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# Extracorporeal Membrane Oxygenation Outcomes in Acute Respiratory Distress Treatment: Case Study in a Chinese Referral Center

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Statistical Analysis C
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Manuscript Preparation E
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**Background:** No definitive conclusions have been drawn from the available data about the utilization of extracorporeal membrane oxygenation (ECMO) to treat severe acute respiratory distress syndrome (ARDS). The aim of this study was to review our center's experience with ECMO and determine predictors of outcome from our Chinese center.

**Material/Methods:** We retrospectively analyzed a total of 23 consecutive candidates who fulfilled the study entry criteria between January 2009 and December 2015. Detailed clinical data, ECMO flow, and respiratory parameters before and after the introduction of ECMO were compared among in-hospital survivors and nonsurvivors; factors associated with mortality were investigated.

**Results:** Hemodynamics and oxygenation parameters were significantly improved after ECMO initiation. Thirteen patients survived to hospital discharge. Univariate correlation analysis demonstrated that APACHE II score ($r$=–0.463, $p$=0.03), acute kidney injury ($r$=–0.574, $p$=0.005), membrane oxygenator replacement ($r$=–0.516, $p$=0.014) and total length of hospital stay ($r$=0.526, $p$=0.012) were significantly correlated with survival to hospital discharge, and that the evolution of the levels of urea nitrogen, platelet, and fibrinogen may help to determine patient prognosis. Sixteen patients referred for ECMO from an outside hospital were successfully transported to our institution by ambulance, including seven transported under ECMO support. The survival rate of the ECMO-transport group was comparable to the conventional transport or the non-transport group (both $p$=1.000).

**Conclusions:** ECMO is an effective alternative option for severe ARDS. APACHE II score on admission, onset of acute kidney injury, and membrane oxygenator replacement, and the evolution of levels of urea nitrogen, platelet, and fibrinogen during hospitalization may help to determine the in-hospital patient prognosis. By establishing a well-trained mobile ECMO team, a long-distance, inter-hospital transport can be administered safely.

**MeSH Keywords:** Critical Illness • Extracorporeal Membrane Oxygenation • Respiration, Artificial • Respiratory Distress Syndrome, Adult

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## Background

Acute respiratory distress syndrome (ARDS) is a syndrome characterized by progressive respiratory distress and refractory hypoxemia caused by severe intrapulmonary and extrapulmonary disease. It is one of the most common causes of ICU inpatient admission [1]. Despite continuous advancements in intensive care technology, the case fatality rate in critical ARDS is still as high as 80–100% [2]. Applying the low tidal volume "pulmonary protection" ventilation strategy does help improve patient prognosis, however, it is hard to achieve effective gas exchange in those patients with an oxygenation index <100 via this strategy; mechanical ventilation with high-pressure often leads to ventilator-induced lung injury (VILI) [2].

Extracorporeal membrane oxygenation (ECMO) is a mobile extracorporeal life support device that provides temporary, complete cardiopulmonary function support [3]. The respiratory support mode (veno-venous ECMO) gains valuable time to improve pulmonary functions and transition into isolated mechanical ventilation by enhancing oxygenation without increasing average alveolar pressure [4,5]. Positive results reported in a recent multi-central, randomized controlled trial [6] and subsequent success during an influenza A/H1N1 panepidemic [7–9] has consistently demonstrated that an ECMO-based management protocol significantly improves survival compared to conventional mechanical ventilation.

However, there has been relatively little research on treating critical ARDS with ECMO in developing countries, and likewise very few studies on predicting the impact of biochemical parameter evolution on survival to hospital discharge. In this study, we evaluated the effectiveness and safety of rescuing critical ARDS patients with ECMO when conventional treatment was ineffective, and identify the factors related to patient prognosis in a Chinese ECMO referral center.

## Material and Methods

### Patient selection

This study was a retrospective review of a single institution's experience with severe ARDS adults (>18 years old) who were treated with ECMO at our center from January 2009 to December 2015.

### Inclusion and exclusion criteria

According to the Extracorporeal Life Support Organization (ELSO) [10], ECMO can be initiated when risk of death exceeds 80%, where $PaO_2/FiO_2$ is less than 100 mm Hg on $FiO_2$ more than 90%, and Murray score is 3–4, or in the case of hypercapnia as indicated by $PaCO_2$ over 80 mm Hg or inability to achieve safe inflation pressures (plateau pressure <30 cm $H_2O$). Patients were excluded if they 1) had been on mechanical ventilation for more than 10 days, 2) showed contraindication to anticoagulation, 3) had irreversible multiple organ failure, 4) had severe chronic pulmonary parenchymal disease, or 5) were in the terminal stage of cancer.

