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Extracorporeal Life Support for the Adult Respiratory Distress Syndrome due to Severe *Legionella* Pneumonia

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Abstract

Background—*Legionella* is a common cause of community-acquired pneumonia (CAP) and is second only to Pneumococcal pneumonia as a cause of severe CAP that requires treatment in an intensive care unit. We report a case series of patients with severe *Legionella* pneumonia who developed the adult respiratory distress syndrome (ARDS), failed ventilator management, and required extracorporeal life support (ECLS).

Methods—We performed a retrospective review of all patients treated with ECLS at the University of Michigan for severe ARDS as a result of *Legionella* pneumonia from 1994 to 2006.

Results—A total of twelve patients with a diagnosis of *Legionella* pneumonia were treated with venovenous (V-V) ECLS over this time period. Nine of these twelve (75%) were successfully treated and weaned off ECLS and 8 patients (67%) survived to hospital discharge. Two of these twelve (13%) died of multisystem organ failure, one patient (8%) died from global hypoxic encephalopathy, and one patient (8%) was weaned from ECLS but ultimately died of liver failure. Renal failure requiring some form of continuous dialysis occurred in seven patients (58%) and the survival for this sub-set of patients was 43%.

Conclusion—Extracorporeal life support for severe ARDS associated with *Legionella* pneumonia is an effective treatment option when mechanical ventilation fails. *Legionella* associated renal failure is associated with a worse prognosis.

Keywords

ECLS; *Legionella* pneumonia; ARDS; renal failure

INTRODUCTION

Since the first known outbreak of Legionnaires' disease at a 1976 meeting of the Pennsylvania Chapter of the American Legion, *Legionella* have been recognized as a common cause of community-acquired pneumonia.^{1,2} Cigarette smoking, chronic lung disease, and immunosuppression (especially that caused by corticosteroid therapy) have

been consistently implicated as risk factors for the development of severe *Legionella* pneumonia.^{3,4}

Legionella pneumonia is often clinically and radiographically similar to other forms of pneumonia, although presentations may range from mild flu-like symptoms to a fulminating course complicated by multiple organ failure. The species *Legionella pneumophila* accounts for 85–90% of cases and is separated into over 40 serogroups (of which serogroups 1, 4 and 6 most commonly cause illness).⁵ The severity of the disease is often determined by the patient's immunocompetency as well as the timeliness of appropriate antibiotic treatment.^{6,7} Those patients admitted to the ICU for severe *Legionella* pneumonia have a mortality rate of 33%.⁸

Extracorporeal life support (ECLS) is an established option for treating severe ARDS for various etiologies when mechanical ventilation fails.⁹ Others have described cases in which ECLS was used successfully to treat ARDS stemming from *Legionella* pneumonia.^{10,11} In one series of sixteen patients treated with ECMO at a major UK ECLS center from 1989 to 2001, eleven survived.^{12,13} Two other groups have reported single cases in which ECLS was successfully used to treat a patient with ARDS complicating Legionellosis.^{10,11}

We performed a retrospective review of the patients with severe *Legionella* pneumonia treated at our institution with ECLS to compare this institution's mortality rate to previously published data and to identify factors that may be associated with beneficial use of ECLS.

METHODS

We reviewed the medical records of those adult patients treated with ECLS for ARDS secondary to *Legionella* pneumonia at the University of Michigan between 1994 and 2006; $n = 12$. These twelve patients represent a small fraction of all patients treated for *Legionella* pneumonia over that same time period; while most were successfully managed with conventional ventilation, these twelve failed maximal ventilatory management and met the institution's criteria for ECLS (listed in Table 1).

We collected data on demographics, comorbidities, hemodynamic parameters, and ventilatory support used before ECLS. Outcome measures included survival to hospital discharge, duration of ECLS, days on the ventilator, days in an intensive care unit, total length of hospital stay, adjunct therapies and procedures, and complications. All patients underwent veno-venous bypass (the standard mode of ECLS for an adult patient with respiratory failure who does not require cardiac support). Although the time between the patient's first presentation for medical attention and the actual initiation of antibiotics is a relevant factor in the treatment of legionellosis (as with other forms of pneumonia), we did not have enough information from the medical records to adequately assess this factor.

Veno-venous bypass requires the percutaneous placement of a 23 French venous drainage cannula within the femoral vein and a 21 French re-infusion line within the right internal jugular vein. All patients require systemic heparinization to maintain an activated clotting time (ACT) between 180–200 sec. Pump flow achieved with the use of a roller-pump system is typically maintained between 3–6 L/min. Patients are sedated and paralyzed. The patients'

pulmonary mechanics are reviewed daily, as is oxygen diffusion across the native lung. Once a patient is ready to have ECLS discontinued, the circuit is temporarily clamped to allow his or her respiratory status to be fully characterized before decannulation.

Ventilator management for these patients typically consists of inverse ratio pressure-controlled ventilation with a peak inspiratory pressure of 30 mm Hg and a positive end expiratory pressure (PEEP) usually maintained at 10 mm Hg. The fraction of inspired oxygen (FiO_2) is maintained at 30 to 40%. This ventilator strategy helps to minimize both barotrauma and oxygen toxicity during ECLS.

