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Clinical paper

A retrospective comparison of survivors and non-survivors of massive pulmonary embolism receiving veno-arterial extracorporeal membrane oxygenation support

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ABSTRACT

Introduction: While the optimal care of patients with massive pulmonary embolism (PE) is unclear, the general goal of therapy is to rapidly correct the physiologic derangements propagated by obstructive clot. Extracorporeal membrane oxygenation (ECMO) in this setting is promising, however the paucity of data limits its routine use. Our institution expanded the role of ECMO as an advanced therapy option in the initial management of massive PE. The purpose of this project was to evaluate ECMO-treated patients with massive PE at an academic medical center and report shortterm mortality outcomes.

Methods: Thirty-two patients placed on ECMO for confirmed, massive PE from January 2012 to December 2015 were retrospectively analyzed. All patients had PE confirmed by computerized tomography and/or invasive pulmonary angiography.

Results: In our population of patients managed with ECMO, 21 (65.6%) patients survived to decannulation and 17 (53.1%) survived index hospitalization. Baseline characteristics and clinical variables showed no difference in age, gender, right ventricular-to-left ventricular ratios, or peak troponin-T between survivors and non-survivors. Non-survivors tended to have a previous history of malignancy. Cardiac arrest prior to ECMO cannulation was associated with worse outcomes. All 5 patients who received concomitant systemic thrombolysis died, while 11 of 15 patients who received catheter-directed thrombolysis survived. A lactic acid level ≤6 mmol/L had an 82.4% sensitivity and 84.6% specificity for predicting survival to discharge.

Conclusion: The practical approach of utilizing ECMO for massive PE is to reserve it for those who would receive the greatest benefit. Patients with poor perfusion, for example from cardiac arrest, may gain less benefit from ECMO. Our findings indicate that a serum lactate > 6 mmol/L may be an indicator of worse prognosis. Finally, in our patient population, catheter-directed thrombolytics was effectively combined with ECMO.

Introduction

A significant cause of morbidity and mortality worldwide, acute pulmonary embolism (PE) can range in presentation from asymptomatic with incidental discovery to hemodynamic instability with cardiovascular arrest. The mortality rate for massive PE ranges from 18 to 65% with up to 10% of patients dying suddenly [1–3]. The goals of pulmonary artery reperfusion therapy are to provide recanalization of distal flow, correct ventilation/perfusion mismatches, reduce pulmonary vascular resistance, and ultimately decrease the hemodynamic load on the right ventricle. While systemic thrombolysis has been validated in the highest risk scenarios, the limitations involving bleeding have offset some of the potential benefit [4–6]. There is a paucity of data on the utility of extracorporeal membrane oxygenation (ECMO) in the setting of massive PE as ECMO requires a substantial infrastructure to employ routinely. Our institution has expanded the role of ECMO in patients with massive PE and we sought to evaluate our experience.

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Methods

We retrospectively analyzed our institution's ECMO database to identify all the patients placed on ECMO for confirmed, high-risk PE between January 2012 and December 2015. Most patients (26) presented through the emergency department. PE was confirmed by computerized tomography and/or pulmonary angiography prior to the initiation of ECMO. Massive PE was defined as a systolic blood <90 mmHg for >15 min, requiring vasopressors, and/or demonstrating evidence of organ dysfunction[7]. ECMO cannulation was performed by either an interventional cardiologist or a cardiothoracic surgeon. The majority (27/30) patients had their cannulation performed in the cardiac catheterization laboratory with the remainder receiving emergent bedside cannulation. The typical procedure involved placement of a 6-French short sheath in the femoral artery and another in the femoral vein. A 6-French Proglide Perclose would be used to preclose the femoral arteriotomy. After serial dilatation, a 17-French cannula was advanced to the descending aorta while a 25-French cannula was placed at the level of the SVC. The circuit was primed, de-aired, and initiated. After patient stabilized on circuit, care was transferred to cardiology or cardiothoracic critical care service managed by cardiology and/or anesthesiology inpatient services. Therapeutic anticoagulation for the ECMO circuit was provided. Hypothermia could be provided through the ECMO circuit, though it was difficult to determine if this was routinely done.