### Establishment and management of ECMO

We considered the veno-venous mode to be the best choice for hemodynamically stable patients. Transfemoral venous and transjugular percutaneous puncture and catheterization were performed under local anesthesia. Systemic heparinization was performed to keep the activated clotting time (ACT) between 160 and 200 seconds, and blood flow was maintained between 3 L/minute to 4 L/minute. Depending on the blood gas results, oxygen concentration and flow were adjusted. The respirator parameter settings were gradually downregulated to implement a "lung rest" strategy following ECMO, which included pressure control ventilation, low tidal volume (4 mL/kg), low pressure (PEEP 10–15 cm $H_2O$, peak airway pressure <30 cm $H_2O$), low frequency (8–12 times/minute) and low oxygen concentration ($FiO_2$ <50%), and remained unchanged throughout the entire process.

### ECMO removal

ECMO flow was gradually decreased until being removed when the flow reached 1 L/minute. The oxygen flow decreased to zero as the ECMO was removed. The blood flow and anticoagulation intensity were kept unchanged, and respirator parameters were upregulated simultaneously as hemodynamic indexes and gas exchange conditions were closely monitored. The ECMO could be removed once arterial conditions, $PO_2$ >60 mm Hg and $PCO_2$ 30–45 mm Hg, were constant for more than two hours.

### Inter-hospital referral and transportation

"Inter-hospital referral and transportation" was used to indicate critical patients who were referred, accepted, and transferred to our center. The patients meeting these indications and able to tolerate the conventional transfer method were considered transferrable to our institute with the assistance of mechanical ventilation. Patients with oxygenation or hemodynamic instability who were unable to tolerate conventional transfer were brought to the institute with ECMO support. The equipment for transport included a Medtronic Bio-Console 550/560 centrifugal pump, pipe package and cannula, surgical instruments, oxygen cylinders, respirator (Savina respirator, Drager Co. Germany), ACT detector, blood-gas analyzer, monitor, defibrillator, and 5% albumin.





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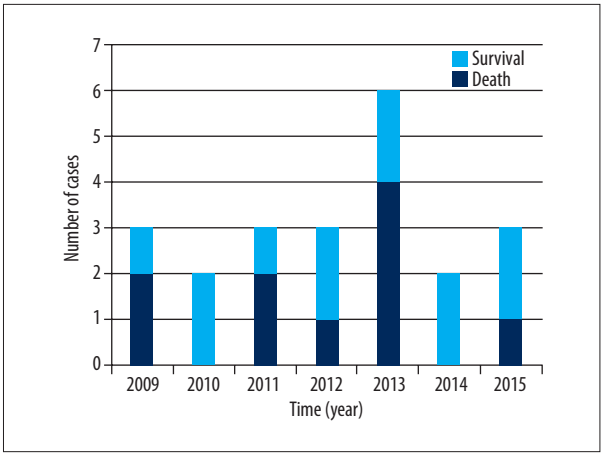


**Figure 1.** Change trends of cases and survival rates since 2009.

### Statistical analysis

Statistical analyses were performed using SPSS 16.0 (Chicago, Illinois, USA) and Prism 6 (GraphPad Prism 6.00, San Diego, California, USA). The comparison of the quantitative data between the two groups were determined via *t*-test or *t'* test depending on its distribution. The differences in constituent ratio among various groups were compared via Fisher's exact test, and univariate correlation analysis was conducted according to the Spearman method. Multiple longitudinal comparisons of parameters between survivors and nonsurvivors were made by two-way repeated-measures analysis of variance to test the influence of time on the variables. When a difference was detected, LSD method was used to adjust for multiple comparisons. All *p* values were two-sided and considered statistically significant if $p<0.05$.

