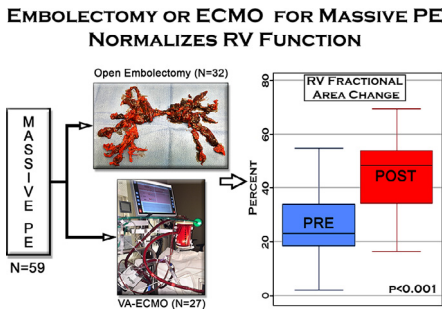
Comparison of Surgical Embolectomy and Veno-arterial Extracorporeal Membrane Oxygenation for Massive Pulmonary Embolism

Joshua B. Goldberg, MD,[†] Daniel M. Spevack, MD,[‡] Syed Ahsan, MD,[‡] Yogita Rochlani, MD,[‡] Suguru Ohira, MD,[†] Philip Spencer, MD,[†] Masashi Kai, MD,[†] Ramin Malekan, MD,[†] David Spielvogel, MD,[†] and Steven Lansman, MD, PhD[†]

Massive pulmonary embolism (MPE) is associated with a 20-50% mortality rate with guideline directed therapy. MPE treatment with surgical embolectomy (SE) or venoarterial extracorporeal membrane oxygenation (VA-ECMO) have shown promising results. In the context of a surgical management strategy for MPE, a comparison of outcomes associated with VA-ECMO or SE was performed. A retrospective review of a single institution cardiac surgery database was performed, identifying MPE treated with SE or VA-ECMO between 2005-2020. Primary outcome was in-hospital survival. 59 MPE [27 (46.8%) VA-ECMO vs 32 (54.2%) SE] were identified. All presented with elevated cardiac biomarkers, tachycardia (mean heart rate 113 ± 20 beats/minute), hypotension (mean systolic blood pressure 85 ± 22 mm Hg) and vasopressors requirement, without significant differences between cohorts. Preoperative CPR was performed in 37.3% (22/59), without a significant difference between cohorts. More VA-ECMO presented with questionable neurologic status (GCS ≤ 4) [9/27 (33.3%) vs 2/32 (6.2%), $P = 0.008$] and more VA-ECMO failed thrombolysis [8/27 (29.6) vs 2/32 (6.3), $P = 0.014$]. All presented with severe RV dysfunction, by discharge all had normalization of echocardiographic RV function. Overall mortality was 10.2%, with a trend toward higher mortality among VA-ECMO [14.9% (4/27) vs 6.3% (2/32) $P = 0.14$]. CPR was independently associated with death (OR 10.8, $P = 0.02$) whereas treatment modality was not (OR 0.24). In an extremely unstable MPE population VA-ECMO and SE were safely performed with low mortality while achieving RV recovery. Adverse outcomes were more closely associated with preoperative CPR than with treatment modality.

Semin Thoracic Surg 34:934–942

Keywords: Pulmonary embolism, Right ventricular failure, Surgical embolectomy, Extracorporeal membrane oxygenation, Survival



Our treatment algorithm by which MPE are treated with either Surgical Embolectomy or VA-ECMO results in RV recovery as evidenced by TTE assessment of RV function including improvement in RV Fractional Area Change (FAC).

Central Message

Surgical embolectomy and venoarterial extracorporeal membrane oxygenation result in excellent right ventricular recovery and survival in the setting of massive pulmonary embolism.

Perspective Statement

Guideline directed therapy of massive PE is associated with up to 50% mortality. In contrast, these data describe 10.2% mortality and excellent RV recovery with surgical embolectomy or VA-ECMO. VA-ECMO was used in

Abbreviations: AHA, American Heart Association; BMI, Body Mass Index; CPR, Cardiopulmonary Resuscitation; CVP, Central Venous Pressure; CT, Computed Tomography; GCS, Glascow Coma Scale; MPE, Massive Pulmonary Embolism; PASP, Pulmonary Artery Systolic Pressure; PE, Pulmonary Embolism; RBC, Red Blood Cell; RV, Right Ventricle; RVFAC, Right Ventricle Fractional Area Change; RV:LV, ratio of the diameter Right Ventricle to the Left Ventricle; SE, Surgical Embolectomy; SMPE, Submassive Pulmonary Embolism; TTE, Transthoracic Echocardiogram; VA-ECMO, Venoarterial Extracorporeal Membrane Oxygenation

[†]Section of Cardiothoracic Surgery, Westchester Medical Center, New York Medical College, Valhalla, New York
[‡]Department of Cardiology, Westchester Medical Center, New York Medical College, Valhalla, New York

IRB: The Institutional Review Board of New York Medical College/Westchester Medical Center approved this study under "consent exempt" category #12190.

Funding: None.

Conflicts of Interest: The authors have no conflicts of interest.

Address reprint requests to Joshua B. Goldberg, MD, Section of Cardiothoracic Surgery, Westchester Medical Center, 100 Woods Road - Macy Pavilion,114W, Valhalla, New York 10595. E-mail: joshua.goldberg@wmchealth.org

1043-0679/$–see front matter
https://doi.org/10.1053/j.semtcvs.2021.06.011

patients with worse clinical severity which drove outcome differences rather than treatment modality. Surgical embolectomy or VA-ECMO should be considered for massive PE patients.

