Circulation

AHA SCIENTIFIC STATEMENT

Surgical Management and Mechanical Circulatory Support in High-Risk Pulmonary Embolisms: Historical Context, Current Status, and Future Directions: A Scientific Statement From the American Heart Association

This statement is endorsed by the American Association for Thoracic Surgery.

This statement is endorsed by the Society of Thoracic Surgeons.

The Society for Cardiovascular Angiography and Intervention affirms the value of this statement.

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ABSTRACT: Acute pulmonary embolism is the third leading cause of cardiovascular death, with most pulmonary embolism–related mortality associated with acute right ventricular failure. Although there has recently been increased clinical attention to acute pulmonary embolism with the adoption of multidisciplinary pulmonary embolism response teams, mortality of patients with pulmonary embolism who present with hemodynamic compromise remains high when current guideline-directed therapy is followed. Because historical data and practice patterns affect current consensus treatment recommendations, surgical embolectomy has largely been relegated to patients who have contraindications to other treatments or when other treatment modalities fail. Despite a selection bias toward patients with greater illness, a growing body of literature describes the safety and efficacy of the surgical management of acute pulmonary embolism, especially in the hemodynamically compromised population. The purpose of this document is to describe modern techniques, strategies, and outcomes of surgical embolectomy and venoarterial extracorporeal membrane oxygenation and to suggest strategies to better understand the role of surgery in the management of pulmonary embolisms.

Key Words: AHA Scientific Statements ■ cardiopulmonary bypass ■ cardiopulmonary resuscitation ■ embolectomy ■ extracorporeal membrane oxygenation ■ heart failure ■ pulmonary embolism ■ survival

Acute pulmonary embolisms (PEs) are common, affecting patients of all ages and comorbidity profiles.[1,2] In 2016, there were an estimated 370 000 cases of PE in the United States, with PE hospital admissions tripling over the prior 2 decades. The estimated residual lifetime risk of developing a PE at 45 years of age is 8.1% and can be significantly higher when risk factors are present. Furthermore, PE represents the third leading cause of cardiovascular death in the United States, with associated 30-day and 6-month all-cause mortality rates of 9.1% and 19.6%, respectively, in the Medicare population.[2,3]

It is estimated that up to 45% of PEs present with or progress to a more clinically severe presentation, including hemodynamic instability. Options for the treatment

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Table 1. PE Classification System

Category	Features
Low risk	No RV strain Hemodynamically stable
Intermediate risk	RV strain Hemodynamically stable
High risk, fulminate	RV strain Hemodynamically unstable ≥1 of the following: SBP <90 mm Hg for 15 min Drop of >40 mm Hg from baseline SBP Vasopressor support MCS Cardiac arrest Severe (refractory) hemodynamic instability

MCS indicates mechanical circulatory support; PE, pulmonary embolism; RV, right ventricular; and SBP, systolic blood pressure.

RV strain is defined as an RV:left ventricle ratio on computed tomography or transthoracic echocardiography >0.9 or elevated cardiac biomarkers (troponin or BNP [brain natriuretic peptide]).

of hemodynamically significant PE include systemic anticoagulation alone, systemic thrombolysis, catheter-directed thrombolysis, catheter-based embolectomy, and advanced surgical therapies such as surgical embolectomy (SE) and mechanical circulatory support (MCS). In an attempt to navigate this wide array of treatment options, often supported by relatively low-quality data, multidisciplinary PE response teams have been established at many institutions to help risk-stratify and direct optimal patient management.[4] However, the effect of these teams on survival is unknown, especially for those who present with hemodynamic instability (ie, high risk), for whom contemporary high-quality observational studies suggest that in-hospital mortality rates are in excess of 40% with little improvement in the past 50 years.[5,6]

A recent American Heart Association scientific statement evaluating the existing evidence on the use of catheter-based therapies for acute PE did not comment extensively on their use in patients with high-risk PE because of a dearth of evidence within the transcatheter literature.[7] In contrast, the majority of the surgical PE literature consists almost exclusively of high-risk patients. Nevertheless, guidelines for the management of high-risk PE published by the major cardiovascular societies extend findings from intermediate-risk patients to the high-risk population. PE management guidelines published by the American Heart Association and the European Society of Cardiology recommend thrombolytic and transcatheter therapies in high-risk patients while reserving surgical therapy for circumstances in which all other treatment options have failed or are contraindicated.[8,9] Over the past 2 decades, there has been a growing body of literature describing the use of surgical treatments, including SE and MCS, in acute PE, particularly in high-risk patients.[10–13]

This scientific statement focuses on the surgical management of acute PE, clarifying the most modern evidence for various surgical techniques, the potential shortcomings of historical literature and the impact on current practice, and important gaps in knowledge in this field. Secondary to referral and practice patterns, most of the patients with PE discussed throughout this document are high-risk patients. Although clot in transit, defined as a mobile clot within the right side of the heart, is a classic surgical indication in the setting of PE, it is not a focus of discussion in this document. Rather, this scientific statement focuses on surgical strategies addressing right ventricular (RV) dysfunction leading to high-risk PE, which may not uniformly be present with isolated clot in transit. In addition, this document does not address the management of chronic thromboembolic pulmonary hypertension with surgical thromboendarterectomy, which is a markedly different disease process that requires different surgical techniques. This scientific statement is organized into 2 main sections: SE and MCS for acute PE. It is important to note that these 2 sections and treatment strategies are not mutually exclusive and that there is considerable crossover between strategies. Last, the authors of this scientific statement recognize that MCS is performed and managed by surgeons and nonsurgeons alike. The rationale for including MCS under the umbrella of surgery has to do with the historical association of MCS and embolectomy use, as well as the overall use of MCS in almost exclusively high-risk patients, who are the focus of this scientific statement.