## Results

### Demographic characteristics of study population

Twenty-three consecutive patients (82.6% were male) were ultimately enrolled in this study. The number of cases and the survival rate of discharge annually since 2009 was shown in Figure 1. Sixteen (69.6%) patients were transferred by ambulance from peripheral hospitals, and notably, seven (30.4%) patients were transported back to our institution on ECMO, including three cases where the patients were transferred from Hebei Province to Tianjin. There were five patients (21.7%) with influenza A (H1N1) including two patients who had been transferred to our hospital immediately after Cesarean procedures in another hospital. Bilateral pneumothorax or mediastinal emphysema occurred in these two patients and four other patients who were given cardiopulmonary resuscitation before ECMO establishment (Table 1).

**Table 1.** Study population demographics.

| Parameter | Value |
|---|---|
| Age | 46.1±18.5 |
| BMI (kg/m$^2$) | 25.1±2.3 |
| APACHE II score | 31.5±9.9 |
| Murray score | 3.3±0.2 |
| Etiology of ARDS *n* (%) | |
| Severe pneumonia | 19 (82.6) |
| Sepsis | 4 (17.4) |
| Comorbidities *n* (%) | |
| Coronary artery disease | 3 (8.7) |
| Hypertension | 7 (30.4) |
| Diabetes mellitus | 2 (8.7) |
| Stroke | 4 (17.4) |
| Septic shock *n* (%) | 6 (26.1) |
| Pattern of hospitalization *n* (%) | |
| Intra-hospital transport | 3 (13.0) |
| Inter-hospital transport on MV | 9 (39.1) |
| Inter-hospital transport on ECMO | 7 (30.4) |
| Admission via EMS | 4 (17.4) |

ARDS – acute respiratory distress syndrome; BMI – body mass index; ECMO – extracorporeal membrane oxygenation; EMS – emergency medical services; MV – mechanical ventilation.

### Clinical data during ECMO bypass

The median time for mechanical ventilation was 24.0 (4.0–56.8) hours before ECMO establishment, and the average time of ECMO assistance was 114.4±65.4 hours (range 26–305 hours). Veno-venous mode was applied in eighteen cases (78.3%), veno-arterial mode in four (17.4%), and conversion from V-V to V-A mode in one case (4.3%). The time for mechanical ventilation was 164.0 hours (105.6–259.3 hours) after ECMO establishment. Complications included: membrane oxygenator replacement (4 cases), major hemorrhage, including surgical sites or intracranial hemorrhage (9 cases), arterial/venous system embolism (4 cases), and catheter- related septicopyemia (2 cases). The length of ICU stay and the total length of hospital stay were (15.3±19.0) days and (20.6±19.3) days, respectively. The rate of survival to discharge without disability was 56.5%.





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**Table 2.** Comparison of clinical characteristics between survival and nonsurvival group.

| Parameter | Non-survival group (*n*=10) | Survival group (*n*=13) | *P* value |
|---|---|---|---|
| Male n (%) | 9 (90) | 9 (69.2) | 0.594 |
| Age | 51.7±18.5 | 40.8±18.4 | 0.180 |
| BMI (kg/m$^2$) | 25.80±3.02 | 24.55±1.39 | 0.216 |
| APACHE II score | 36.1±6.7 | 27.6±10.6 | 0.035* |
| NEmax prior to ECMO (ug/kg·min) | 0.80 (0.43–6.25) | 0.50 (0.31, 3.93) | 0.283 |
| Intervals | | | |
| MV-ECMO (h) | 43.3 (4.8, 222.0) | 12.5 (4.0–24.0) | 0.093 |
| Duration of MV after ECMO (h) | 118.3 (48.4, 444.0) | 176.0 (123.88, 226.75) | 0.456 |
| ICU stay (days) | 4.5 (2.0, 18.8) | 14.8±10.1 | 0.077 |
| Hospital stay (days) | 4.5 (2.0, 18.8) | 24.6±9.2 | 0.015* |
| Duration of ECMO support (h) | 117.1±87.2 | 112.2±44.0 | 0.867 |
| Transfusions | | | |
| Albumin (g) | 106.3 (68.8, 376.9) | 122.5 (48.1, 189.6) | 0.722 |
| Plasma (ml) | 0 (0, 2650.0) | 400 (0, 1627.5) | 0.900 |
| Packed red blood cell (ml) | 0 (0, 2650.0) | 600 (0, 1725.0) | 0.596 |
| Acute kidney injury n (%) | 9 (90) | 4 (30.8) | 0.011* |
| Septic shock *n* (%) | 3 (30) | 3 (23.1) | 1.000 |
| Pre-ECMO CPR *n* (%) | 3 (30) | 0 (0) | 0.078 |
| ECMO-related complications *n* (%) | | | |
| Oxygenator replacement | 4 (40) | 0 (0) | 0.029* |
| Embolization of arterial/venous system | 1 (10) | 3 (23.1) | 0.594 |
| Catheter related infection | 3 (30) | 5 (38.5) | 0.675 |

BMI – body mass index; CPR – cardiopulmonary resuscitation; NEmax – maximal dosage of norepinephrine prior to ECMO; MV – mechanical ventilation; * *P*<0.05.