BACKGROUND

Acute pulmonary embolism (PE) is the third leading cause of cardiovascular death and the number one cause of preventable in-hospital death in the United States.[1,2] The vast majority of PE associated deaths are due to acute RV failure from a sudden increase in RV afterload. As a result, PE has been classified bythe clinical extent of RV failure, with massive PE (MPE) defined as patients with severe RV dysfunction and hemodynamic instability and submassive PE (SMPE) defined as hemodynamically stable patients with objective evidence of RV dysfunction.[3] Despite renewed focus on PE treatment over the last several years, the adoption of multidisciplinary PE treatment teams, and advances in medical and transcatheter therapies, MPE associated mortality remains exceedingly high, at 20-50%.[4]

Evidence based guidelines for MPE recommend primary treatment with thrombolytic therapy, despite numerous associated bleeding and stroke complications and a considerable portion of patients in whom the treatment is contraindicated.[5] Yet the efficacy of thrombolytics among MPE patients is questionable, as mortality remains high and the vast majority of the supporting literature does not focus on MPE patients.[5] Nevertheless, American Heart Association (AHA), European Society of Cardiology (ESC) and the American College of Chest Physicians (CHEST) guidelines recommend thrombolysis as first line therapy.[3,6,7] Similarly, the vast majority of the transcathether PE treatment literature does not focus on MPE patients.[8,9]

In contrast, a growing body of literature supports the safety and efficacy of surgical embolectomy (SE) or venoarterial extracorporeal membrane oxygenation (VA-ECMO) as treatment of MPE.[10-16] SE is definitive treatment for acute PE, as it removes the RV afterload while allowing the struggling RV to recover in an unloaded state on cardiopulmonary bypass. ECMO decompresses and unloads the failing RV and provides hemodynamic support while the body's native fibrinolytic mechanisms lyse the thrombus. Although SE and VA-ECMO have been performed with low morbidity and mortality rates in MPE, it is unclear which procedure is superior. Thus, we compared clinical features and outcomes between SE and VA-ECMO in a large, single center series.

METHODS

The Institutional Review Board of New York Medical College/Westchester Medical Center approved this study under "consent exempt" category #12190. A retrospective review of our prospectively maintained cardiac surgery database was performed to identify all patients who underwent SE and/or VA-ECMO for acute PE between January 2005 and September of 2020. Basic demographics and clinical data were reviewed.

Based upon AHA defined criteria,[3] MPE was defined as a PE with associated hemodynamic instability (systolic blood pressure less than 90 mm Hg for ≥ 15 minutes or need for pressors or inotropes) and evidence of RV dysfunction. RV dysfunction was defined as an elevated RV:LV ratio (>0.9), measured by transthoracic echocardiography (TTE) or CT scan, and/or elevated brain natriuretic peptide (BNP) or troponin-I.

Patient Management Algorithm

The decision to proceed with VA-ECMO or SE for MPE was made via consensus opinion between at least two attending physicians (2 cardiac surgeons or 1 cardiac surgeon and 1 cardiologist). The treatment algorithm is depicted in Figure 1. VA-ECMO was selected if a patient had ongoing CPR, recurrent CPR, uncertain neurologic status post cardiac arrest, unstable hemodynamics despite inotropes and pressors, had recently received systemic thrombolytics (within 4-6 hours) or was deemed a high risk for sternotomy. All others were treated with SE. The primary treatment modality was defined as the treatment initially employed (SE or VA-ECMO) and the secondary treatment modality was defined as any additional procedure, concomitant or delayed, for management of the PE. Of note, most MPE patients were emergently transferred from

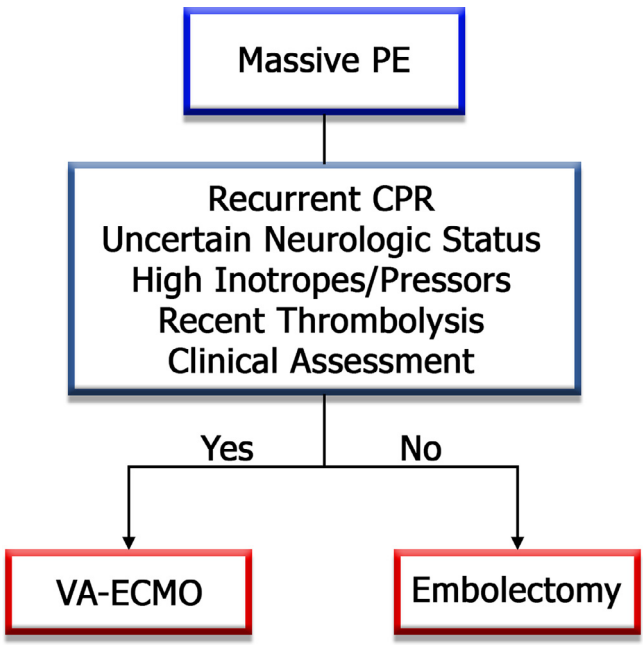


Figure 1. Pulmonary Embolism Patient Management Algorithm. The decision tree at our institution for selecting the primary management strategy for patients presenting with acute PE. Management decisions were made based on a consensus opinion between either two cardiac surgeons or a cardiac surgeon and a cardiologist. Patients with recurrent CPR, uncertain neurologic status, high inotrope and/or pressor requirement, recent thrombolysis or clinical concern for sudden decompensation were treated with ECMO, others were treated with surgical embolectomy.

multiple institutions, spanning a 100-mile radius; medical therapy and all instances of systemic thrombolytic therapy were initiated at these referring institutions, and reliable data on treatment prior to transfer, and indeed the number of MPE patients not transferred, were not available. Postoperative care was tailored to patients' physiology. Standardized RV support with inotropes or nitric oxide was not universally administered to patients post operatively. While specific data on postoperative medications are not available for the entire study population, the vast majority of patients were weaned off of cardiopulmonary bypass or ECMO on inotropy (epinephrine or milrinone) and a minority of patients required nitric oxide. Treatment was determined by objective assessment of RV function based on PA catheter numbers and echocardiogram findings. Furthermore, IVC filters were rarely inserted and were done so only if the patient could not tolerate anticoagulation. Discharge anticoagulation was determined by hematology and has gravitated to direct oral anticoagulants.

