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# Effectiveness of ECMO for burn-related acute respiratory distress syndrome

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ABSTRACT

*Introduction:* Acute respiratory distress syndrome (ARDS) is a complication that affects approximately 40% of burn patients and is associated with high mortality rates. Extracorporeal membrane oxygenation (ECMO) therapy is a management option for severe refractory hypoxemic respiratory failure; however, there is little literature reporting the effectiveness of this therapy in burns. Our study objective was to review patient outcomes in burns following severe ARDS treated with ECMO.

*Methods:* We retrospectively reviewed all patients treated with ECMO for ARDS who received their burn care at a single regional burn center between 9/1/2006 and 8/31/2016. Primary patient outcome examined was discharge disposition.

*Results:* We identified 8 patients who had ARDS secondary to burn who were placed onto ECMO during this 10-year period. The average APACHE score, SOFA score, and P/F ratio were 21±3, 9±2, and 59±8, respectively, at the time of decision for ECMO. No ECMO-related complications were identified. Out of the 8 patients reviewed, 1 died, 4 were discharged to acute rehabilitation or a long-term acute care facility, and 3 were discharged to home.

*Conclusion:* Mortality in burn patients with ARDS who are managed with ECMO is extremely low. Careful selection and timely intervention with ECMO contributed to good clinical outcomes.



## 1. Introduction

Acute respiratory distress syndrome (ARDS) is a complication of burn injury that affects approximately 40% of mechanically ventilated patients [1]. Lung injury in burn trauma can be attributed to smoke inhalation, fluid resuscitation, ventilator acquired pneumonia, or inflammation secondary to the burn injury itself. Pulmonary failure is a major determinant of both morbidity and mortality in burn patients [2]. Mortality rates associated with ARDS have been reported at 40% without any additional comorbidities such as burn wounds or multi-organ failure [3,4]. Mortality rates in severe ARDS associated with burns have been reported to be as high as 50% [1]. Classically, ARDS treatment is supportive with low tidal volume ventilation [5]. In severe cases of ARDS, traditional management methods have often proven insufficient, resulting in the use of rescue strategies including advanced ventilator modes, prone positioning, and inhaled nitric oxide.

Extracorporeal membrane oxygenation (ECMO) is a therapy sometimes used for severe refractory hypoxemic respiratory failure. ECMO works as an artificial lung, facilitating gas

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exchange outside of the body, which allows time for lung recovery. The effectiveness of ECMO has improved since its introduction [6]; however, little has been reported on its effectiveness in the setting of severe ARDS associated with burn injuries. Furthermore, the literature that exists consists primarily of small retrospective case studies, case reports, and case-control studies [7–15]. These studies report a wide range of mortality rates. A meta-analysis performed in 2013 indicated that the use of ECMO for salvage from hypoxemic respiratory failure may be beneficial for scalds and when used for limited time frames, but ultimately concluded that understanding the utility of ECMO for burn patients with respiratory failure would require a larger patient population with similar ECMO selection critera [9].

The hypothesis for this study was that the use of ECMO in appropriately selected patients would result in decreased mortality associated with hypoxemic respiratory failure and burn injury.

## 2. Methods

This retrospective review included adult and pediatric patients with severe acute lung injury and acute burn injury admitted to a single regional Burn Trauma Intensive Care Unit (BTICU) between September 1, 2006 and August 31, 2016. Inclusion criteria for patients consisted of severe hypoxemic respiratory failure with veno-venous ECMO following acute burn injury. Patients were excluded from this study if their respiratory failure was not associated with an acute burn injury. Patients were identified using the institutional National Burn registry and the institutional ECMO/Extracorporeal Life Support registry at the primary facility housing the burn center and the associated children's hospital. Exemption from the Institutional Review Board of both facilities was obtained for this study.

The decision to consult cardiothoracic surgery for initiation of ECMO was at the discretion of the attending burn surgeon based on the patient's failure to respond to salvage maneuvers for hypoxemia. Each patient referred for ECMO consultation met Berlin Criteria for severe acute respiratory distress with PaO2/FiO2 ratio of less than 100 [6].

The primary measured outcome was patient mortality. Data points collected included demographics (age, sex, and body mass index), injury information (burn mechanism, TBSA burn injury), clinical data prior to ECMO initiation (APACHE II Score, SOFA Score, Murray Score, days with PaO2/FiO2 ratio less than 100, timing of burn excision in relationship to placement on ECMO, infectious complications, blood gas values, and ventilator settings) and clinical data during ECMO (duration of ECMO, presence of ECMO-related bleeding or thrombosis, cerebrovascular accident (CVA) related to ECMO). The effects of debridement and excision prior to ECMO were compared to ECMO related bleeding. Components of APACHE II and SOFA scores were averaged for the 24 h prior to initiation of ECMO. Patient outcomes were then compared to predicted mortality according to APACHE II scores, SOFA scores, and ARDS severity.