### Clinical data among patients with different prognoses

The difference in APACHE II scores, proportion of acute kidney injury (defined by the standard from the Acute Kidney Injury Network [11]), membrane oxygenator replacement between the survivor group and nonsurvivor group were statistically significant ($p<0.05$) (Table 2). The univariate correlation analysis showed that a high APACHE II score ($r=-0.439$, $p=0.041$), occurrence of acute kidney injury ($r=-0.574$, $p=0.005$), membrane oxygenator replacement ($r=-0.516$, $p=0.014$) were significantly negatively correlated with prognosis. The biochemical index evolution analysis showed that there were significant changes in blood platelet count, albumin, total bilirubin, blood urea nitrogen, oxygenation index ($PO_2/FiO_2$), and fibrinogen evolution in the overall group within the first 72 hours after ECMO establishment. The blood platelet counts and fibrinogen levels significantly decreased over time after assistance while the albumin, oxygenation index, total bilirubin, and blood urea nitrogen all significantly increased (Table 3). The results of intragroup comparison among these parameters are shown in Figure 2. Further intergroup comparative analyses demonstrated that fibrinogen level at 24 hours and platelet count at 72 hours in the nonsurvivor group were much lower than those of the survivor group; however, the level of blood urea nitrogen at 24 hours and 48 hours were significantly higher in the nonsurvivor group than the survivor group.





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**Table 3.** Evolution of laboratory tests in the first 72 h after ECMO initiation in survival and nonsurvival groups.

| Parameter | Group | T -0 | T -24h | T- 48h | T -72h |
|---|---|---|---|---|---|
| White blood cell (×10$^9$/L) | Death | 9.7±5.9 | 8.9±5.2 | 9.5±4.8 | 11.3±6.1 |
| | Survival | 13.6±7.1 | 13.8±6.0 | 13.1±6.0* | 14.0±5.5* |
| Hemoglobin (g/L) | Death | 105.6±19.4 | 105.0±15.2 | 106.6±6.7 | 96.9±7.7 |
| | Survival | 107.7±20.0 | 107.1±10.8 | 105.8±10.2 | 106.7±11.3 |
| Platelet count (×10$^9$/L) | Death | 132.4±89.4 | 95.0±63.1 | 74.4±70.0* | 53.0±43.4* |
| | Survival | 126.6±62.7 | 107.0±47.7 | 95.9±41.5 | 100.5±42.0 |
| Albumin (g/L) | Death | 28.8±5.3 | 31.8±6.2 | 37.2±12.6 | 35.4±3.5 |
| | Survival | 29.3±6.5 | 33.8±5.1 | 35.1±6.0* | 34.8±4.6* |
| Total of bilirubin (umol/L) | Death | 20.5±14.9 | 24.5±12.8 | 37.2±21.3 | 44.1±28.4 |
| | Survival | 31.9±20.2 | 41.0±30.9 | 51.0±41.2 | 58.3±44.5 |
| Urea nitrogen (mmol/L) | Death | 11.6±8.5 | 14.2±7.2* | 17.5±8.3* | 17.4±9.7 |
| | Survival | 7.2±3.7 | 8.8±4.8 | 9.7±5.1 | 10.7±7.3 |
| Serum creatinine (umol/L) | Death | 152.1±151.0 | 146.0±124.5 | 156.0±118.2 | 151.1±115.9 |
| | Survival | 87.8±75.4 | 93.8±66.1 | 96.3±70.8 | 89.4±57.4 |
| Lactates (mmol/L) | Death | 5.14±2.52 | 3.34±1.32 | 3.53±2.55 | 2.93±1.33 |
| | Survival | 3.32±2.70 | 3.02±1.00 | 2.83±1.36 | 2.05±1.27 |
| Oxygenation index (mmHg) | Death | 76.1±55.7 | 229.5±95.7 | 259.4±104.0 | 255.5±134.0 |
| | Survival | 101.1±80.8 | 238.3±88.6 | 311.6±116.1 | 298.3±63.5 |
| Prothrombin (%) | Death | 59.7±21.1 | 61.4±26.4 | 57.4±17.6 | 59.0±17.3 |
| | Survival | 71.0±28.4 | 71.3±23.6 | 88.0±30.9 | 79.4±34.9 |
| Fibrinogen (g/L) | Death | 3.50±1.78* | 2.86±1.65 | 2.42±1.43 | 2.44±1.30 |
| | Survival | 5.53±2.42 | 5.27±3.08 | 4.11±2.68* | 3.69±2.10* |