TERMINOLOGY

Modern operational definitions and classifications of acute PE were described in the prior American Heart Association scientific statement on interventional PE therapies and are used throughout this document[7] (Table 1). Specifically, we use the term high risk to refer to patients with hypotension, defined as a systolic blood pressure <90 mm Hg, a drop of >40 mm Hg for at least 15 minutes, the need for vasopressor support or MCS, any period of pulselessness, or persistent profound bradycardia <40 bpm not attributable to causes other than PE. These patients have been described as having massive PE in prior literature. The 2020 updated American Heart Association guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care further describe a subgroup of patients with massive PE, or fulminant PE, defined as patients presenting with cardiac arrest or severe hemodynamic instability.[14] We use the term intermediate risk to refer to normotensive patients with objective evidence of RV dysfunction as judged by transthoracic echocardiography, computed tomographic angiography, or the presence of positive serum cardiac biomarkers. These patients have been classified as having submassive PE in prior literature. Last, low risk refers to patients who do not meet the criteria for high risk or intermediate risk. It is important to note that there is fluidity between classification strata; patients can rapidly and unpredictably change from a lower

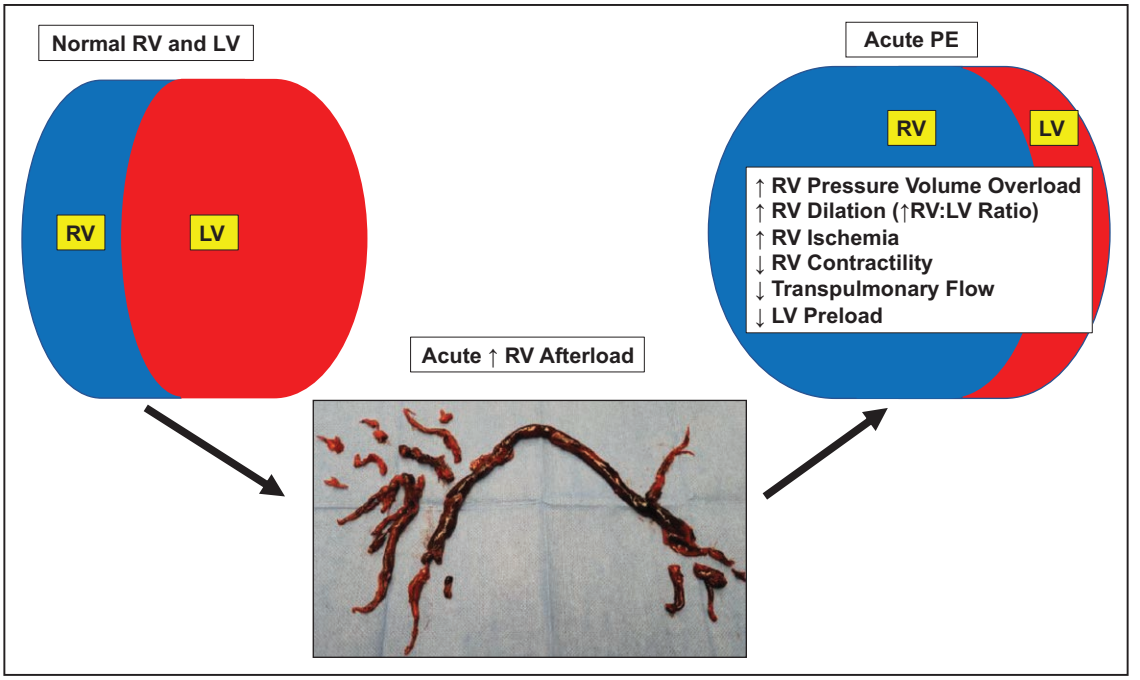

Figure 1. Effect of a hemodynamically significant PE on biventricular function.
Graphical description of changes that occur to biventricular function with a hemodynamically significant pulmonary embolism (PE). The figure depicts a normal right ventricle (RV) with an RV:left ventricle (LV) ratio of ≈0.6 and bowing of the interventricular septum to the right. With an acute, hemodynamically significant PE (photograph), there is an acute increase in RV afterload, resulting in RV pressure and volume overload. The RV dilates as reflected by an increased RV:LV ratio (>0.9) and a flattening or leftward shift of the interventricular septum (increased interventricular interdependence). There is subsequent increased wall tension; RV ischemia decreased RV contractility. In combination with outflow obstruction from the acute thrombus, there is decreased transpulmonary flow, leading to decreased LV preload, which is further exacerbated by the increased interventricular interdependence. Once compensatory mechanisms are exhausted, the patient becomes hypotensive.

to a higher risk category. This scientific statement focuses primarily on high- and intermediate-risk patients in whom the RV has been directly affected by the PE. Throughout this document, death and PE-related death, unless otherwise indicated, refer to death attributed to the acute PE presentation rather than a chronic illness such as cancer.

PE PATHOPHYSIOLOGY

In patients with hemodynamically significant PEs, RV dysfunction attributable to an acute increase in RV afterload represents the main pathophysiological insult leading to death. The RV is accustomed to the afterload of the pulmonary arterial circulation, a highly compliant and low-pressure system (normal mean pulmonary artery [PA] systolic blood pressure <20 mm Hg). Acute PE causes a sudden increase in RV afterload, requiring the RV to generate pressures that can reach 4 to 5 times greater than normal[10,15–18] (Figure 1). The quickly escalating, vicious pathophysiological cycle begins with RV pressure and volume overload, which can lead to both RV ischemia and a decrease in RV output. Through a combination of decreased transpulmonary flow and increased ventricular interdependence, there is a reduction in left ventricular (LV) preload, resulting in a sharp decrease in systemic cardiac output and ultimately hemodynamic compromise and shock. Hypoxic pulmonary vasoconstriction[19] and neurohumoral mediated pulmonary vasoconstriction contribute further to increased pulmonary vascular resistance, decreased pulmonary arterial compliance, and increased RV afterload.[20] Systemic hypoxemia is caused largely by ventilation/perfusion mismatch, as well as possible right-to-left shunting if a persistent patent foramen ovale is present.[21] Significant RV distention and dysfunction are readily diagnosed by imaging studies (increased RV:LV ratio, RV free wall hypokinesis, interventricular septal flattening [McConnell sign]) and elevated biomarkers (troponin or BNP [brain natriuretic peptide]), which are hallmark pathophysiological features of hemodynamically significant acute PE (Figure 2).