## 3. Results

During the ten-year review period 8 patients (6 pediatric, 2 adult) admitted to a regional BTICU with burn injury complicated by severe ARDS were referred for ECMO. The median hospital stay was 69 days (IQR: 45–80) and the median time on ECMO was 11 days (IQR: 6–15), with the minimum and maximum time on ECMO of 4 days and 29 days. The median time from burn injury to ECMO was 7.5 days (IQR: 3.75–11). There were 6 males and 2 females. Median age was 5.9 (IQR: 3.2–13.6) years with a minimum of 11 months and maximum of 24 years; two of the eight patients were over age 15. The mechanism of burn injury in the study included flame (3, 37.5%), scald (2, 25%), electrical (2, 25%), and friction and contact (1, 12.5%). The median total body surface area (TBSA) percentage effected by burn injury was measured as 17% (IQR: 13.5–29.9) (Table 1). Of the patients included, 3 (37.5%) were diagnosed with or had suspected inhalation injury at the time of admission and 1 (12.5%) presented with a pneumothorax. Prior to ECMO cannulation 4 participants developed ventilator acquired pneumonia, and 3 were in distributive shock refractory to their hypoxemic respiratory failure with vasopressor support.

At the time of initiation of ECMO, all patients met the Berlin Criteria for severe ARDS (PaO2/FiO2 ratio < 100) with a median PaO2/FiO2 ratio of 57.2 (IQR: 52.1–68.9); all of the patients were considered to be in severe ARDS by Berlin criteria for less than 24 h prior to ECMO cannulation. PEEP measurements ranged from 6.6 to 18 mmHg with a median of 14 mmHg (IQR: 12–16.5). Median APACHE II, SOFA, and Murray scores were 22 (IQR: 19–23), 10 (IQR: 8–11), and 3.38 (IQR: 3–3.5) respectively (Table 1).

Of the potential ECMO related complications – thrombus, bleeding, CVA, and infection – only bleeding was reported. Of the 5 patients with bleeding while on ECMO, 3 underwent

**Table 1 – Patient burn injury and acuity of illness data.**

| Patient | TBSA burn injury (%) | PaO2/FiO2 ratio | PEEP (mmHg) | APACHE II | SOFA | Murray |
|---|---|---|---|---|---|---|
| 1 | 34 | 68.3 | 14 | 23 | 11 | 3.5 |
| 2 | 20 | 70.5 | 15 | 20 | 8 | 3.75 |
| 3 | 31 | 49.8 | 6.6 | 21 | 12 | 3 |
| 4 | 29.5 | 72.4 | 18 | 24 | 12 | 3.5 |
| 5 | 13.8 | 51 | 18 | 24 | 9 | 3.5 |
| 6 | 14 | 56 | 14 | 26 | 11 | 3 |
| 7 | 12.5 | 52.5 | 14 | 23 | 13 | 3.25 |
| 8 | 9.5 | 58.3 | 10 | 18 | 6 | 3 |

excision of wounds prior to initiation of ECMO. These patients' bleeding was localized to the area of their excised wounds. In the remaining 2 patients who received 2 or more units of pRBCs, bleeding occurred at the site of ECMO cannulation. Bleeding was significantly more likely in patients who underwent wound excision prior to ECMO versus patients who did not (Fisher' exact test, p=0.0179). However, excised and unexcised patients had no difference in mortality.

Of the 8 ECMO patients, 1 died, 4 were discharged to acute rehabilitation or a long-term acute care facility, and 3 were discharged home (Fig. 1). Overall survival was 87.5%. The single patient who died during ECMO suffered fungal sepsis, multi-organ failure and DIC, which were thought to be sequelae of burn wound infection and not directly related to ECMO.

## 4. Discussion

In this study 7 of 8 patients treated with ECMO for severe ARDS following burn injury survived. APACHE II scores have been used to predict mortality rates of individuals admitted to ICUs. Based upon APACHE II scoring, the predicted mortality of our study cohort prior to ECMO was 40%. A SOFA score of 9–12 is correlated with a morality rate of 40%–50% according to previous described methods [16,17]. Using the Berlin criteria for ARDS all of the study participants met the diagnostic criteria for the severe form (PaO2/FiO2 < 100). The ARDS Definition Task Force (ADTF) found mortality rates of severe ARDS have been 45% (95% confidence interval: 42–48%) [6]. These mortality rates did not take into account additional ARDS comorbidities. All three mortality prediction models would indicate our patients had an expected mortality rate of 40%–50%, which is a markedly worse than our observed mortality rate (Fisher's exact test, p=0.08).