* $P$<0.05compared to the survival group at the same time point. T-0 just after ECMO establishment; T-24h, -48h, -72h represent time points of 24, 48, and 72 hours after ECMO establishment.

### Patients transferred by different means

Sixteen patients referred for ECMO in outside hospitals were successfully transported to our institution by ambulance. Nine were transferred on a standard ventilator and the other seven were transferred to our institution on ECMO, which was initiated by our team at the original hospital. Table 4 compares the clinical characteristics of transportation with the two methods. We discovered that the patients were older (though not statistically significant) and with poorer Murray scores and oxygenation indexes before transfer in the ECMO assistance group compared with those in the conventional transfer group, however, patient oxygenation indexes improved significantly and ventilator conditions were substantially downregulated after transfer in the case of an equivalent average transfer distance. Hemodynamic indexes, such as heart rate and systolic pressure, also improved, although this observation may not constitute a statistical difference due to the small number of cases.

## Discussion

Following major improvements in ECMO technology and supportive evidence obtained in a series of recent clinical trials [6–9], ECMO is, as of now, utilized frequently to treat severe ARDS patients. Early application of ECMO may help to avoid substantial lung and sequential organ dysfunction via inhibited systemic release of inflammatory mediators induced by high concentrations of oxygen and high-volume ventilation [12–14]. Through a 15-year retrospective analysis,





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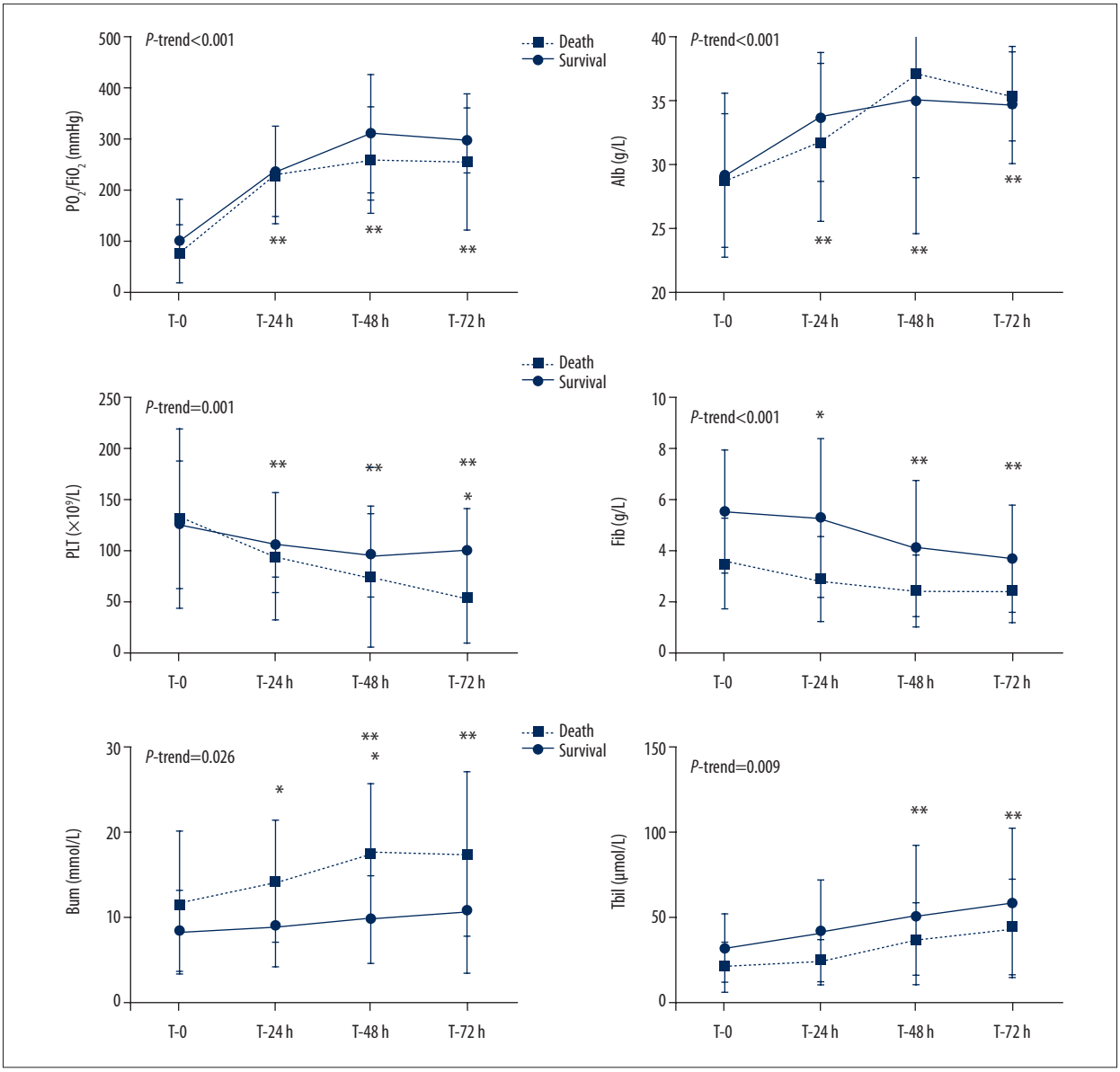