It is important to note that LV function in the initial phase is preserved, although the LV cavity is typically underfilled. Together with other compensatory responses, including vasoconstriction and tachycardia, this helps explain why many patients, even in the setting of severe RV dysfunction, do not become overtly hemodynamically unstable in the initial phase and may, in some cases, even present with systemic hypertension. However, in the presence of severe pulmonary obstruction to blood flow, cardiac output is relatively fixed. Any sudden decrease in sympathetic tone, for example, from anesthesia induction, drug-related vasodilation, or a decrease in venous return from positive pressure ventilation or postural changes, may accelerate the vicious

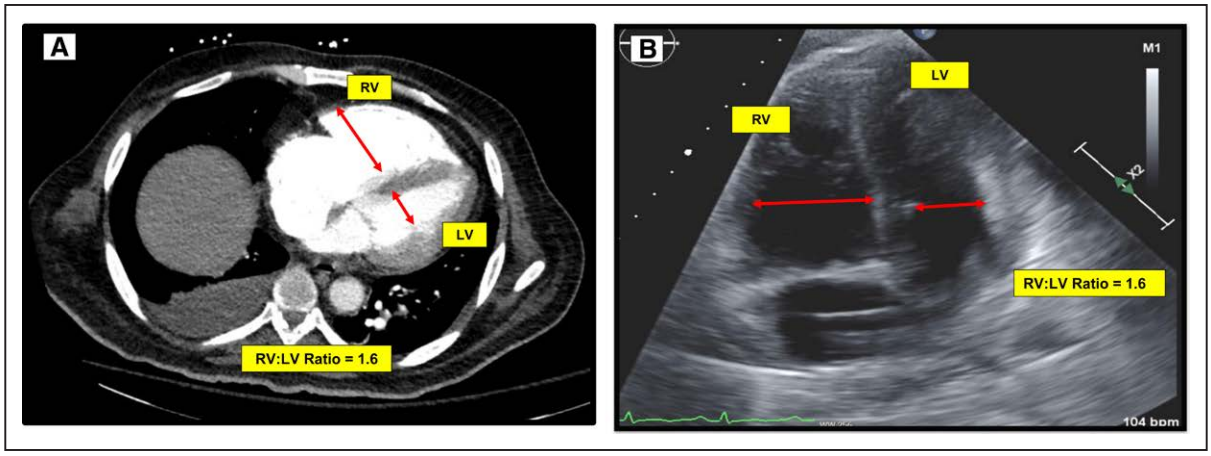

Figure 2. Acute RV dilation associated with pulmonary embolism as seen on CT and TTE.
A, Computed tomography (CT) pulmonary angiogram in the setting of an acute pulmonary embolism (PE) demonstrating a dilated right ventricle (RV). **B**, Transthoracic echocardiography (TTE) of the same patient with acute PE demonstrating a dilated RV. Normal RV:left ventricle (LV) ratio is <0.9.

cycle of hypotension and coronary ischemia, which can rapidly precipitate cardiac arrest. In the compensatory state, blood pressure alone is a poor metric of hemodynamic stability, in particular for risk-stratifying patients who may rapidly deteriorate. Investigation is needed into other metrics such as clinical findings (eg, syncope, exacerbation of symptoms with minor activity [transferring from bed to chair, positional changes, short-distance ambulation], imaging findings, and novel biomarkers] to better predict hemodynamic stability.

Because PE represents a mechanical obstructive problem, methods to increase RV inotropy or to pharmacologically decrease PA pressures typically have limited effectiveness. Furthermore, CPR is largely ineffective in the setting of cardiac arrest resulting from PE because the LV cannot fill from the obstructing clot burden. To directly treat RV dysfunction in acute PE, the volume pressure overload must be addressed by offloading the RV through resolution of the mechanical obstruction or decompression of the RV by diversion of the blood causing the distention.

Summary

- In acute PE, RV dysfunction attributable to a sudden increase in RV afterload is the main pathophysiological insult, resulting in mortality.
- Because PE affects primarily the RV while sparing the LV, systemic hypotension is typically a late marker of PE severity; thus, systemic blood pressure alone may not be a reliable determinant of clinical stability.
- Further research is needed to determine more accurate predictors of patient stability because systemic blood pressure, which is currently used to risk-stratify patients, may be inadequate for selecting patients who may decompensate.
- Definitive, acute treatment of PE-associated RV dysfunction requires RV offloading by resolving the mechanical disruption or diverting the RV preload causing the distention.

HISTORY OF SE AS A TREATMENT FOR PE

Acute PE has a long historical association with cardiac surgery. Dr Friedrich Trendelenburg recognized the acute effect of PE on the RV and was the first to publish his animal research and pulmonary embolectomy technique in 1908, 18 years before the first clinical use of heparin.[22] However, it was not until 1924 that a patient survived the operation. Unfortunately, surgical pulmonary embolectomy with the Trendelenburg procedure continued to result in dismal outcomes for many decades, with a reported 87% mortality rate in the literature of that era (only 12 reported survivors between 1908 and 1954).[23]

Conceptually, removal of the thrombus causing the RV failure was sound. However, the Trendelenburg procedure was doomed to fail because of flaws in its application and implementation. First, diagnosis was challenging and based solely on clinical suspicion because no imaging modalities were available. Second, it was common practice to defer surgery until a patient experienced or was very near cardiac arrest. In this emergency circumstance, a left anterior thoracotomy was performed rapidly, followed by occlusion or partial occlusion of the PA and aorta to permit adequate visualization and to prevent excessive blood loss (Figure 3). A pulmonary arteriotomy was then performed, the clot was extracted, and the PA was closed. In retrospect, multiple factors contributed to the exceedingly high mortality associated with the Trendelenburg procedure, including imprecise PE diagnosis, intervention at the end stages of hemodynamic decompensation, and perhaps most important, occlusion of the PA, leading to even larger increases in afterload to an