RESULTS

Between 1994 and 2002, twelve patients (three women and nine men) with an average age of 47.0 ± 7.7 years (range 33–57 years) were treated with V-V ECLS for severe *Legionella* pneumonia at the University of Michigan. Their demographic characteristics are summarized in Table 2. Eight patients (67%) had co-morbid illnesses, the most common being diabetes (4/12, 33%). Six patients (50%) had a smoking history. Seven patients (58%) had an elevated creatinine on admission and were classified as having renal failure. All seven of these patients required continuous renal replacement therapy during ECLS. The survival among this sub-set of patients was 43%.

ECLS became necessary for these twelve patients due to worsening oxygenation and in some cases hemodynamic instability. The clinical course of these twelve patients is briefly summarized in Table 3. Of the twelve patients, nine (75%) eventually recovered lung function well enough to undergo decannulation from ECLS. Survival to hospital discharge for these twelve patients was 67%. Two patients (13%) ultimately died of sepsis and multisystem organ failure while on ECLS. One patient (8%) was diagnosed with global hypoxic encephalopathy. One patient (8%) with a history of alcoholic hepatitis was able to be successfully weaned from ECLS but ultimately died from liver failure prior to hospital discharge.

These patients underwent an average of 283.3 ± 167.6 hours of ECLS. Those who survived to discharge underwent an average of 188.9 ± 70.5 hours of ECLS, while those who did not survive underwent 472.3 ± 141.7 hours. This difference was statistically significant ($U=1.0$, $P=0.011$). The mean length of stay was 25.5 ± 14.2 days and did not differ significantly between survivors and nonsurvivors (28.0 ± 16.8 vs 20.5 ± 6.0 ; $U=13$, $P=0.57$).

Eleven of the twelve (92%) patients underwent a tracheostomy. Ten of these were performed while the patient was on ECLS, at an average of 2.9 ± 1.9 days after initiation of ECLS. Seven of twelve patients (58%), including the four patients who died before discharge, required either continuous venovenous hemofiltration or continuous venovenous hemodialysis. Other complications (besides the acute renal failure in those patients) included bleeding at surgical sites, urinary tract infection, and abdominal compartment syndrome.

The surviving patients did not differ significantly from those who died in the number of days spent on the ventilator prior to ECLS therapy (mean 1.6 ± 2.4 vs. 1.8 ± 1.0 days; $U=11$, P

=0.38). The mean age of those who survived was 41 ± 6 years, significantly lower than the mean age of those who died (53 ± 3 years; $U=1.5$, $P=0.013$).

DISCUSSION

Of twelve patients treated with ECLS for ARDS stemming from *Legionella* pneumonia, 75% were able to be weaned from ECLS, and 67% survived to hospital discharge. The most common complication was renal failure (58% of patients required hemodialysis). These patients spent an average of 12 days on ECLS and had a mean length of stay of 26 days.

Patients with *Legionella* pneumonia who require ICU admission and the use of mechanical ventilation have a high mortality rate. Three studies reported mortality rates of 30, 33, and 36% among patients with legionellosis in the ICU.^{6,8,14}

Survival rates for adult patients requiring ECLS varies according to the etiology of cardio-respiratory failure. In adult patients receiving ECLS for cardiac support, studies have reported survival rates of 36% and 38%.^{15,16} Survival rates among patients undergoing ECLS for trauma have been reported at 50% and 63%.^{17,18} Survival rates for patients requiring ECLS for ARDS is 52%.⁹ In this context, the 67% survival rate for our cohort with legionellosis is noteworthy, especially given that their expected mortality without ECLS would have approached 100%.

The majority of patients who failed conventional management within our review had a rapid progression from hospital admission to maximal ventilator support. We speculate that ECLS is most successful if started when patients are in the early stages of a precipitous decline, reducing the damage from barotrauma. Patients, of course, worsen at varying speeds and begin ECLS at various stages in their illness, which prevents us from inferring anything more concrete on this topic.

Venovenous (V-V) ECLS was used in all twelve cases, since these patients experienced respiratory distress only and did not require cardiac support. V-V ECLS has been shown to be sufficient support in previous series of adults undergoing ECLS for purely respiratory indications, while reducing neurologic complications relative to venoarterial ECLS.¹⁹

Comorbidities of the patients in this study included diabetes (4 patients, 33%), chronic obstructive pulmonary disease (COPD) and immunosuppression following bone marrow transplant (one each). These comorbidities are associated with worse outcomes in *Legionella* pneumonia.⁶ Smoking, present in half of the twelve patients, is associated with the development of legionellosis and with mortality once infected.²⁰

Three patients had bleeding complications related to the anticoagulation necessary for ECLS. These complications included bleeding at cannulation sites, and some less common ones also related to hematologic factors (e.g., stroke, intraabdominal bleeding causing abdominal compartment syndrome). Lowering the risks due to anticoagulation remains one of the most pressing issues in the clinical use of ECLS and in research relating to ECLS.