**Figure 2.** Biochemical index evolution of survivors and nonsurvivors within the first 72 hours after ECMO establishment. Plots show mean versus time, bars represent standard deviation. * $p<0.05$ intergroup comparison between survivors and nonsurvivors at the same time point; ** $p<0.05$ intragroup comparison with the value at the first time point (LSD method). Alb – albumin; Bun – blood urea nitrogen; Fib – fibrinogen; PLT – platelet count; Tbil – total bilirubin.

Hemmila et al. found that the actual survival rate of severe ARDS patients given ECMO reached 52%, though it was expected to be less than 20% [15].

The data we gathered in this study showed that a significant improvement in hemodynamic function and normalization of blood gases with simultaneous reduction of inotropic requirements and ventilator parameter settings occur within the first 24 hours of ECMO support. As an ECMO referral center, we have implemented ECMO support for severe ARDS patients since 2009. Our results demonstrate quite favorable results – an over 50% survival rate – after a mean support interval of approximately five days. Notably, 16 cases of inter-hospital transportation were completed sucessfully in this series, including seven transports with mobile ECMO and the first domestic inter-provincial transport over a distance of 125 km by ground.

Although general guidelines for ECMO initiation do exist, it remains difficult to make a decision on cannulation in real-world clinical practice. Early objective individual risk assessment is needed to aid the proper selection of candidates, compare success rates across different centers, and augment the predictive





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**Table 4.** Clinical comparison between patients transferred conventionally and on ECMO support.

| Parameter | Conventional mode (n=9) | ECMO-assisted mode (n=7) | *P* value |
|---|---|---|---|
| Age | 38.9±15.4 | 58.9±22.0 | 0.050 |
| APACHE II score | 25.7±11.6 | 33.4±6.9 | 0.139 |
| Murray score | 3.2±0.2 | 3.5±0.2 | 0.039* |
| Inter-provincial transport n (%) | 4 (44.4) | 3 (42.9) | 1.000 |
| Distance of transport (km) | 47.0±39.8 | 13 (8.7, 114.7) | 0.837 |
| Duration of transport (min) | 66.0±37.9 | 60.6±43.8 | 0.794 |
| CPR during transport n (%) | 3 (33.3) | 0 (0) | 0.213 |
| Heart rate before transport | 126.5±12.3 | 139.3±12.5 | 0.060 |
| SBP before transport | 125.6±10.2 | 120.5±16.9 | 0.465 |
| $FiO_2$ before transport (%) | 100 | 100 | 1.000 |
| PIP before transport (cmH2O) | 37.8±2.2 | 39.6±2.7 | 0.163 |
| OI before transport (mmHg) | 130.5±65.9 | 54.3±33.7 | 0.015* |
| HR after transport | 115.3±37.3 | 105.8±27.6 | 0.582 |
| SBP after transport | 120.2±14.6 | 132.7±10.9 | 0.080 |
| $FiO_2$ after transport (%) | 95.2±9.2 | 46.4±5.9 | <0.001* |
| PIP after transport ($cmH_2O$) | 35.3±2.8 | 22.5±3.0 | <0.001* |
| OI after transport (mmHg) | 103.2±69.5 | 218.3±57.8 | 0.003* |
| Multiple organ failure *n* (%) | 4 (44.4) | 3 (42.9) | 1.000 |
| ICU stay (days) | 19.8±27.6 | 13.6±13.4 | 0.595 |
| Hospital stay (days) | 24.0 (2.5,31.5) | 20.9±15.2 | 0.758 |
| Survival to discharge n (%) | 4 (44.4) | 4 (57.1) | 1.000 |