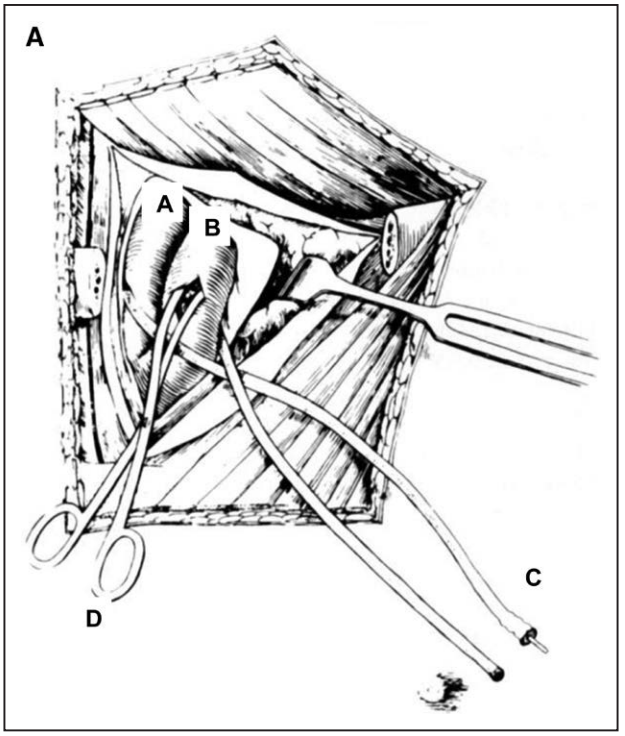

Figure 3A. Original Trendelenburg procedure.
This figure demonstrates the original Trendelenburg procedure, an early surgical embolectomy procedure, during which the ascending aorta and proximal pulmonary artery are encircled with a tourniquet to occlude blood flow while a pulmonary arteriotomy is performed to extirpate the clot. A, Ascending aorta. B, Pulmonary artery. C, Tourniquet around the ascending aorta and main pulmonary artery used to occlude blood flow during pulmonary arteriotomy and clot extraction. D, Extraction of clot from an arteriotomy in the pulmonary artery. Reprinted from Johnson.[23a] Used with permission of Johns Hopkins Press; permission conveyed through Copyright Clearance Center, Inc.

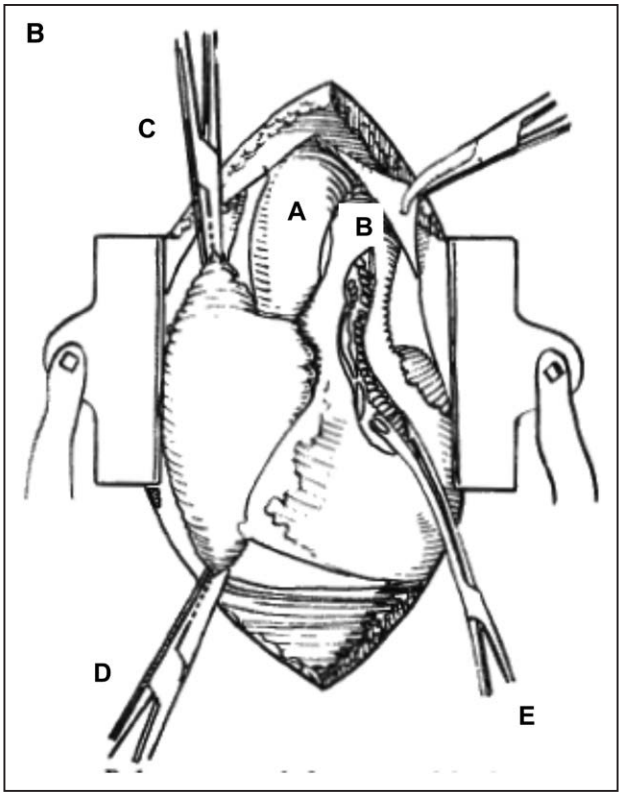

Figure 3B. Inflow occlusion technique.
This figure demonstrates the inflow occlusion technique, another early surgical embolectomy procedure, during which the vena cava is occluded to eliminate venous inflow to the right ventricle while a pulmonary arteriotomy is performed to extirpate the clot. A, Ascending aorta. B, Pulmonary artery. C, Clamp occluding venous return from the superior vena cava. D, Clamp occluding venous return from the inferior vena cava. E, Extraction of clot from an arteriotomy in the pulmonary artery. Reprinted from Clarke.[24] Used with permission of The Royal College of Surgeons of England; permission conveyed through Copyright Clearance Center, Inc.

already failing RV, resulting in further RV dysfunction, systemic hypoperfusion, and death.[23]

To avoid the lethality of exacerbating RV failure through PA occlusion, a surgical strategy of inflow occlusion was developed. Inflow occlusion was performed by cessation of flow to the right atrium by occlusion of the superior vena cava and inferior vena cava, followed by pulmonary arteriotomy, embolectomy, and PA closure (Figure 3). Although inflow occlusion does not cause further increase in RV afterload by avoiding PA occlusion, it was still associated with dismal outcomes, with mortality rates exceeding 55%.[23,24] Inflow occlusion outcomes were poor for 2 reasons. First, as with the Trendelenburg procedure, patients presented late in the disease process, profoundly hemodynamically unstable, and often in a peri–cardiac arrest state. In addition, the low cardiac output secondary to decreased LV preload characteristic of PE pathophysiology was profoundly exacerbated by inflow occlusion, which, by eliminating all preload into the heart, commonly precipitated profound systemic hypotension and cardiac arrest. The failure of the Trendelenburg procedure and inflow occlusion techniques highlighted the importance of combining removal of thrombus with the ability to decompress and support the RV while maintaining systemic perfusion.