Primary analysis compared patients with PE who survived or died during index hospitalization. As tested variables were not normally distributed as assessed by the Shapiro-Wilk test, we compared continuous variables between groups using a Mann-Whitney *U* test and summarized them as median and 25–75% interquartile ranges (IQR). The Chi-square test for association was used to compare categorical variables between groups, which were presented as numbers and percentages. The ability of pre-ECMO lactic acid to predict successful weaning from ECMO and survival to discharge was assessed using receiver operating characteristics (ROC) curves. Optimum cutoff values of pre-ECMO lactic acid were those that provided the highest combined sensitivity and specificity for predicting the outcome. Other than ROC curve analysis which was performed by MedCalc software, the rest of the statistical analysis was performed using IBM SPSS 21.0 statistical software (IBM SPSS Version 21.0. Armonk, NY). All statistical significance was assessed using a 2-sided *p*-value. A *p*-value <0.05 was considered statistically significant.

Results

Baseline characteristics and clinical variables showed no difference in age, gender, right ventricular-to-left ventricular ratios, or peak troponin-T between survivors and non-survivors (Tables 1 and 2). Non-survivors tended to have a previous history of malignancy. Table 3 shows outcomes. Ultimately, 21 (65.6%) patients survived to ECMO decannulation and 17 (53.1%) survived index hospitalization, though with significantly longer ICU and total length of stay. Cardiac arrest prior to ECMO cannulation was associated with worse outcomes. All 5 patients who received concomitant systemic thrombolysis died, while 11 of 15 patients who received catheter-directed thrombolysis survived. Systemic lysis involved administration of a 10 mg bolus of alteplase followed by a 90 mg bolus over 2 h. The catheter-directed lytic patients underwent placement of the EndoWave System (EKOS Corporation, Bothwell, MA, USA) consisting of placement of 5-French 106-cm long catheters containing micro-infusion pores for alteplase delivery with an ultrasound core wire that transduced high frequency ultrasound waves. ECMO was initiated prior to CDT whereas patients who received systemic thrombolytics, had ECMO placed after. Two patients received surgical thrombectomy – one survived to decannulation but none survived to hospital discharge. Four patients received aspiration thrombectomy with three surviving to decannulation and two surviving to discharge.

The Whisker plot in Fig. 1 illustrates the relationship between pre-ECMO serum lactate and survival to decannulation. The receiver operator curve had an area under the curve (AUC) of 0.841 (95% confidence interval: 0.66–0.95, p < 0.005) and demonstrated

Table 1
Baseline Demographics.

	Survived Index Hospitalization (n = 17)	Died During Index Hospitalization (n = 15)	p-value
Median age, years (IQR)	56 (43, 70)	56 (50, 62)	1
Men (%)	7 (41.2)	10 (66.7)	0.178
White (%)	15 (88.2)	14 (93.3)	1
Median BMI, kg/m2 (IQR)	36.5 (26.3, 45)	30.2 (26.6, 34.7)	0.475
Coronary artery disease (%)	4 (23.5)	0 (0)	0.104
Hypertension (%)	9 (52.9)	5 (33.3)	0.308
Diabetes mellitus (%)	9 (52.9)	3 (20)	0.076
Prior DVT/PE (%)	2 (11.8)	1 (6.7)	1
Malignancy (%)	0 (0)	4 (26.7)	**0.038**

Table 2
Clinical Characteristics.

	Survived Index Hospitalization (n = 17)	Died During Index Hospitalization (n = 15)	p-value
Cardiac arrest before ECMO (%)	4 (25)	11 (73.3)	**0.012**
RV:LV on CT – median; (IQR)	1.1 (1, 1.6)	0.9 (0.7, 1.3)	0.143
RV:LV on echo – median; (IQR)	1 (0.9, 1.3)	0.9 (0.8, 1.2)	0.193
Peak troponin-T, ng/mL – median; (IQR)	0.26 (0.13, 0.98)	0.37 (0.17, 1.45)	0.589
Initial hemoglobin, g/dL – median; (IQR)	12.7 (10.4, 14)	11.6 (9.3, 12.7)	0.206
Initial platelet, k/uL – median; (IQR)	217 (155, 274)	174 (90, 214)	0.059
Initial creatinine, mg/dL – median; (IQR)	1.2 (1, 1.3)	1.45 (1.1, 1.69)	0.117
Lactate before ECMO, mmol/L – median (IQR)	4.1 (2, 5.5)	11.5 (7.4, 16)	**0.004**
Received systemic thrombolysis (%)	0 (0)	5 (33.3)	**0.015**
Catheter-directed thrombolysis performed (%)	11 (64.7)	4 (26.7)	**0.042**