CPR – cardiopulmonary resuscitation; HR – heart rate; PIP – peak inspiratory pressure; OI – oxygenation index, equal to $PaO_2/FiO_2$); SBP – systolic blood pressure; * $P<0.05$.

performance of prognosis. In the specific population investigated here, factors associated with poor outcomes according to the literature include old age [6,15–22], lengthy duration of mechanical ventilation prior to ECMO [15,16,18,19,22,23], high levels of organ failure [15,16,19,20–22,24], and immunosuppression [18,22,24].

In this study, we found that patients less than 45 years of age had a markedly better prognosis. In fact, in younger patients, favorable outcomes were achieved even independent of other organ failure. Based on this and information from a previous study with similar findings [21], we presumed that ECMO should not be contraindicated on the basis of organ dysfunction in young patients.

Lengthy duration of mechanical ventilation prior to ECMO, a well-known predictor of poor prognosis, inextricably indicates severe VILI [2,25]. Two valuable predictive models both demonstrated mechanical ventilation more than seven days before ECMO support was the cutoff point for decline in prognosis [18,22], but that ECMO exerted the most beneficial effect when initiated early to within less than 48 hours [18]. We also found that the nonsurvivor group had a longer interval of pre-ECMO mechanical ventilation, although the difference was not statistically significant. During the H1N1 pandemic (2009–2010) we received some young adults who had been given prolonged ventilation prior to arriving at our center, as they were young, previously fit (some even having given birth just prior to treatment). The ECMO outcome was indeed disappointing for those who had been ventilated for more than seven days. The ELSO database also showed that the duration





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of mechanical ventilation was no longer associated with mortality in the most recently treated patients, which may be attributed to the fact that the number of patients treated after seven days of mechanical ventilation decreased with time [16].

Excessive organ failure (marked by high APACHE or SOFA score), as determined prior to administering ECMO [21] or at day 1 after ECMO initiation [17,24], was consistently shown to be a strong predictor of poor prognosis. We discovered that the incidence of acute kidney injury during assistance was one of the mortality risk factors, however, interpreting the prognostic value of changes in hepatic functions proved highly complex. As a component of medical therapy, an abundance of albumin was transfused into the two groups which had different prognoses to maintain adequate colloid osmotic pressure; accordingly, the albumin levels of both groups were shown to increase significantly within 72 hours after assistance began and there was no significant difference between the groups. The levels of blood urea nitrogen 24 hours and 48 hours after ECMO establishment in the nonsurvivor group were significantly higher than those of the survivor group, which indicated differing intensity of catabolism between the groups despite their shared trend of significant increase over time. We inferred that the balance between anabolism and catabolism at early stages may be an important factor in prognosis. We further suggest that the causes of the abnormal rise in total bilirubin level in the survivor group may be: 1) the total bilirubin levels at different points in time in the survivor group, including two patients with the etiology of sepsis, were significantly higher than those in the pneumonia group; and 2) the three patients with multiple organ failure in the nonsurvivor group died within 72 hours after ECMO establishment (which was excluded in the statistics). We also found that the occurrence of coagulopathy within 72 hours may be a valuable marker for predicting intrahospital prognosis. Although both groups presented significant decreasing trends in platelet count and fibrinogen within the first 72 hours of ECMO support, said decrease occurred at a quicker rate in the nonsurvivor group compared to the survival group; to be specific, the intergroup difference at the same time point reached statistical significance at 72 hours for platelet count and at 24 hours for fibrinogen. The fibrinogen level of the nonsurvivor group at any time point was much lower than that of the survivor group. Our data confirmed the previous finding that high fibrinogen concentration following ECMO initiation has a protective effect and positive predictive value of treatment success, which may be attributable to its indication of effective immune response and relative scarcity of bleeding disorders [26].

