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Veno-Venous Extracorporeal Life Support in Hemodynamically Unstable Patients with ARDS

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Abstract

When clinicians consider ECLS support for ARDS patients with hemodynamic instability, both Veno-arterial and Veno-venous (VV) ECLS are therapeutic possibilities. We analyzed seventeen patients with ARDS on inotropic or vasopressor support requiring ECLS for refractory hypoxemia. After implementing Veno-venous ECLS, pressor requirements (based on norepinephrine equivalents) were significantly lower in all patients. (p=0.0001 for overall comparison across time points). None of the 17 patients required conversion from VV ECLS to veno-arterial (VA) ECLS (95% CI 0% - 20.0%). In this sample of 17 patients with substantial baseline vasopressor support and hypoxemic respiratory failure, initiation of VV ECLS was associated with reduced pressor requirements. Such a strategy may help avoid complications of VA ECLS in patients with both respiratory and hemodynamic failure.

Introduction

Patients with severe ARDS have a high risk of morbidity and mortality.(1) Current supportive therapy includes limiting ventilator induced lung injury, source control, and adjunctive strategies such as early neuromuscular blockade and prone positioning.(2-5)

Extracorporeal life support can also be an effective bridge to recovery in patients with severe acute respiratory distress syndrome (ARDS) refractory to standard medical management. (6) However, clinicians considering ECLS support in patients with both hypoxemic respiratory failure and hemodynamic instability often must decide between Veno-venous support, which addresses gas exchange, and veno-arterial support, which also offers circulatory support..

We designed our mobile ECLS program to permit VV ECLS implementation in patients with severe ARDS with hemodynamic instability deemed acute and reversible post-ECLS. To our knowledge, no study has examined the hemodynamic effect of initiating VV ECLS in ARDS patients with concomitant shock. To address this knowledge gap, we retrospectively examined hemodynamic outcomes in these patients, including conversion to VA ECLS and trend in post-VV ECLS pressor requirements.

Methods

This study was approved by the Institutional Review Board (University of Pennsylvania Institutional Review Board irb@pobox.upenn.edu phone: 215-573-2540), and the requirement for written informed consent was waived. We conducted a retrospective study of all consecutive patients with severe ARDS and hemodynamic instability presenting for ECLS from outside hospitals through our mobile ECLS program from Jan 2, 2015 until December 31, 2015. Hemodynamic instability was defined as requiring vasopressor or inotropic support to maintain a mean arterial pressure greater than 60 mm Hg or a systolic blood pressure greater than 100 mm Hg after normalizing volume status. Patients > 18 years of age were considered for ECLS support for ARDS with a Murray Score > 3.0 or a pH < 7.20. Exclusion criteria included contraindication to heparinzation, ventilator support for > 10 days, or a history of severe chronic lung disease.

ECLS was implemented in standard fashion according to our program's protocol. To assure that we do not place patients on VV ECLS with inadequate cardiac function, our program requires that a cardiac echocardiogram be performed before ECLS is implemented. If the patient has severe ventricular dysfunction associated with severe hemodynamic instability, he/she is considered a candidate for VA ECLS only. In circumstances when patients are too unstable to be transported and the referring facility is unable to obtain a cardiac echo, we obtain the echo ourselves using a portable TEE machine (Phillips CX50 with a TEE probe) that we bring along. This option is possible since our mobile team consists of a cardiac anesthesiologist, cardiovascular surgeon, and a perfusionist.

In our patient cohort, ECLS was initiated as follows: First, both groins and the right neck were draped and prepped in sterile fashion with chloraprep. The right femoral vein and right internal jugular (IJ) veins were accessed and 0.35 Amplatz wires advanced and positioned within the right atrium using fluoroscopic confirmation. After an intravenous bolus of 100 units/kilogram of heparin was administered, a 25 French long femoral venous inflow cannula was inserted and a 16 French right IJ outflow cannula. In one patient a right internal jugular Avalon catheter was placed instead of bicaval cannulation. After fluoroscopic confirmation of position, the cannulas were connected to a Maquet Cardiohelp portable ECLS machine. ECLS flow was then started and slowly with gradually increased to 4-6

liters/minute. The gas flow sweep was initially set at 2 liters with a fraction of inspired oxygen (FIO2) of 100%. After ECLS had reached steady state, pressors were titrated to maintain MAP>60mmHg and ultra-low stretch ventilator settings were used as tolerated, with PEEP set to 10-12 cm H2O and tidal volumes set to 2-4 mL/kg.

Retrospective data collection included patient age at time of ECLS implementation, site of ECLS implementation, hospital length of stay (LOS), intensive care unit (ICU) LOS, duration of ECLS support, and in-hospital mortality. In addition, pH, positive end expiratory pressure or mean airway pressure (for patients on APRV), and PaO2 were collected pre (immediately prior) and post (2 hours after) ECMO implementation.