Rates of hemorrhage associated with ECMO range from 10 to 30% [18,19]. Hemorrhage can occur at multiple locations including surgical sites, cannulation sites, or into the site of a previous invasive procedure [20]. Hemorrhage with transfusion of more than 2 units of PRBCs was the most common ECMO-related complication in our patients. Bleeding from excision sites occurred in all patients whose wounds were excised prior to ECMO. In burn patients the decision for timing of excision is complicated by the known association of early excision with improved survival, which obviously must be weighed against the risk of hemorrhage and associated complications in patients who are developing severe ARDS and may benefit from referral to ECMO. It is worth noting we did not collect detailed information regarding transfusion use in patients who did have ECMO-related bleeding.

The decision to utilize ECMO requires thoughtful patient selection. Patients in this study who showed signs of advanced respiratory failure were identified early and considered for ECMO by the burn surgeons involved in their care. Use of ECMO was not pursued until these patients failed other rescue strategies including inverse ratio ventilation and chemical paralysis. In addition to failing advanced respiratory techniques, referred patients also met the Murray Criteria with a median score of 3.38 (IQR: 3-3.5). The Murray Score was developed to help identify potential candidates of ECMO cannulation; the score includes lung compliance, PaO2/FiO2, lung consolidation, and PEEP. Those who receive a score above 3 are recommended to be transferred to an ECMO-capable center to significantly improve survival without severe disability [21]. The patients in this study also met the Berlin Criteria for severe ARDS (PaO2/FiO2 > 100) for the duration of 1 day or less prior to ECMO cannulations. The rapid progression of their hypoxemic respiratory failure highlights the importance of moving toward consideration of ECMO early in the patient's care course. Based upon the experience at our center, we recommend early consideration of ECMO consultation in burn patients with rapidly declining pulmonary function and no other organ system failure.

Several limitations must be considered in this study. First, the retrospective nature of this study has inherent limitations, primarily the availability and accuracy of information within the medical record [22]. Second, the cohort was demographically skewed in respect to age, with a preponderance of pediatric patients. The median age was 9.6 (IQR 3.7–13.2), with only two adult patients. While our burn center admits significantly more adult than pediatric patients, this may represent cognitive bias on the part of the surgeons to "do everything" for pediatric patients; the decision making process around ECMO merits further exploration. Notably, the Extracorporeal Life Support (ECLS) registry reported similar rates of survival for patients treated with ECMO for pulmonary indications as 66% and 67% for adults and pediatrics, respectively. The rates of survival to discharge were reported

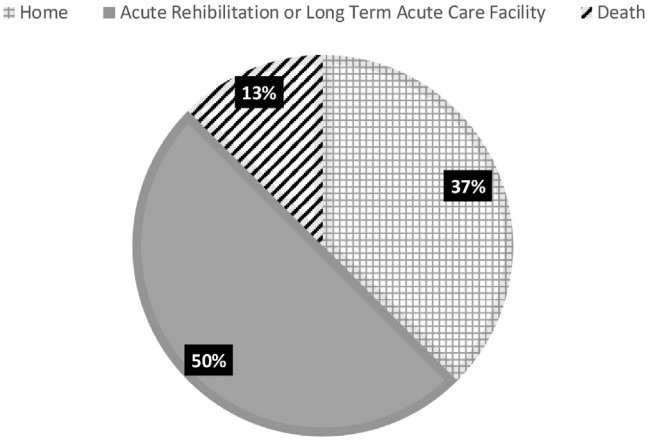


**Fig. 1 – Discharge destination summary of all patients in this cohort.**

as 57% for both groups [20,23]. Finally, this study had a relatively small number of patients due to rarity of ECMO support in the setting of ARDS in burn patients. The patient cohort for this study came from a single center BTICU over a ten-year span, yielding only 8 patients who were placed on ECMO. Due to the rarity of this intervention, future prospective multi-center observational or interventional studies would better assess patient selection criteria and outcomes.

## 5. Conclusions

Severe burn injury is commonly complicated by ARDS, especially in patients with inhalation injury. Unlike burn injuries, lung injury is treated mainly through supportive care. ECMO has been shown to improve outcomes of patients with severe ARDS, though data on the use of ECMO in burn patients with associated ARDS remains scarce. This study sought to show that ECMO improved survival in patients with burns and ARDS. Timely decision for ECMO and appropriate patient selection can result in excellent patient outcomes in burn-associated ARDS and hypoxemic respiratory failure. Multi-center observational studies would help to definitively establish the role, timing, and decision for ECMO in burn patients with ARDS.

## Conflict of interest

The authors have no competing interests to declare for this work.

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