Utilization of Veno-Arterial Extracorporeal Membrane Oxygenation for Massive Pulmonary Embolism

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Background. **The management of massive pulmonary embolism remains challenging, with a considerable mortality rate. Although veno-arterial extracorporeal membrane oxygenation (VA-ECMO) for massive pulmonary embolism has been reported, its use as salvage therapy has been associated with poor outcomes. We reviewed our experience utilizing an aggressive, protocolized approach of VA-ECMO to triage, optimize, and treat these patients.**

Methods. **All patients with a massive pulmonary embolism who were placed on VA-ECMO, as an initial intervention determined by protocol, were retrospectively reviewed. ECMO support was continued until organ optimization was achieved or neurologic status was determined. At that time, if the thrombus burden resolved, decannulation was performed. If substantial clot burden was still present with evidence of right ventricular (RV) strain, operative therapy was undertaken.**

Results. **Twenty patients were identified. Before cannulation, all patients had an RV-to-left ventricular ratio greater than 1.0 and severe RV dysfunction. The median duration of ECMO support was 5.1 days, with significant improvement in end-organ function. Ultimately, 40% received anticoagulation alone, 5% underwent catheter-directed therapy, and 55% underwent surgical pulmonary embolectomy. Care was withdrawn in 1 patient with a prolonged pre-cannulation cardiac arrest after confirmation of neurologic death. In-hospital and 90-day survival was 95%. At discharge, 18 of 19 patients had normal RV function, and 1 patient, who received catheter-directed therapy, had mild dysfunction.**

Conclusions. **VA-ECMO appears to be an effective tool to optimize end-organ function as a bridge to recovery or intervention, with excellent outcomes. This approach may allow clinicians to better triage patients with massive pulmonary embolism to the appropriate therapy on the basis of recovery of RV function, residual thrombus burden, operative risk, and neurologic status.**

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Massive pulmonary embolism (PE), defined as PE resulting in hemodynamic instability, remains a grave condition, with mortality rates ranging from 15% to 80% [1–6]. Although select studies have reported improved outcomes with massive PE over the past decade, all primary interventions for patients who present in cardiogenic shock, including systemic anticoagulation, systemic or catheter-based lytic therapies, and surgical pulmonary embolectomy, continue to be associated with excessive mortality rates [4, 7, 8].

In refractory patients, veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has been reported, but has also been associated with considerable rates of morbidity and mortality [9–11]. However, its reported use in the treatment of these patients has been limited to salvage interventions, often after other interventions have failed. Given the large experience with ECMO at our institution, we began using an early and aggressive, protocolized approach to VA-ECMO for massive PE. We report our cannulation and management strategies and outcomes for these patients over a 3-year period.

Patients and Methods

With institutional review board approval (HP-00066712), a retrospective review was performed of all patients from January 2014 to August 2016 who were placed on VA-ECMO as an initial intervention for massive PE according to protocol. A manual review of patient charts was then undertaken to confirm the diagnosis and to obtain preoperative, perioperative, and postoperative variables and outcomes. PE was confirmed by computed tomographic angiography in all patients. Right ventricular (RV) dysfunction was recorded according to a preoperative and

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postoperative (before discharge) transthoracic echocardiogram (TTE). Postoperative RV dysfunction (none, mild, moderate, or severe) was delineated by an independent cardiologist, who both quantitatively and qualitatively assessed RV function to obtain an overall assessment of dysfunction.

Massive PE was defined, according to the American Heart Association, as patients with a systolic blood pressure less than 90 mm Hg for at least 15 minutes or who required inotropic support, not due to a cause other than PE, or persistent profound bradycardia (heart rate <40 beats/min with signs or symptoms of shock).