The other noteworthy complication (and comorbidity), acute renal failure, is commonly associated with legionellosis. The mortality rate of legionellosis increases from 15% to 53% with associated renal failure.²¹ Furthermore, renal failure is also associated with ECLS and with worse outcomes of ECLS.²² However, all seven of the twelve patients (58%) had elevated creatinine levels prior to ECLS, suggesting that the etiology was primarily related to their legionellosis. Of these seven patients, only three (43%) survived. Thus, the higher mortality in this subgroup of patients suggests that *Legionella*-associated renal failure is associated with worse survival in patients that eventually require ECLS.

Unsurprisingly, age and ECLS run time were associated with lower survival, although the small number of cases presented limits the conclusions that can be drawn. Also, an important consideration in judging the baseline risk of mortality for patients with any form of pneumonia, which we were unable to examine in this study, is the time from presentation with and clinical suspicion of pneumonia to the initiation of intravenous antibiotics.²³

Tracheostomies and continuous hemodialysis or hemofiltration were used in a majority of patients. Early tracheostomies are consistent with generally accepted principles of ECLS, since they have been shown to reduce mortality in the critically ill.²⁴ Despite the increased risk of bleeding from ECLS, only one of eleven patients undergoing tracheostomy had bleeding at the tracheostomy site, suggesting that ECLS therapy should not preclude necessary procedures that may carry an increased bleeding risk.

ECLS is an established therapy for severe respiratory distress from various indications.^{9,18} This study suggests that extracorporeal life support for severe ARDS associated with *Legionella* pneumonia is an effective treatment option when mechanical ventilation fails, although renal failure in this setting carries a worse prognosis.

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Table 1Criteria for Extracorporeal Life Support²⁵

Hypoxemic Respiratory Failure
Failure of mechanical ventilation (PC-IRV) to reverse hypoxemia and improve lung compliance
Diffusely abnormal chest radiograph
Transpulmonary shunt > 30% on FiO ₂ > 0.6
Total static lung compliance < 0.5 ml/cm H ₂ O/kg (or <30ml/cm H ₂ O at Vt 10ml/kg)
Lack of PEEP recruitment response (PEEP 5 to 15 cm H ₂ O)
Hypercarbic Respiratory Failure
Uncorrectable hypercarbia with pH < 7 and PIP > 45, or
PaCO ₂ > 45 despite Ve > 200 ml/kg/min

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Table 2

Demographics and clinical summary of twelve patients with *Legionella* pneumonia requiring extracorporeal life support.

Patient #	Age	Sex	Comorbidities	Smoking history	Renal failure	Survived to Discharge
1	37	F	Breast Cancer / BMTx	No	No	Yes
2	41	M	Diabetes	No	No	Yes
3	39	M	Diabetes	Yes	No	Yes
4	50	M	Diabetes	Yes	No	Yes
5	55	M	Diabetes	No	Yes	No
6	52	M	Alcoholism	Yes	Yes	No
7	42	M	--	No	No	Yes
8	55	M	--	No	Yes	No
9	36	M	--	Yes	Yes	Yes
10	49	F	Cervical Cancer, COPD	No	Yes	Yes
11	49	M	--	Yes	Yes	No
12	33	M	--	Yes	Yes	Yes

Note: BMTx = bone marrow transplant

Table 3
Clinical course summary of twelve patients with *Legionella* pneumonia requiring extracorporeal life support.

Patient #	Renal failure	Days on Ventilator before ECLS	Last ABG before ECLS (pH / paCO ₂ / paO ₂ / pHCO ₃ / SaO ₂)	Hours on ECLS	Length of Stay	Underwent Tracheostomy	Survived to Discharge	Complications (not including renal failure)
1	No	0	7.32 / 75 / 44 / 23 / 93%	158	19	Yes	Yes	--
2	No	0	7.36 / 68 / 38 / 21 / 92%	134	14	Yes	Yes	--
3	No	0	7.22 / 56 / 46 / 18 / 83%	135	20	No	Yes	Mild bleeding at cannula site
4	No	2	7.44 / 61 / 32 / 21 / 92%	162	20	Yes	Yes	--
5	Yes	1	7.34 / 48 / 46 / 24 / 81%	295	13	Yes	No	global hypoxic encephalopathy
6	Yes	1	7.28 / 40 / 38 / 17 / 63%	499	23	Yes	No	sepsis
7	No	3	7.41 / 50 / 36 / 23 / 82%	138	24	Yes	Yes	--
8	Yes	3	7.36 / 44 / 43 / 24 / 77%	639	27	Yes	No	Bleeding at tracheostomy and chest tube sites, sepsis
9	Yes	7	7.25 / 79 / 47 / 21 / 93%	257	40	Yes	Yes	Urinary tract infection
10	Yes	0	7.45 / 46 / 44 / 31 / 82%	330	65	Yes	Yes	Mild bleeding at cannula site
11	Yes	2	7.26 / 39 / 39 / 17 / 57%	456	19	Yes	No	Liver failure, sepsis
12	Yes	1	7.17 / 58 / 38 / 22 / 67%	197	22	Yes	Yes	Abdominal compartment syndrome