Summary

- Early SE was associated with exceedingly high mortality attributable to imprecise diagnosis, late intervention (all patients had fulminant PEs), and surgical techniques that exacerbated RV failure and systemic malperfusion.

CARDIOPULMONARY BYPASS: MECHANISM OF ACTION

One of the single most important advancements in the field of cardiac surgery and in the surgical treatment of PE occurred in 1931 when Dr John Gibbon observed a patient die of an attempted Trendelenburg procedure.

He realized that for patients to survive the procedure, surgeons needed the ability to temporarily support corporeal perfusion. Thus, he developed the cardiopulmonary bypass (CPB) machine, which was first used to support a patient during pulmonary embolectomy in 1961 by Dr Denton Cooley.[25]

The CPB machine functions as an external heart and lung. Venous blood is drained into a reservoir, oxygenated, and pumped back to the arterial system. With full CPB, the heart is essentially isolated with the majority of blood bypassing the heart and lungs, allowing cardiac decompression while maintaining corporeal perfusion. Full anticoagulation, typically with heparin, measuring a target activated clotting time >480 seconds is required. The reservoir distinguishes CPB from extracorporeal membrane oxygenation (ECMO) by creating an open circuit, allowing the addition to or subtraction of volume from the circuit. ECMO constitutes a closed circuit lacking the ability to add or subtract volume directly to the circuit (Figure 4).

Venous cannulation for CPB can be achieved through any central vein(s) (femoral, internal jugular, innominate, inferior vena cava, superior vena cava, or right atrium). Arterial access for blood return from the CPB machine is typically through the aorta or axillary, innominate, or femoral artery. Aside from ascending aorta and right atrial cannulation, other cannulation sites can be achieved percutaneously in locations other than the operating room (emergency department, intensive care unit, and regular ward), as routinely done by some institutions before the introduction of ECMO, which is much more mobile than the large, cumbersome CPB machine[26–28] (Figure 4).

CPB is effective in the setting of PE for several key reasons. Diversion of the venous return to the CPB circuit immediately decompresses the RV and the pulmonary circulation, thereby interrupting the vicious cycle of RV distention, increased workload, and myocardial ischemia that accompanies a large PE. Systemic perfusion is reinstituted, ending or preventing acute end-organ ischemia, which may occur in a low-cardiac-output state. In addition, CPB without aortic cross-clamping and cardioplegia-induced myocardial arrest, which is not typically required in patients with acute PE, allows active recovery of the RV by allowing it to contract with minimal preload or afterload (Figure 5).

Summary

- CPB permits RV recovery by decompressing the dilated and dysfunctional RV through diversion of the cardiac output to a pump and oxygenator, allowing the RV to beat in a fully decompressed state with minimal preload and afterload.
- CPB fully supports systemic perfusion.
- ECMO is a closed circuit that functions similarly to CPB while allowing more flexibility in MCS initiation outside of traditional operative room settings.

ANESTHESIA CONSIDERATIONS

As previously described, patients presenting with acute PE typically have decreased cardiac output and rely on compensatory mechanisms such as increased adrenergic tone to maintain blood pressure and systemic perfusion. As a result, anesthesia induction can be hazardous because most anesthetics lead to a loss of adrenergic tone, resulting in a cycle of decreased venous return and perfusion pressure, which, unless intervened on rapidly, may culminate in profound hemodynamic instability and cardiac arrest.[10,26,27,29,30] For example, in a study of 52 patients undergoing emergency pulmonary embolectomy, hemodynamic collapse requiring CPR after anesthesia induction occurred in 19% of patients.[31] In a modern series of 59 patients with high-risk PE, anesthesia induction precipitated the need for CPR in 50% of patients who required preoperative CPR.[32]

Several strategies are commonly used to mitigate the anesthesia-related risk of further hemodynamic compromise. At a minimum, hemodynamic monitoring, including invasive continuous blood pressure monitoring and secure intravenous access, must be established before anesthesia induction. Although PA catheters can provide information on RV function and potential early detection of RV failure progression, they are not essential, and preoperative placement should not delay surgery if a patient is unstable or if there is clot in transit. If patients with high-risk PE are not supported by MCS preoperatively, patients should be prepped and draped, and the surgeon should be scrubbed before anesthesia induction to facilitate chest opening if the patient becomes unstable or arrests. Preinduction placement of femoral arterial and venous sheaths should be considered because this expedites the surgeon's ability to place the patient on peripheral CPB or venoarterial ECMO (VA-ECMO) if a patient decompensates. Alternatively, the risk of anesthesia-induced instability can be avoided altogether by placing a patient on CPB or VA-ECMO through the femoral artery and vein before anesthesia induction, thereby ensuring hemodynamic stability and avoiding the risk of decompensation. Intraoperative transesophageal echocardiography is also valuable because it helps with the assessment of changes in the severity of RV strain, response to anesthetic drugs, and pharmacological treatment of RV failure; it also confirms the diagnosis and detects additional findings that may affect surgical and CPB management.

Currently, there are few descriptive studies and no comparative studies analyzing the safety and