Indications for VA-ECMO and Management of ECMO Support

All patients included in this study followed an approach determined by protocol. Patients with a massive PE resulting in end-organ dysfunction or unclear neurologic status were placed on VA-ECMO. All patients, regardless of age or comorbid conditions, were considered candidates for this intervention, unless their predicted survival independent of the PE, was less than 1 year. Cannulation was performed under ultrasound guidance, with a 23F to 25F venous drainage cannula placed in a femoral vein and a 17F to 19F arterial return cannula placed in a femoral artery in the contralateral groin (Maquet, Rastatt, Germany). A 6F distal perfusion cannula was placed in the superficial femoral artery a priori, unless the patient was actively requiring cardiopulmonary resuscitation (CPR), to allow for better ultrasound visualization of the superficial femoral artery. In patients who actively required CPR, the drainage and return cannulae were placed before the distal perfusion cannula, to re-establish adequate perfusion as quickly as possible, and the distal perfusion cannula was placed after stabilizing the patient's hemodynamics.

In non-intubated patients, moderate sedation with 0.5 mg/kg ketamine and local anesthetic agent with 20 to 30 mL of 2% lidocaine was used before cannulation. Once adequately sedated, the patient was positioned flat on the table, and cannulation was performed awake.

ECMO flow was titrated up until the right ventricle was decompressed by TTE. However, some pulmonary blood pulmonary flow was maintained to allow for fibrinolysis of the thrombus. Systemic anticoagulation was maintained with a partial thromboplastin time of 72 to 113 seconds.

Duration of Support and Further Intervention

ECMO support was continued until all of the following criteria were met: (1) neurologic status was determined, if unclear before cannulation; (2) optimization of end-organ function; and (3) 3 to 5 days of heparin therapy to allow for potential endogenous fibrinolysis. ECMO support was terminated early in patients with concerning findings, such as an ECMO-related complications.

If the patient was found to have a neurologic death, organ donation was offered to the family and care was withdrawn. If neurologically intact, a repeat TTE was performed after all the above criteria were met. RV evaluation was performed with the ECMO flow turned down to evaluate function with the right ventricle and left ventricle loaded. This was performed similar to an inverse left ventricular assist device ramp study (ie, 100%, 50%, and 25% flows). In patients in whom RV size and function were normal, ECMO decannulation was performed by a surgical cut-down in the operating room. However, in patients in whom RV function continued to be abnormal, a triple rule-out computed tomographic angiography scan was performed to concurrently re-evaluate extent of pulmonary thrombus and to rule out coronary disease. In the subset of patients who failed heparin therapy, defined as continued RV dysfunction with persistent pulmonary thrombus, surgical pulmonary embolectomy was performed, as previously described [12]. Briefly, all patients were placed on cardiopulmonary bypass with mild hypothermia. Central aortic and bicaval venous cannulation was used. Separate incisions were made into the right and left main pulmonary arteries, and thrombus was removed in its entirety up to the subsegmental level. The operation was routinely performed on a beating heart without placement of an aortic cross-clamp, unless required for a concomitant procedure. If the patient was deemed an inappropriate surgical candidate (n = 1), alternative therapy, such as catheter-based intervention, was undertaken. All patients received an inferior vena cava filter before discharge.

Clinical Outcomes

The primary outcome of this study was in-hospital and 90-day survival. Secondary outcomes included acute kidney injury that required renal replacement therapy, new hemodialysis at discharge, sepsis, tracheostomy, RV dysfunction at discharge, and ECMO-related complications, including bleeding that required blood product transfusion on ECMO, stroke after cannulation, and vascular complications related to ECMO.

Statistical Analysis

Continuous variables are presented as median with interquartile range (IQR) and were compared using the Wilcoxon rank-sum test. Categorical variables are presented as number (%). A p value of less than 0.05 was considered statistically significant. For analysis purposes, the descriptive terms used by the echocardiographer were converted to numerical values according to the following rubric: none = 0, trivial = 0.5, mild = 1, mild-moderate = 1.5, moderate = 2, moderate-severe = 2.5, and severe = 3. In addition to reporting the appropriate medians (IQRs), paired preoperative and postoperative measurements of RV dysfunction were compared using the test of marginal homogeneity.

Results

Patient Demographic Characteristics and Clinical Presentation

Twenty consecutive patients were identified with a median age of 47 years. Common risk factors for PE included