Surgical Technique

SE was performed via a sternotomy, with the heart beating, on cardiopulmonary bypass. Patients were cooled to 32 °C, permitting short periods of reduced cardiopulmonary bypass flow during embolectomy to optimize distal pulmonary artery visualization. Two pulmonary arteriotomies were made: one in the main pulmonary artery (PA) extending into the left PA and a separate incision in the main right PA extending to the takeoff of the right upper lobe branch. This wide exposure permits visualization to perform an extended embolectomy with removal of clot extending into secondary and tertiary branches.

Peripheral arterial access for VA-ECMO was obtained via the axillary or femoral artery. Axillary artery cannulation was performed via a right infraclavicular incision with an end-to-side anastomosis of an 8 mm or 10 mm Dacron graft, depending on vessel size. Femoral artery cannulation was performed by one of three techniques, each incorporating a method of distal limb perfusion, a critical consideration for avoiding ischemic limb complications: 1) open femoral artery exposure with anastomosis of a Dacron graft in end-to-side fashion; 2) open femoral artery exposure with placement of a percutaneous arterial cannula and antegrade distal perfusion catheter via Seldinger technique; or 3) percutaneous placement of an arterial cannula and an antegrade distal perfusion catheter using ultrasound and/or fluoroscopic guidance. Antegrade distal perfusion catheters (6-8 French) were inserted in the distal common femoral artery or proximal superficial femoral artery and connected to the arterial limb of the ECMO circuit. Venous cannulation was performed via the femoral vein with a long venous cannula. The choice of ECMO arterial cannulation strategy depended on a number of factors, including surgeon preference, patient condition, patient habitus and clinical location. In general, we prefer open femoral artery exposure with cannulae placement under direct visualization performed with local anesthesia, which we have found to be expeditious while avoiding vessel injury and bleeding problems that may complicate percutaneous access attempts. Hemodynamics, PA catheter pressure measurements and RV function on TTE were assessed for readiness to wean from ECMO. If the RV continued to have significant dysfunction and the patient had an intact neurologic exam, then a CT scan was performed to assess residual clot burden. If significant clot burden remained in the setting of significant persistent RV dysfunction, then an interval embolectomy was performed. Alternatively, if the RV had improved during VA-ECMO, then a CT scan was not repeated, and the patient was weaned off of ECMO.

Outcomes

The primary outcome was in-hospital mortality and the secondary outcome was RV recovery. Early RV recovery was determined by normalization of central venous pressure (CVP) and/or pulmonary artery systolic pressure (PASP), as measured by a PA catheter in the operating room after weaning from cardiopulmonary bypass. Among patients who presented in extremis (CPR or profound hemodynamic instability refractory to pharmacotherapy), PA catheters were not placed due to clinical urgency and these patients tended to be treated with VA-ECMO. Thus, a disproportionate number of ECMO patients did not have preoperative PA catheter data.

Transthoracic Echocardiography (TTE) measurements of RV function [RV:LV ratio and RV fractional area change (RV FAC)] were analyzed postoperatively and comparisons were made with the preoperative studies, when available. All postoperative TTE measurements in the VA-ECMO cohort were obtained after ECMO wean. Subanalysis of survival was performed among patients who presented with preoperative CPR. Additional outcomes were stroke; reoperation for bleeding; red blood cell (RBC) transfusions; new hemodialysis; prolonged ventilation (defined as intubation >72 hours, based upon New York State cardiac surgery public reporting criteria), and overall length of stay.

Data Analysis

Statistical analysis was performed using Stata software, version 11.2 (College Station, TX). Normally distributed data were presented as the mean ± standard deviation (SD). Non-normal data were presented as the median (range). Comparison of means for unpaired data was performed using the two-sample t-test. Paired data from before and after surgical intervention was performed using the paired t-test. Comparison of categorical data was generally performed using the Chi-squared test. When sample sizes were small, categorical data was compared using Fisher's exact test. Comparison of medians was performed using the Mann-Whitney or Kruskal-Wallis tests as appropriate. Two-sided p-values were considered significant if < 0.05.

RESULTS

Of 161 patients that underwent surgical treatment for PE at our institution over the course of the study period, 59 (36.6%) had MPE and constituted the study population. As previously

Table 1. Demographics and Chronic Conditions

	All 59	VA-ECMO 27 (45.8)	Embolectomy 32 (54.2)	*P*
Age	55.5 ± 15.0	55.7 ± 17.7	55.4 ± 12.6	0.93
Male (%)	30 (50.8)	10 (37.0)	20 (62.5)	0.05
African-American (%)	23 (39.0)	11 (40.1)	12 (38.7)	0.87
BMI (kg/m^2) (mean)	36.0 ±8.9	32.1 ± 6.7	39.0 ± 9.3	0.003
Recent Surgery/Trauma (%)	19 (32.2)	9 (33.3)	10 (31.3)	0.45
Hx VTE (%)	10 (16.9)	8 (29.6)	2 (6.3)	0.017
Hx Cancer (%)	11 (18.6)	4 (14.8)	7 (21.9)	0.49
COPD (%)	17 (28.8)	7 (25.9)	10 (31.3)	0.65
Current Smoker (%)	13 (22)	6 (22.2)	7 (21.9)	0.97
Diabetes (%)	17 (28.8)	6 (22.2)	11 (34.4))	0.30
CAD (%)	4 (6.8)	2 (7.4)	2 (6.3)	0.86
CHF (%)	4 (6.8)	2 (7.4)	2 (6.3)	0.86
PVD (%)	3 (5.1)	2 (7.4)	1 (3.1)	0.46
Hx CVA (%)	2 (3.4)	0	2 (6.3)	0.19
Creatine (mg/dL)	1.20 ± 0.47	1.19 ± 0.48	1.22 ± 0.47	0.81
LVEF < 55%	5 (8.5)	2 (7.4)	3 (21.9)	0.79