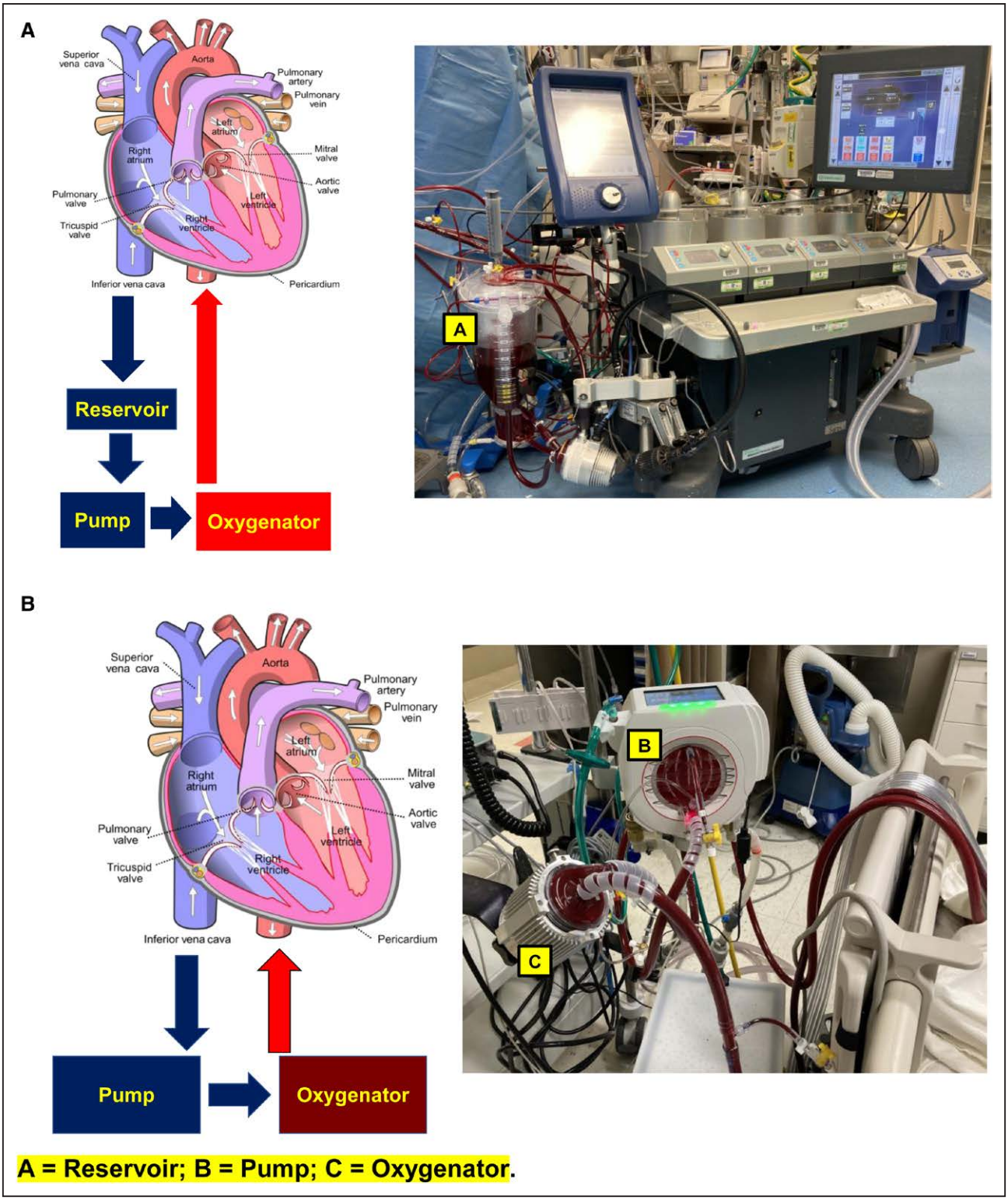

Figure 4. Essential mechanics of CPB and VA-ECMO.
This image describes the basic function and depicts the cardiopulmonary bypass (CPB; **A**) and venoarterial extracorporeal membrane oxygenation (VA-ECMO; **B**). In the case of CPB, a patient's venous return is drained into a reservoir, then pumped through an oxygenator, and finally pumped back into the patient's arterial system. VA-ECMO functions similarly but lacks a venous reservoir.

efficacy of preoperative and anesthetic strategies in the setting of PE. Because the immediate preoperative period is a particularly vulnerable period, future research efforts focusing on anesthesia management, including preinduction MCS/CPB in patients with acute PE, are needed.

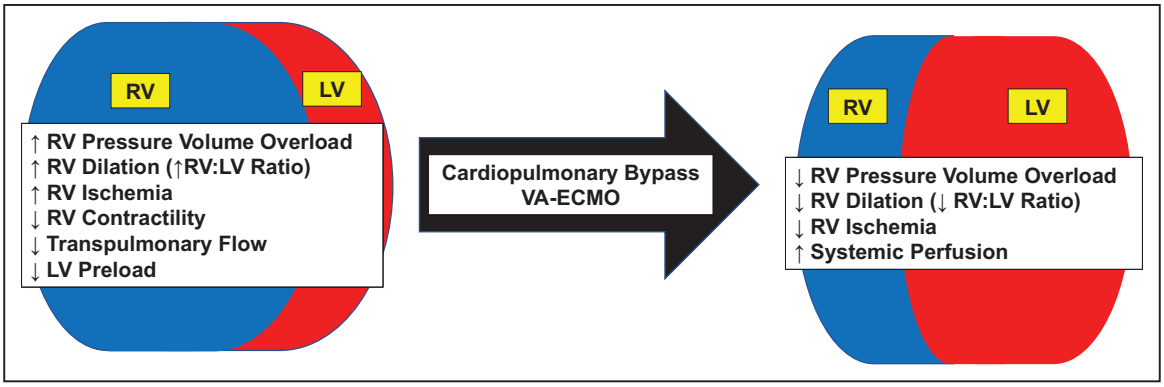

Figure 5. Beneficial effect of CPB and VA-ECMO on biventricular function in the setting of a hemodynamically significant PE. Graphical descriptions of the beneficial effect of cardiopulmonary bypass (CPB) and venoarterial extracorporeal membrane oxygenation (VA-ECMO) on the right ventricle (RV) and left ventricle (LV) in the setting of a hemodynamically significant pulmonary embolism (PE). CPB and VA-ECMO result in immediate decompression of the volume and pressure overload by diverting the RV preload to the CPB or VA-ECMO circuit. This results in rapid reduction in RV size, ischemia, and augmentation of systemic perfusion.

