | 589 | - | VA→VV | 63 | 684 | Survived |
| 3 | 71 | M | 42 | Pneumonia | 596 | 25 | VV | 74 | 192 | Died |
| 4 | 2.1 | F | 15 | Pneumonia, Septic shock | - | - | VA | 80 | 48 | Died |
| 5 | 4.3 | M | 18 | Pneumonia | 645 | 50 | VV | 78 | 240 | Died |
| 6 | 13.3 | M | 40 | Pneumonia, Septic shock | - | - | VA | 58 | 24 | Died |
| 7 | 3.3 | F | 20 | Pneumonia, Septic shock | - | - | VA | 80 | 47 | Survived |
| 8 | 4.3 | F | 18.5 | Pneumonia, Septic shock | - | - | VA | 85 | 108 | Survived |
| 9 | 19.1 | M | 50 | Post-trauma ARDS | 618 | 42 | VV | 76 | 89 | Survived |
| 10 | 24.1 | M | 61 | Post-trauma ARDS | 632 | 36 | VV | 43 | 67 | Survived |

AaDO₂: alveolar arterial oxygen gradient; ARDS: acute respiratory distress syndrome; BW: body weight; ECMO: extracorporeal membrane oxygenation; VA: venoarterial; VV: venovenous.

Table 2. ECMO survival rates

| Variable | Survival rate | |
|----------------------|-------------------|------|
| ECMO mode | VA (n = 4) | 50% |
| | VA → VV (n = 1) | 100% |
| | VV (n = 5) | 40% |
| ECMO setup date | 2001-2002 (n = 5) | 20% |
| | 2003-2005 (n = 5) | 80% |
| Septic shock | Yes (n = 5) | 60% |
| | No (n = 5) | 40% |
| Age | < 10 y/o (n = 6) | 50% |
| | 10-20 y/o (n = 2) | 50% |
| | > 20 y/o (n = 2) | 50% |
| ECMO supporting time | ≤ 7 days (n = 5) | 80% |
| | > 7days (n = 5) | 20% |
| HFOV use | Yes (n = 3) | 67% |
| | No (n = 7) | 43% |

ECMO: extracorporeal membrane oxygenation; HFOV: high-frequency oscillatory ventilation; VA: venoarterial; VV: venovenous.

patients (60%) were less than 10 years old, and two patients (20%) were more than 20 years old. All the patients suffered from severe desaturation (AaDO₂ (alveolar arterial oxygen gradient) > 600 or OI (oxygenation index) > 25) and/or hypotension before ECMO setup. All the venovenous-ECMO patients had PaO₂/FiO₂ ratio less than 60 before ECMO setup.

For the patients with desaturation and persistent hypotension despite use of high dosage of inotropic

agents, venoarterial-ECMO with centrifugal pump (Medtronic Inc., Anaheim, CA, USA) was set up at first through the right carotid artery and right internal jugular vein in children and through the femoral artery and vein in adolescents. It was shifted to venovenous mode if cardiac function improved but respiratory function was still severely impaired. However, venoarterial-ECMO was removed a couple of days later directly without shifting to venovenous mode in case cardiac and respiratory

function improved simultaneously.

For patients with severe desaturation with preserved cardiac function despite maximal use of the ventilator support and medications, venovenous-ECMO with centrifugal pump was set up through the femoral vein and right internal jugular vein.

Technique of ECMO setup

Vascular exploration by cut-down method was performed in 8 patients and percutaneous Seldinger's technique was done for 2 adolescent patients. Before cannulation, heparin 100 units/kg was given intravenously. The size of the cannulas (Medtronic Inc., Anaheim, CA, USA) was chosen by the body weight of the patients. The selection of cannulation site was mentioned above. When removing ECMO, all the vessels in the cannulation site were repaired with prolene suture.

Patient care

After ECMO was set up, the patients were sedated and paralyzed with fentanyl and pancuronium given intravenously. The ventilator was gradually adjusted to low setting (PIP 30 cmH₂O, PEEP 5 cmH₂O) and pressure-controlled mode. High-frequency oscillatory ventilation (HFOV) was used for 3 patients as an adjuvant therapy, one before ECMO setup, and two for an attempt to solve lung collapse and to improve the unsatisfactory lung compliance after running of ECMO more than 1 week. Inotropic agents were tapered according to the hemodynamics. Intravenous infusion of heparin was given to maintain the activated clotting time (ACT) between 160 and 200 seconds. Concomitant peritoneal dialysis was performed for three children, two with hemolytic-uremic syndrome and another one with cardiopulmonary resuscitation before ECMO setup. Blood component therapy was given when necessary. Total parenteral nutrition (TPN) was used for some patients. Usage of antibiotics was adjusted by culture results.

RESULTS

Four patients underwent setup of venoarterial-ECMO, and the initial ECMO blood flow was 63-85 ml/Kg. Six patients underwent setup of venovenous-

ECMO, and the initial ECMO blood flow was 74-100 ml/Kg. ECMO support was shifted to venovenous mode in one venoarterial-ECMO patient after hemodynamics were stabilized but respiratory function was still severely impaired.

Five patients (50%) survived the ECMO. The median ECMO supporting time was 89 hours. The survival rate was 60% in the venoarterial-ECMO group and 40% in the venovenous-ECMO group, with no statistical significance between the two groups. The ECMO survival rate was 20% (1/5) between 2001 and 2002 and was 80% (4/5) between 2003 and 2005. Stratified by age, the ECMO survival rate was 50% in all age groups. The mean follow-up time for the survivors was 15.5±14.2 months (range: 2.0 to 38.9 months). All the surviving patients were discharged from the hospital.