BMI = body mass index; Hx VTE = prior history of venous thromboembolic disease; Hx Cancer = history of cancer; COPD = chronic obstructive pulmonary disease; CAD = coronary artery disease; CHF = congestive heart failure; PVD = peripheral vascular disease; Hx CVA = history of stroke; LVEF<55%= left ventricular ejection fraction < 55%

reported, intermediate high risk submassive PE were treated with either SE (97), catheter directed suction embolectomy (3), or VA-ECMO (2) Procedural incidence by time period is displayed in Supplemental Table 1.

Of the 59 MPE patients, 27 (45.8%) were initially treated with VA-ECMO and 32 (54.2%) with SE. Demographic and comorbidity data, presented in Table 1, indicate that the groups were largely similar, and that cardiovascular disease was uncommon. A greater proportion of SE patients were male (62.5% vs 37.0%, $P = 0.05$). The overall population was obese, with a mean BMI of 36.0 ± 8.9 kg/m^{2}and with greater obesity in the SE patients (39.0 ± 9.0 vs 32.1 ± 6.7, $P = 0.003$). More VA-ECMO patients had a history of VTE (29.6% vs 36.3%, $P = 0.017$).

The presenting symptoms and features are displayed in Table 2. The vast majority presented with dyspnea (98.3%). Syncope (59.3%) or near syncope (35.6%) was common in both cohorts. All patients had severe RV dysfunction and dilation based on preoperative imaging, with RV:LV ratios > 0.9. All patients had elevated troponin and/or brain natriuretic

Table 2. Presenting Symptoms/Features

	All 59	VA-ECMO 27 (45.8)	Embolectomy 32 (54.2)	*P*
Days symptomatic				
Median (range)	2 (1, 21)	2 (1,21)	1 (1, 14)	0.03
Dyspnea (%)	58 (98.3)	27 (100)	31 (97)	0.35
Chest Pain (%)	23 (39.0)	12 (44.4)	11 (34.4)	0.43
Leg pain/swelling (%)	11 (18.6)	5 (18.5)	6 (18.8)	0.98
Syncope (%)	35 (59.3)	18 (66.6)	17 (53.1)	0.29
Near syncope (%)	21 (35.6)	9 (33.3)	12 (37.5)	0.74
Elevated biomarkers	59 (100)	27 (100)	32 (100)	1.0
Heart rate (bpm)	113± 20	112 ± 25	113 ± 14	0.89
SBP (mm Hg)	85 ± 22	81 ± 19	90 ± 24	0.16
Preop Pressors	59 (100)	27 (100)	32 (100)	1.0
CPR (%)	22 (37.3)	10 (37.0)	12 (37.5)	0.97
Prehospital	2 (3.4)	2 (7.4)	0	
InHospital	9 (15.3)	6 (22.2)	3 (9.4)	
PostInduction	11 (18.6)	2 (7.4)	9 (28.1)	
GCS ≤ 4 (%)	11 (18.6)	9 (33.3)	2 (6.3)	0.008
Preop Lytics (%)	10 (16.9)	8 (29.6)	2 6.3)	0.014

GCS = Glasgow Coma Scale; SBP = systolic blood pressure; CPR = cardiopulmonary resuscitation; Preop Lytics = preoperative administration of systemic thrombolytics; Prehospital = CPR initiated prior to admission to a hospital; InHospital = CPR initiated after admission to a hospital not including post anesthesia induction; PostInduction = CPR initiated after anesthesia induction.

peptide levels and all were hemodynamically unstable, as evidenced by tachycardia, hypotension and the need for vasopressors, with no significant differences between groups. Underscoring the critical nature of these patients, 37.3% (22/59) underwent preoperative CPR [VA-ECMO: 10/27 (37.0%) vs SE: 12/32 (37.5%), P = 0.97]. The majority of SE CPR occurred post anesthesia induction (9/12), while the majority of VA-ECMO was initiated either in the prehospital setting (2/10) or after hospital admission but prior to entering the operating room. While the duration of CPR was not available, in general, CPR that occurred post induction was relatively short, and the patients were expeditiously placed on ECMO or cardiopulmonary bypass while they were being resuscitated by cardiac anesthesia. In contrast, prehospital and in-hospital CPR was generally of longer duration and longer intervals elapsed before advanced PE treatment was initiated. Eleven patients (18.6%) presented with unclear neurologic function in association with previous or ongoing cardiac arrest [GCS ≤ 4; VA-ECMO: 9/27 (33.3%) vs SE: 2/32 (6.3%), P = 0.008]. Overall, 16.9% of the population had failed systemic thrombolysis, with more VA-ECMO patients failing thrombolytics than SE patients [8/27 (29.6%) vs 2/32(6.3%), P = 0.014].

Among the 32 primary SE patients, 4 (12.5%) required postcardiotomy VA-ECMO, all of whom had undergone preoperative CPR. The median duration of postcardiotomy ECMO support among SE patients was 4 days (range: 2-9). None of the patients required durable mechanical circulatory support.