Summary

- Anesthesia induction is potentially hazardous because of iatrogenic loss of compensatory mechanisms maintaining cardiac output and systemic blood pressure.
- Various strategies to prevent peri-intubation instability, including instituting CPB/MCS before anesthesia induction or prepping and draping the patient before induction, have been used.
- Placement of femoral arterial and venous sheaths before anesthesia induction can help expedite placement of CPB or VA-ECMO if needed.
- Future research should focus on strategies to prevent peri-induction instability, including the timing and strategy of preinduction CPB or ECMO.

MODERN SURGICAL TECHNIQUE

Modern surgical pulmonary embolectomy is performed on CPB through a midline sternotomy with or without aortic cross-clamping and cardioplegia-induced cardiac arrest. CPB is classically initiated centrally with bicaval or right atrial venous drainage and ascending aorta cannulation. However, given the potential dangers associated with anesthesia induction, some initiate CPB through the femoral vessels before anesthesia induction or transition from peripheral ECMO to CPB. CPB management typically includes moderate hypothermia to ≈32°C. Hypothermia offers additional protection during brief periods of decreased CPB flows often required to optimize distal PA visualization. Aortic cross-clamping and cardioplegic arrest are not necessary except when certain concomitant procedures are required. Avoidance of cross-clamping and cardioplegic arrest prevents associated myocardial edema and dysfunction, which may have a deleterious effect on RV recovery. Avoiding aortic cross-clamping facilitates RV recovery by allowing the RV to contract with minimal preload and afterload with continuous perfusion on CPB during the procedure.[10,11,33,34] A pulmonary arteriotomy is performed through which the clot is extracted. Surgeons have described a variety of techniques, including a single incision in the main PA or 2 incisions, 1 in the main PA extending toward the left PA and a second incision in the right main PA.[10,11,33–35] The 2-incision approach facilitates visualization of both left and right PAs and their major branches, allowing optimal distal clot extraction, whereas the single-incision approach does not provide right PA visualization, which may lead to suboptimal clot extraction. Clot extraction has been augmented by a variety of procedures, including suction, perfusion of blood retrograde through the pulmonary veins with the intention of flushing out the clot from distal branches, manual manipulation of the lung to massage out the clot from distal branches, or the use of balloon-tipped embolectomy catheters to extract the clot from distal branches. There are no comparative studies investigating the safety or efficacy of the various techniques. However, publications describing balloon-tipped catheter use have reported higher rates of postprocedural pulmonary hemorrhage, which may be attributable to iatrogenic injury, including catheter-induced perforation of the small, fragile distal PA branches.[26,34] The large variability in current practice, including the timing and conduct of CPB and the surgical approach, may affect the observed differences in outcomes. The writing committee acknowledges that future research should include a focus on evidence-based best practices for CPB management and surgical techniques.

Summary

- Modern surgical embolectomies are performed on CPB with variability in techniques.
- Future research is needed to determine the impact of heterogeneous surgical techniques and strategies, especially focusing on the timing of CPB given the instability that patients experience after anesthesia induction.

Table 2. Modern Outcomes of SE Performed on CPB

Study	Study years	n (per year of study)	HR, % (n)*	CPR, % (n)	Deaths, % (n)†	Death—CPR, % (n)‡	Death+CPR, % (n)§
Kadner et al,[36] 2008	2000–2007	25 (3.1)	100 (25)	32 (8)	8 (2)	0	25 (2)
Fukuda et al,[37] 2011	1998–2009	19 (1.6)	89.5 (17)	21.1 (4)	5.2 (1)	6.7 (1)	0
Takahashi et al,[15] 2012	2000–2011	24 (2.2)	75 (18)	45.8 (11)	12.5 (3)	0	27.3 (3)
Zarrabi et al,[16] 2013	2004–2010	30 (4.3)	36 (11)	10 (3)	13.2 (4)	NR	NR
Hartman et al,[11] 2015‖	2003–2011	96 (10.7)	25 (24)	NR	4	NR	NR
Neely et al,[38] 2015	1999–2013	115 (7.7)	43 (49)	9.6 (9)	6.6 (7)	2.9 (3)	36.6 (4)
Keeling et al,[39] 2016	1998–2014	44 (2.6)	20.5 (9)	0	2.3 (1)	2.3 (1)	NR
Keeling et al,[13] 2016‖	1998–2014	214 (12.6)	17.8 (38)	13.1 (28)	11.7 (25)	8.1 (16)	32.1 (9)
Edelman et al,[18] 2016	2000–2014	37 (2.5)	54.1 (20)	35.1 (13)	5.4 (2)	NR	NR
Pasrija et al,[34] 2018	2011–2015	55 (11)	32.7 (18)	16.7 (9)	7.3 (4)	4.3 (2)	22 (2)
Goldberg et al,[10] 2020	2005–2019	136 (9.1)	32.4 (44)	14 (19)	4.4 (6)	1.7 (2)	21.1 (4)
QiMin et al,[35] 2020	2005–2019	41 (2.7)	58.5 (24)	4.9 (2)	7.3 (3)	0	100 (3)

CPB indicates cardiopulmonary bypass; CPR, cardiopulmonary resuscitation; HR, high-risk pulmonary embolism; NR, not reported; and SE, surgical embolectomy.
*High risk.
†In-hospital mortality.
‡Mortality among patients who did not require preoperative CPR.
§Mortality among patients who underwent preoperative CPR.
‖Multicenter study.

CURRENT ERA EMBOLECTOMY OUTCOMES

It is paramount to interpret the findings of recent SE literature in the context of current PE treatment recommendations and their impact on patient selection. Stemming from outcomes reported in the early SE literature, current guidelines do not recommend SE as a primary therapy. Rather, SE is largely reserved for high-risk PEs in which all other treatment options failed or are contraindicated. As a result, a considerable proportion of patients with SE present with high-risk PEs (20.5%–89.5%), many of which are fulminant PEs as reflected by a relatively high incidence of preoperative CPR (4.9%–45.8%; Table 2).[1] Reflecting guideline-directed therapy, ≈40% of patients have contradictions to systemic thrombolysis, and ≈20% have failed catheter-directed therapy or systemic thrombolysis.[11,34,38] Furthermore, heterogeneous surgical indications exist: Some series report using SE as a salvage therapy; other series report using SE as a primary therapy.[15,37] In the broader context of determining the safety and efficacy of PE treatment modalities, it is imperative that comparative studies address and adjust for differences in patient selection and acuity, which have a significant impact on outcomes.