In addition to the predictors mentioned, our data also demonstrated that oxygenator replacement was a strong poor prognosis predictor. Patients whose oxygenator had been replaced often showed higher likelihood to be obliged to withdraw ECMO prematurely due to other complications. Similarly, a recent retrospective study on pediatric pneumonia managed with ECMO showed that any need to change ECMO circuit was a strong predictor of death [27]. We speculate, to this effect, that the occurrence of mechanical ECMO complications may be a valuable predictor of poor prognosis.

Another challenge posed in clinical practice is that it is unclear how to best and most safely administer ECMO support over long-distance transport [28]. Severely ill patients should ideally be transported to an ECMO center before they can no longer be transported by conventional means [6], but this is not always possible because sometimes a patient's course can derteriorate extremely quickly. For this reason, inter-hospital transportation techniques for administering ECMO en route to an ECMO center are a valuable, and urgent, consideration.

Though inter-hospital transport on ECMO was first reported in 1986, it was not widely launched until the 2000s [17,20,29–32]. Recently, researchers from a regional referral center found that a proportion of 69% of severe ARDS patients required ECMO during transport, and further, that ECMO treatment resulted in a 60% survival rate [33]. In a series of 124 patients treated at a Danish center, 85% of patients who received ECMO via mobile unit before being transferred to the referral hospital had a survival rate of 71% [17]. Similarly, in a German cohort study [20], adults with severe cardiopulmonary failure benefited from life-saving ECMO administration during long-distance inter-hospital ground transport.

To the best of our knowledge, there is scant literature on ECMO support as it applies to severe respiratory failure patients from China, and there has been practically no research on mobile ECMO unit efficacy over long-distance inter-hospital transport domestically. Transporting severe ARDS adults to centers where they receive specialized tertiary care has become routine – our institution, for example, now has a referral radius of 125 km. Transport on extracorporeal support is obviously more complicated and resource-dependent than conventional transport, as it requires larger vehicles and larger transport teams, and is more equipment-intensive. Any delays from initiating ECMO to departure are closely associated with poorer outcomes [34,35].

Although worse oxygenation indices and Murray scores before transport existed in patients transferred on ECMO in our study, the oxygenation index was significantly improved over the conventional transport group, and the ventilator parameters were much lower post-transport, likely attributable to the fact that the use of ECMO allowed a rapid correction of blood gases and safer transport. Furthermore, the rapid solution of the hypoxia allowed us to adopt a protective ventilation strategy during transport. Although the potential for complications during transport invariably exists, we have been pleased with





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the overall results in our initial experience. The group who were retrieved via a mobile ECMO team in our series had a comparable survival rate to conventional transport (57.1% *vs.* 44.4%, $p$=1.000) or the non-transport group treated with ECMO in our center (57.1% *vs.* 66.7%, $p$=1.000), which is in agreement with other observational studies similar to this one [18,34,36,37].

The utilization of ECMO treatment in severe ARDS in China is still in its initial stages. Retrospective analysis from six domestic ECMO centers from 2002 to 2010 showed that ECMO was used in only 65 cases (about 19% of the total) for respiratory support, and the overall survival rate was not satisfactory (approximately 26%) [38]. Ventilator-associated lung injury secondary to long-term, high-condition mechanical ventilation is the Achilles heel of the recovery of lung function. Regardless, for properly selected severely ill patients, we continue to encourage our colleagues to recommend ECMO support in the future, and to consider transporting patients under ECMO support.

## Conclusions

ECMO is an effective alternative option for severe ARDS. APACHE II score on admission, occurrence of acute kidney injury, membrane oxygenator replacement during ECMO support, and that the evolution of levels of urea nitrogen, platelet, and fibrinogen within the three days of initial ECMO assistance may help to determine the prognosis. By establishing a well-trained mobile ECMO team, a long-distance, inter-hospital transport can be administered safely.

### Disclosure

No conflicts of interest.

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