Among the 27 patients treated with VA-ECMO as initial therapy, the median duration of support was 4.5 days (range:1-10). SE was required at the time of ECMO removal in 6 (22.2%) of the patients, of whom 4 had received pre-ECMO systemic thrombolysis. Femoral arterial cannulation was utilized in 17 (63.0%), right axillary cannulation was utilized in nine (33.3%) and one patient (53.7%) who had undergone sternotomy two days previously was placed on VA-ECMO centrally (ascending aorta and right atrium) during CPR. General anesthesia was avoided in 37% of the VA-ECMO patients, as they were cannulated under local anesthesia.

In the SE cohort, intraoperative PA catheters measurements indicated immediate RV recovery (Fig. 2), with a preoperative CVP of 28 ± 6 mm Hg normalizing to 11 ± 3 mm Hg (P <0.05) and a preoperative PASP of 71 ± 10.0 mm Hg normalizing to 36 ± 10 mm Hg (P <0.05). Due to patient acuity, only a minority (3) of the VA-ECMO cohort had preoperative PA catheters, and thus pre- and postoperative CVP and PASP trends were not analyzed.

Comparison between preoperative and postoperative TTE measurements of RV function are detailed in Supplemental Table 1 and Figure 3. Both cohorts presented with severe RV dysfunction, with SE demonstrating greater median RV:LV

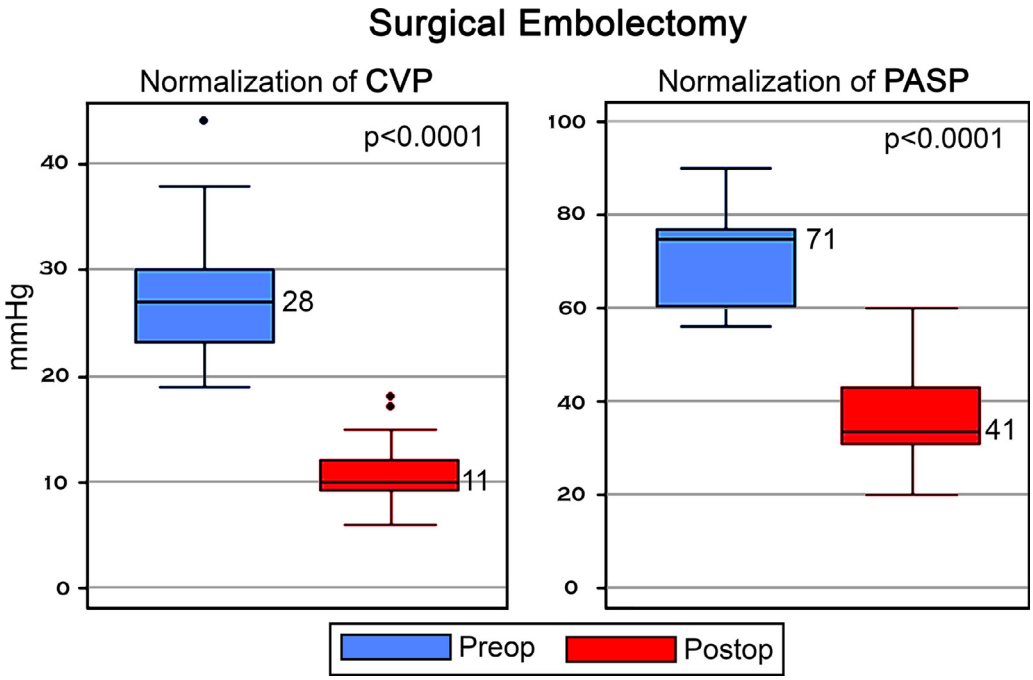


Figure 2. Immediate Postoperative Normalization of RV Filling Pressures after Surgical Embolectomy. Preoperative and postoperative central venous pressure (CVP) and pulmonary artery systolic pressure (PASP) as measured by a PA catheter. Preoperative measurements were obtained in the operating room prior to surgery. Postoperative measurements were obtained in the operating room prior to transport to the intensive care unit. The upper and lower borders of the boxes represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values of non-outliers. Extra dots represent outliers. These data demonstrate that patients presented with invasive hemodynamic evidence of severe RV dysfunction which normalized in the immediate postoperative period. ECMO patients were not included due to the paucity of preoperative PA catheters in the ECMO population.