Vasopressor and inotrope requirements were recorded pre-ECLS implementation (T0), 2 hours post implementation (T+2), 6 hours post implementation (T+6), and 24 hours post implementation (T+24). Since most patients were on multiple vasopressor and inotropic support medications, we generated an equivalency score to convert different pressor doses to norepinephrine equivalents. Specifically, we modified the Vasopressin and Septic Shock Trial (VASST) formula to include vasopressin based on recommendations by Patel et al. (7,8). Vasopressor and inotrope doses were totaled for each patient at each time point and entered into the following formula to calculate norepinephrine equivalents:

$$\begin{aligned}&[\text{norepinephrine} \quad (\mu\text{g}/min)]\\&\quad +[\text{dopamine} \quad (\mu\text{g}/kg/min) \div 2]\\&\quad +[\text{epinephrine} \quad (\mu\text{g}/min)]\\&\quad +[\text{phenylephrine} \quad (\mu\text{g}/min) \div 10]\\&\quad +[\text{vasopressin} \quad (0.01 \quad units/min) \times 2]\end{aligned}$$

Statistical analysis

Vasopressor requirements (in norepinephrine equivalents) at each time point were summarized with medians and interquartile ranges. Comparison of vasopressor requirements across time points was done with the Friedman test, followed by pairwise comparisons using the Wilcoxon signed rank test with the Bonferroni correction to account for repeated obervations. The alpha level for the overall test (Friedman test) was set at 0.05 and was corrected to 0.008 for the post-hoc pairwise comparisons using the Wilcoxon signed rank test. We estimated the correlation between change in vasopressor dose and change in physiologic variables (pH, PEEP, PaO2) using Spearman's rank correlation test. 17 patients were available at the end of the study period. Assuming that 10% of patients would need conversion to VA ECLS, we calculated that our sample would provide 80% power to exclude an upper confidence limit of 35%.

Results

We identified 35 consecutive patients undergoing VV ECLS for severe ARDS from Jan 2, 2015 until December 31, 2015. 18 patients were excluded from analysis because they did not require vasopressor or iontropic support at the time of ECLS implementation. None of the patients referred with ARDS underwent VA ECLS. ECLS was initiated off-site by a mobile

team on 12/17 patients, and 5/17 patients had ECLS initiated at our institution after transfer from the outside hospital. Single vein cannulation with a dual lumen catheter inserted via the right internal jugular vein was performed in one patient. All other patients underwent bicaval cannulation. None of the patients sustained cannulation related complications.

The pressor requirements at each time point are shown in Table 1. After Veno-venous ECLS implementation, pressor requirements were significantly lower at 6 hours (p=0.0003), 24 hours (p=0.0003), and overall across all time points (p=0.0001) None of the patients required conversionfrom VV ECLS to VA ECLS (0/17 [0%, 95% CI 0% - 20.0%]). ECLS was successfully weaned off 15/17 patients. Hospital mortality was 35.3% (6/17 patients) in this patient cohort.

5 of the patients in our series had ECLS implemented at the bedside with TEE guidance of cannula insertion and position due to perceived risk of cardiovascular collapse with patient movement. In all 5 cases, patient movement prior to ECLS implementation resulted in severe hypotension or hypoxia. The remaining 12 were transported to the operating room and cannulation was performed with fluoroscopic guidance.

We found in our cohort that an increase in pH 2 hours after ECMO implementation correlated with a reduction in pressor requirements at 6 hours, but not 24 hours (see Table 2). Changes in peep and PaO2 associated with ECMO implementation did not correlate with the reduction in pressor requirements.

Discussion

We found that in patients with respiratory failure and hemodynamic instability requiring pressors/inotropes, implementation of VV ECLS decreased the pressor requirement at 6 hours and 24 hours. Two patients still required high dose pressors 24 hours after initiation of ECLS (23 and 17.5 NE equivalents), but lower than prior to insertion. One patient had influenza A pneumonia complicated by MRSA pneumonia and bacteremia, and the other had aspiration syndrome. The minimal level of cardiac function required to tolerate VV ECLS remains unknown, but we would be cautious using VV ECLS in patients with severe right or left ventricular dysfunction. Despite the limitations of this retrospective study, the findings provided important information for guiding clinical decision making in patients undergoing ECLS for acute respiratory failure.

In conclusion, we describe the use of Veno-venous ECLS in 17 patients with refractory hypoxemia due to ARDS and hemodynamic instability on pressors/inotropes. In nearly all patients, ECLS not only improved oxygenation but reduced the need for vasoactive agents. In our cohort, an increase in pH was the only ECMO related effect that correlated with the reduction in pressor requirements we observed. Further work is needed to identify factors predicting the successful use of Veno-venous ECLS in patients with combined respiratory failure and hypotension.

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Table 1

Pressor requirements in norepinephrine equivalents (mcg/min)

patient	NE at time of insertion	NE after 2 hrs	NE after 6 hrs	NE after 24 hrs
1	20	0	0	0
2	35	2	3	9
3	11.5	6.25	2.5	0
4	1.5	1	1.5	1.25
5	5	0	0	0
6	23	8	5	0
7	43	40	13	3
8	6	2	2	0
9	12	17	0	2
10	15	6	7	7
11	5	9	3.5	0
12	49	45	28	23
13	96	28	16	0
14	25	21	23	11
15	28	18	18	9
16	15	5	4	3
17	58	68	52	17.5
Group median (IQR) *	20 (11.5-50)	8 (2-21)	4 (2-16) **	2 (0-9) **

NE=norepinephrine equivalents; IQR=interquartile range

* Significant difference across time points, p=0.0001 (Friedman test)

** Significant difference versus insertion, p=0.0003 (Wilcoxon signed rank)

Table 2

Correlations between change in physiologic variables with change in vasopressor support[**]

Variable[***]	Change at 6 hours correlation coefficient[*] (95%CI)	p	Change at 24 hours correlation coefficient[*] (95%CI)	p
Change in pH	−0.50 (−0.79, −0.01)	p=0.04	−0.39 (−0.75, 0.13)	p=0.13
Change in PEEP	−0.06 (−0.52, 0.44)	p=0.83	0.09 (−0.40, 0.55)	p=0.71
Change in PaO2	−0.05 (−0.53, 0.46)	p=0.85	−0.14 (−0.59, 0.38)	p=0.59

[*] calculated with the Spearman's rank correlation test

[**] Change calculated as pre-insertion value - post-insertion value at 6 and 24 hours

[***] Change calculated as pre-insertion value - 2-hour post-insertion value