The cause of mortality was hypoxic encephalopathy in 2 patients, intra-cranial hemorrhage in 1 patient, deteriorated pulmonary function in 1 patient and uncontrolled sepsis in 1 patient. The hypoxic encephalopathy was probably due to unstable hemodynamics before setup of venoarterial ECMO. The intra-cranial hemorrhage was a side effect of the systemic anticoagulation with heparin. One pediatric patient had no improvement of pulmonary function despite venovenous ECMO use; her pulmonary compliance remained poor and lung parenchyma did not re-expand.

With regard to complications in the survivors, one child had mild left hemiparesis, probably due to prolonged ECMO use (684 hours). His neurologic function improved gradually. He could run independently. No major complications occurred in other survivors. All the survivors were in functional class I of the New York Heart Association.

DISCUSSION

“Acute Lung Injury” (ALI) describes a pulmonary syndrome, characterized by non-cardiogenic pulmonary edema, caused by a number of insults. According to the American-European consensus conference on ARDS, ALI has a specific definition⁵: a PaO₂/FiO₂ ratio of less than 300, bilateral infiltrates on chest x-ray, and a pulmonary capillary wedge pressure of less than 18 mmHg. A severe form of ALI is ARDS, which has the same def-

initiation⁵ as ALI except that the PaO₂/FiO₂ ratio is less than 200. The majority of recent studies for ALI or ARDS report mortality in the 35% to 60% range.^{6,7} Severe ARDS⁸ patients are characterized by profound hypoxemia (PaO₂/FiO₂ ratio < 100 and/or AaDO₂ < 600 mmHg) despite optimal conventional treatment. This group of patients with severe ARDS has an 80% to 100% risk of mortality with conventional treatment only.^{9,10} The use of ECMO is indicated in these critically ill patients for the last chance of survival.

ECMO use during severe ARDS maintains oxygen and carbon dioxide gas exchange while providing an optimal environment for recovery of pulmonary function. More recently, improved survival with ECMO in severe ARDS patients failing all other means of respiratory support has been reported.^{8,11} Our results also improved in recent years. In 2001 and 2002, only 20% survived, but from 2003 to 2005, the survival rate increased to 80%.

Nearly 50% of patients with severe sepsis will develop ALI or ARDS.² Poor prognosis is predicted for those patients with septic shock. Under ECMO support, septic patients seemed to have higher mortality rate than non-septic patients, but sepsis was not a statistically significant prognostic factor by multivariate analysis.¹² Our data also showed no statistically significant difference in the survival rate for the venoarterial-ECMO group and the venovenous-ECMO group. This may encourage our effort to treat the severe ARDS patients even in the status of septic shock.

HFOV is an alternative mode of ventilation that theoretically fulfills the goals of lung-protective ventilation.¹³ By the use of HFOV, ventilation is achieved through variable oscillations around a set of mean airway pressure, with both active inspiration and active expiration. Kachel et al,¹⁴ reported that HFOV or inhaled nitric oxide was the first choice of treatment in an attempt to avoid ECMO use. In our series, for patients with severe shock, we set up ECMO first and used HFOV as an adjuvant therapy for selected cases with an attempt to solve lung collapse and to improve the unsatisfactory lung compliance after running of ECMO for more than 1 week.; for some patients with desaturation but relative stable hemodynamics, we tried HFOV before ECMO use.

In addition to certain gas exchange, ECMO support improves patient survival and facilitates lung recovery

by eliminating the problems of high-pressure and high-oxygen mechanical ventilation. Ventilator-induced lung injury also causes renal failure, liver failure, and cardiac failure.¹⁵ Furthermore, the remaining normal lung tissue was destroyed continuously, and inflammatory mediators from the damaged lung were persistently released when high-pressure mechanical ventilation was continued.¹⁶

In conclusion, ECMO can rescue more patients with severe ARDS, even in the condition of septic shock. Improved results were reported in the literature, and our series also shows similar trend. For those patients with severe ARDS whose conditions cannot be improved or even deteriorate under conventional therapy, ECMO can provide a chance of survival.

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以體外維生系統治療急性呼吸窘迫症候群： 單一醫院之經驗

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背景 急性呼吸窘迫症候群常伴隨有相當高的併發症與死亡率。我們報告對於重度急性呼吸窘迫症候群病患以體外維生系統的治療結果。

病患與方法 從 2001 年 12 月至 2005 年 7 月，共有 10 位病患因急性呼吸窘迫症候群（或合併敗血性休克）接受體外維生系統的治療。六位男性病患，四位女性病患，年齡的中位數為 4.3 歲（範圍：2.1 至 71 歲）。對於低血氧合併有低血壓的病患，使用靜脈動脈型的體外維生系統；對於低血氧但無低血壓的病患，使用靜脈靜脈型的體外維生系統。

結果 五位病患（50%）可成功脫離體外維生系統。體外維生系統治療的成功率在 2001 年至 2002 年為 20%（1/5），在 2003 年至 2005 年為 80%。體外維生系統使用期間的中位數為 89 小時。病患死亡的原因如下：兩位缺氧性腦病變、一位顱內出血、一位肺功能持續惡化、一位敗血症無法控制。所有五位成功脫離體外維生系統的病患都可順利出院。

結論 對於重度急性呼吸窘迫症候群病患，甚至在敗血性休克的情況下，體外維生系統的使用有機會可挽救病患的生命。文獻上可見治療的結果逐漸有改善，而我們的報告亦有相似的趨勢。對於重度急性呼吸窘迫症候群病患，無法以傳統治療穩定病情時，體外維生系統可提供一線生存的機會。

關鍵詞：急性呼吸窘迫症候群、體外維生系統、敗血性休克。