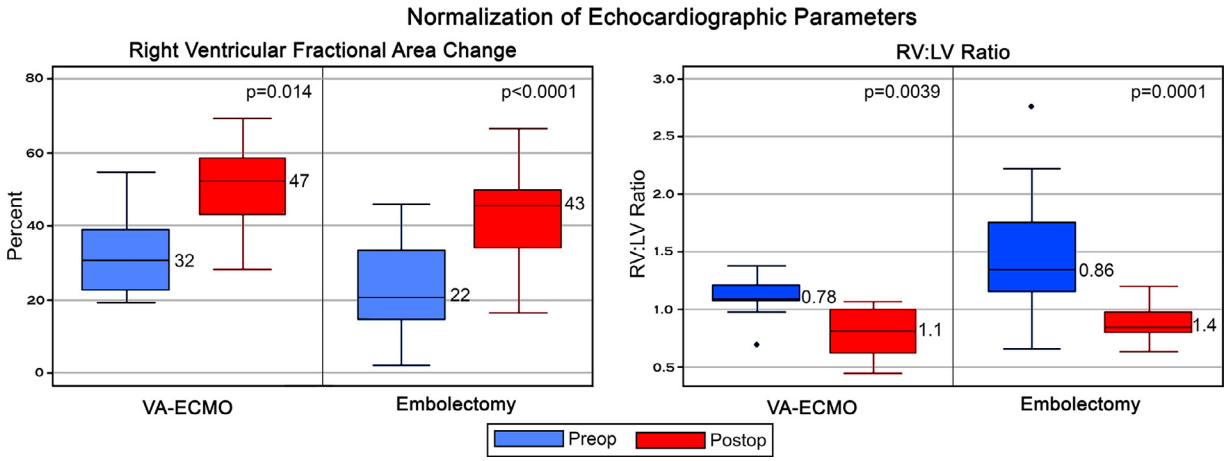


Figure 3. Normalization of Echocardiographic Parameters of RV Function after VA-ECMO or Surgical Embolectomy. Comparison of pre- and postoperative transthoracic echocardiographic (TTE) diameters of right ventricle to left ventricle ratio (RV:LV ratio) and right ventricular fractional area change (RVFAC). The upper and lower borders of the boxes represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values of non-outliers. Extra dots represent outliers. These data demonstrate that patients presented with echocardiographic evidence of severe RV dysfunction which normalized postoperatively.

ratio [1.3 (1.1-1.8) vs 1.1 (1.1, 1.2) P = 0.03] and lower median FAC [20.5 (14.4, 33.5) vs 30.8 (22.4, 39.0) P = 0.05]. Postoperatively, both cohorts had significant (P <0.001) improvement and normalization of TTE parameters of RV function without a significant difference between treatment modalities [RV:LV Ratio: SE 0.84 (0.79, 0.97) vs VA-ECMO 0.81 (0.6, 1.0) P = 0.4] [FAC: SE 45.6 (33.6, 49.8) vs VA-ECMO 45.2 (42.7, 58.6) P = 0.19].

Postoperative outcomes are described in Table 3. Overall, in hospital mortality was 10.2% [VA-ECMO: 14.9% (4/27) vs SE: 6.3% (2/32) P = 0.14]. Details of the mortalities are described in Supplemental Table 2. Five of six deaths required preoperative CPR and all five died of anoxic brain injury attributed to preoperative arrest. The four VA-ECMO deaths underwent preoperative CPR, presented with a GCS≤4, died of anoxic brain injury secondary to preoperative arrest, and their families chose to withdraw care. Two of the VA-ECMO deaths had care withdrawn after one day of support, before TTE assessment of postoperative RV function had been obtained; the remaining two were successfully weaned from ECMO with improved RV function. Of the two SE deaths, one experienced cardiac arrest in the operating room. Due to body habitus (BMI 55.3) it was more expeditious to employ central bypass via sternotomy than peripheral VA-ECMO. This patient required post cardiotomy-ECMO, which was successfully weaned after three days of support, with improved RV function. Unfortunately, the patient suffered anoxic brain injury from the arrest and the family chose to withdraw care. The other SE mortality was a 57-year-old male with a BMI of 54.6 kg/m^2, who developed heparin induced thrombocytopenia and sepsis, and who died with biventricular and multisystem organ failure.

Given the acuity of the population, the postoperative morbidity was relatively low and largely associated with having undergone preoperative CPR (Table 4). Logistic regression demonstrated that CPR was independently associated with mortality (OR 10.8, P = 0.02), while treatment modality was

Table 3. Outcomes

	All 59	VA-ECMO 27 (46.8)	SE 32 (54.2)	*P*
Mortality	6 (10.2)	4 (14.9)	2 (6.25)	0.14
Stroke	2 (3.4)	1 (3.7)	1 (3.1)	0.80
MI	0	0	0	NA
Sternal infection	0	0	0	NA
Reop for Bleeding	1 (1.7)	0	1 (3.1)	0.40
Hemodialysis	8 (13.6)	7 (25.9)	1 (3.1)	0.004
Vent >72 hours	16 (27.1)	8 (29.6)	8 (25)	0.41
HIT	11 (18.6)	6 (28.6)	5 (16.7)	0.31
RBC Transfusion	25 (42.4)	16 (59.3)	9 (28.1)	0.002
LE Ischemia	0	0	0	NA
LOS mean	17.0±15.1	21.8±20.1	13.8±9.9	0.07

MI = Myocardial Infarction; Reop = reoperation; Vent = ventilator; HIT = Heparin Induced Thrombocytopenia; RBC = Red Blood cells; LOS = length of stay; LE = lower extremity

Table 4. Morbidity and Mortality Stratified by Preoperative CPR

	CPR 22 (37.3)	No CPR 37 (62.7)	*P*
Mortality (%)	5 (18.2)	1 (2.7)	0.02
Stroke (%)	2 (9.1)	0	0.08
Renal failure (%)	6 (27.3)	2 (5.4)	0.04
Prolonged Vent (%)	9 (40.9)	7 (18.9)	0.15
RBC Transfusion (%)	12 (54.5)	13 (35.1)	0.36

Vent = ventilator; RBC = red blood cell

not (OR 0.24). One patient in each group suffered a postoperative stroke, both of whom had preoperative CPR. There were no myocardial infarctions nor were there any sternal wound infections. Overall,13.6% (8/47) of the patients required HD with a greater incidence in the ECMO cohort [VA-ECMO 25.9% (7/27) vs SE: 3.1% (1/32), $P = 0.002$]. The incidence of HD was closely associated with preoperative CPR, as 27.3% (6/122) patients who had undergone CPR required HD compared to 5.4% (2/37) who had not undergone CPR ($P = 0.04$). Just over 27% (16/59) of the population required prolonged mechanical ventilation [VA-ECMO: 29.6% (8/27) vs SE: 25% (8/32), $P = 0.41$]. Blood transfusions were more common in the VA-ECMO group [59.3% (16/27) vs 28.1% (9/32), $P = 0.002$] and one patient in the SE cohort required reoperation for bleeding. Postoperatively, heparin induced thrombocytopenia developed in 18.6% (11/459) [VA-ECMO: 28.6% (6/27) vs SE: 16.7% (5/32), $P = 0.31$]. None of the patients experienced lower extremity ischemia.

DISCUSSION

This analysis of 59 MPE patients treated with a surgical management strategy of either SE or VA-ECMO demonstrates excellent outcomes in an extremely unstable population. All patients had severe RV dysfunction and hemodynamic instability requiring intravenous vasopressors, with 37% undergoing preoperative CPR. Nevertheless, the overall in-hospital mortality was only 10.2%, which was largely driven by the sequelae of preoperative CPR; the mortality for those who did not undergo CPR was only 2.7%, which is comparable to the survival of the SMPE population (1.1%) that we previously published.[17] Based on our institution's treatment algorithm, the most unstable patients were preferentially treated with VA-ECMO, including patients who had uncertain neurologic status after CPR. As a result, the VA-ECMO population had higher mortality and hemodialysis rates. VA-ECMO was definitive therapy in 77.8% of patients treated with VA-ECMO as primary therapy, as these achieved sufficient RV recovery to permit weaning from ECMO without the need for any additional procedures. However, 22.2% required subsequent SE in order to achieve RV recovery sufficient to permit ECMO weaning.

Of note, none of the deaths were secondary to RV failure, indicating the success of SE and VA-ECMO at rescuing the RV. Furthermore, none of the patients treated required durable RV mechanical circulatory support. Thus, our treatment algorithm, using primary SE or VA-ECMO to treat massive PE, is safe and highly effective at achieving RV recovery, with relatively low morbidity and mortality. While this study was not sufficiently powered to determine treatment superiority it illustrates the effect of preoperative status and patient selection on procedural outcomes.

A growing body of literature documents the safety and efficacy of surgical management of MPE. Pasrija *et al.* published a series of MPE treated with VA-ECMO, reporting RV recovery and 95% survival in a population in which 25% had preoperative cardiac arrest.[13] The only death in that series was due to anoxic brain injury from preoperative CPR, not RV failure. Underscoring the effectiveness of ECMO in treating PE, ECMO combined with systemic anticoagulation achieved RV recovery and survival in 40% of their patients without any additional invasive procedures. Similarly, in a series of 12 MPE patients treated with VA-ECMO at a Japanese medical center, 83% survival was achieved and reported deaths were not due to RV failure but to the consequences of anoxic brain injury from pre-ECMO cardiac arrest.[18]

Modern series describing the treatment of MPE with SE also report excellent survival and RV recovery. Among 49 MPE patients treated with SE for acute PE, Neely *et al.* reported an overall mortality of 10.2%, but only 2% among patients who had not undergone preoperative CPR;[19] these findings are very similar to our outcomes (respectively10.2% and 2.7%). Similarly, Pasrija *et al.* published a series of 27 MPE patients treated with SE, 33% of whom had undergone preoperative CPR. Survival was 88% among MPE patients who had not undergone CPR and 78% among those who underwent CPR. All deaths were the result of preoperative stokes or preoperative multisystem organ failure and all survivors had RV recovery.[11]

In accordance with our treatment algorithm, the VA-ECMO cohort was more severely compromised, with a much greater proportion presenting with uncertain neurologic function after cardiac arrest (GCS ≤ 4: 33.3% vs 76.3%, $P = 0.008$), and anoxic brain injury was the sole cause of death among VA-ECMO cohort. These facts certainly contributed to the higher mortality (14.9% vs 6.25%, $P = 0.14$), renal failure (25.9% vs 3.1%, $P = 0.002$) and blood transfusions (59.3% vs 28.1%, $P = 0.006$) among VA-ECMO patients.

While our study and others describe the safety and efficacy of SE and VA-ECMO for PE, there are no studies that compare the two treatments. Based on these data, since SE and VA-ECMO both achieved RV recovery with relatively low morbidity and mortality, who should be treated with VA-ECMO and who should be treated with SE? First and foremost, care providers must be astutely aware of the mercurial nature of PE physiology and the tendency for "stable patients" to suddenly and profoundly decompensate requiring vigilante observation on part of the treatment team. In patients who are not determined to need immediate treatment, they are observed in an ICU setting on bed rest until

they are able to mobilize without significant symptomatology (syncope, presyncope, dyspnea etc.) In experienced centers, VA-ECMO can be initiated quickly in a variety of clinical settings (e.g. ER, ICU, cath lab, operating room). Thus, highly unstable patients (e.g. on-going CPR, instability despite vasopressors, uncertain neurologic status) or those who are high risk for sternotomy (e.g. prior sternotomy, recent thrombolytics) should be considered for ECMO first. VA-ECMO may be definitive therapy, as was the case in 78% of our ECMO population or may be a bridge to SE or catheter directed therapy once the patient has stabilized. However, VA-ECMO is not without risks: although the VA-ECMO cohort in our series experienced relatively few morbidities, reported series of VA-ECMO use for cardiogenic shock note relatively high rates of bleeding, stroke and limb ischemia. Thus VA-ECMO should be reserved for extremely unstable, high risk patients.[20] For more stable MPE patients, who can tolerate sternotomy, SE is preferred. It is important to note that thrombus burden in and of itself is not an indication for embolectomy as it has not been shown to be a predictor of adverse outcomes. Rather, we use the effect the thrombus has on the RV as the key determining factor for intervention.

Currently, the standard of care for treating MPE is systemic thrombolysis, based on the guidelines published by CHEST, AHA, and ESC.[3,6,7] However, current management strategies are associated with a 30-50% mortality, which is unacceptable by any standards. These guidelines either do not mention SE or VA-ECMO as a treatment option or recommend they be used only as salvage therapy, when all other treatment options are contraindicated or have failed. Our study mortality rate of 10.2% in a population in which nearly 40% had undergone CPR, along with similar findings from other studies, begs one to question the traditional strategy. In the era of multidisciplinary PE management teams, our data, and the data of similar surgical series, establish the importance of a well-timed surgical intervention as a primary treatment modality.

The limitations of this study are those inherent in a retrospective chart review. Our study lacks a nonsurgical or alternative therapy control group, such as thrombolysis or catheter-based therapy, but the study population was referred to our center from numerous institutions over a 100-mile radius, and data on alternative therapies administered at those centers are not available. Further research is needed with matched patient populations in order to compare the various treatment modalities.

This study described excellent survival and RV recovery after either SE or VA-ECMO in a highly unstable population with MPE. Untoward outcomes were largely associated with preoperative features, such as the need for CPR or uncertain neurologic status, rather than the treatment modality itself. This experience demonstrated excellent RV recovery and relatively low mortality, suggesting that primary treatment of MPE with VA-ECMO or SE should be considered as first line therapy.

SUPPLEMENTARY MATERIAL

Scanning this QR code will take you to the article title page to access supplementary information.

REFERENCES

1. Office of the Surgeon General NH, Lung, and Blood Institute. The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism. Rockville (MD) 2008.
2. Beckman MG, Hooper WC, Critchley SE: Venous thromboembolism: a public health concern. Am J Prev Med 38:S495–S501, 2010
3. Jaff MR, McMurtry MS, Archer SL, et al: Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the. American Heart Association. Circulation. 123:1788–1830, 2011
4. Secemsky E, Chang Y, Jain CC, et al: Contemporary Management and Outcomes of Patients with Massive and Submassive Pulmonary Embolism. Am J Med 131:1506–1514, 2018, . e1500
5. Hao Q, Dong BR, Yue J, Wu T, et al: Thrombolytic therapy for pulmonary embolism. Cochrane Database Syst Rev 12:CD004437, 2018
6. Konstantinides SV: 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J 35:3145–3146, 2014
7. Kearon C, Akl EA, Ornelas J, et al: Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest 149:315–352, 2016
8. Kuo WT, Gould MK, Louie JD, et al: Catheter-directed therapy for the treatment of massive pulmonary embolism: systematic review and meta-analysis of modern techniques. J Vasc Interv Radiol 20:1431–1440, 2009
9. Loyalka P, Ansari MZ, Cheema FH, et al: Surgical pulmonary embolectomy and catheter-based therapies for acute pulmonary embolism: A contemporary systematic review. J Thorac Cardiovasc Surg 156:2155–2167, 2018
10. Keeling WB, Sundt T, Leacche M, et al: Outcomes After Surgical Pulmonary Embolectomy for Acute Pulmonary Embolus: A Multi-Institutional Study. Ann Thorac Surg 102:1498–1502, 2016
11. Pasrija C, Kronfli A, Rouse M, et al: Outcomes after surgical pulmonary embolectomy for acute submassive and massive pulmonary embolism: A single-center experience. J Thorac Cardiovasc Surg 155:1095–1106, 2018, . e1092
12. Leacche M, Unic D, Goldhaber SZ, et al: Modern surgical treatment of massive pulmonary embolism: results in 47 consecutive patients after rapid diagnosis and aggressive surgical approach. J Thorac Cardiovasc Surg 129:1018–1023, 2005
13. Pasrija C, Kronfli A, George P, et al: Utilization of Veno-Arterial Extracorporeal Membrane Oxygenation for Massive Pulmonary Embolism. Ann Thorac Surg 105:498–504, 2018
14. Ain DL, Albaghdadi M, Giri J, et al: Extra-corporeal membrane oxygenation and outcomes in massive pulmonary embolism: Two eras at an urban tertiary care hospital. Vasc Med 23:60–64, 2018
15. Corsi F, Lebreton G, Brechot N, et al: Life-threatening massive pulmonary embolism rescued by venoarterial-extracorporeal membrane oxygenation. Crit Care 21:76, 2017
16. Goldberg JB, Spevack DM, Ahsan S, et al: Survival and Right Ventricular Function After Surgical Management of Acute Pulmonary Embolism. J Am Coll Cardiol 76:903–911, 2020

17. Goldberg JBRY, Nag T, Kai M, et al: Surgical management of 108 cases of acute massive and submassive pulmonary embolism yields recovery of right ventricular function with low mortality. In: American Heart Association 2018 National Meeting, Chicago, Il; 2019
18. Hashiba K, Okuda J, Maejima N, et al: Percutaneous cardiopulmonary support in pulmonary embolism with cardiac arrest. Resuscitation 83:183–187, 2012
19. Neely RC, Byrne JG, Gosev I, et al: Surgical Embolectomy for Acute Massive and Submassive Pulmonary Embolism in a Series of 115 Patients. Ann Thorac Surg 100:1245–1251, 2015. discussion 1251-1242
20. Eckman PM, Katz JN, El Banayosy A: Veno-Arterial Extracorporeal Membrane Oxygenation for Cardiogenic Shock: An Introduction for the Busy Clinician. Circulation 140:2019–2037, 2019