Survival

Despite the critically ill nature of patients with SE in these modern series, postoperative in-hospital mortality has improved dramatically, now ranging from 2.3% to 13.2%, with mortality associated largely with preoperative CPR (Table 2). The mortality of patients with SE who do not require CPR (2.9%) is approximately the same as the operative mortality (2.7%) of patients undergoing coronary artery bypass grafting in the Society of Thoracic Surgeons Adult Cardiac Surgery Database, despite nearly all patients undergoing SE experiencing acute RV failure at the time of surgery, which is uncommon in the setting of coronary artery bypass grafting.[40] In addition, heterogeneity exists within the subset of patients requiring preoperative CPR. For example, the duration and location of CPR (out of hospital, in hospital, intraoperative) affect postoperative morbidity and mortality. Patients who require a brief period of intraoperative CPR compared with those who present to the operating room after prolonged CPR are expected to have different risks for a poor outcome. Currently, within the PE literature, CPR is treated as a dichotomous variable without granularity of CPR circumstances, which are essential for risk stratification and for comparing different treatment modalities among patients with high-risk PE. Despite virtually all patients in surgical series presenting with severe RV dysfunction, postoperative RV failure is rarely reported as a cause of death in modern series of SE. Anoxic brain injury from preoperative cardiac arrest or exacerbation of underlying illness such as coronary artery disease, cancer, or infection more frequently causes mortality.[10,18,35–38]

RV Recovery

In addition to improved survival, modern series report normalization of RV function after SE.[10,15–18] Reported proxies for RV function include PA catheter hemodynamics and echocardiography measures.[10,15–18] For instance, 1 study demonstrated intraoperative improvement

of central venous pressure from 26.6 to 10 mm Hg ($P<0.001$) and PA systolic pressure from 66.4 to 31.7 mm Hg ($P<0.001$) after embolectomy.[10] Of note, hemodynamic data to assess improvement in RV function are subject to numerous confounders, including lack of data in the sickest patients, who are often too unstable for placement of preoperative PA catheters. Such a lack of data may result in underestimation of the magnitude of preoperative RV dysfunction and, consequently, underestimation of postoperative RV recovery.[10] Furthermore, lower postoperative PA catheter pressures may also reflect a reduction in intravascular volume status from bleeding or hemoconcentration. In addition, mechanical ventilation, general anesthesia, and inotrope use will confound PA catheter assessment of RV function.

The echocardiographic surrogates for RV function also normalize by discharge after SE.[10,18,34,41] Heterogeneity exists in the measurement of RV function in the surgical and nonsurgical literature. In the future, more uniform reporting criteria would facilitate outcome comparisons.

In recent series, the need for postoperative VA-ECMO or RV assist device (RVAD) to treat persistent RV failure after embolectomy was rare (ranging from 0%–8.7%) and strongly associated with prolonged preoperative CPR.[10,11,13,18,34–38,42] It is speculated that the rates of continued MCS after SE may decrease with more liberal use of ECMO in the most acutely ill patients.[18,32]

RV recovery is an important outcome metric of treatment efficacy in analyses of any treatment modality used in patients with high-risk PE. Mortality alone is an imprecise assessment of treatment efficacy, especially with high-risk and fulminant PE. With the high incidence of preoperative CPR and associated anoxic brain injury, patients have been reported to achieve full RV recovery after SE only to succumb to the sequelae of their anoxic brain injury attributable to preoperative cardiac arrest.[10,34] Mortality in such situations reflects the patient's preoperative acuity rather than the inability of SE to rescue the RV. The key element here is a distinction between randomized and observational analyses of high-risk PE interventions. In randomized evaluations of high-risk PE interventions (which are lacking), there is little question that early mortality should be the primary outcome because multiple clinical confounders can be controlled by the randomization process. In observational data sets, because of the inability to truly adjust for confounders in such an ill and heterogeneous population, more nuance is necessary for assessed outcomes such as measurement of RV function.

Morbidity

Relative to the severity of illness on presentation, morbidity in modern series is low and associated largely with preoperative CPR. Among patients who presented neurologically intact, postoperative stroke rates were low, ranging from 0% to 4.4%. Postoperative renal failure requiring new hemodialysis ranged from 0% to 5.5%. Postprocedural bleeding, defined as a drop in hemoglobin or the need for transfusion, is an important metric for thrombolytic and catheter-directed therapies. Arguably, similar bleeding criteria to assess post-SE complications are inappropriate because the nature and conduct of CPB commonly result in anemia and the need for transfusion even in the elective surgical population rather than reflecting a true bleeding complication.[43] Return to the operating room for bleeding and postoperative tamponade may be more accurate measures of true bleeding complications after SE, all of which are low (0%–10.5%), with many series reporting no occurrences.

Impact of Failed Thrombolytic Therapy on SE Outcomes

Reflecting consensus guideline recommendations to primarily treat high-risk PEs with systemic thrombolytics (ST) while reserving SE for patients in whom ST fails or is contraindicated, most surgical series include a subset of patients with SE who failed ST.[8,9,44] Although ST failure (defined as progression of PE pathophysiology after administration of ST requiring SE) is common among surgical series, only a few studies have analyzed this subpopulation. The conclusion of this sparse literature is that failed ST portends greater morbidity and mortality. For example, a single-institution, nonrandomized comparison of 108 patients with high-risk PE (30 with SE versus 78 with ST) separately analyzed the outcomes of 17 patients who failed ST (21.8%) and subsequently underwent SE.[41] The SE cohort, which included both those who did not receive ST and those who failed ST, was more unstable, as reflected by a 40% incidence of preoperative CPR compared with 0% among patients with ST. Nevertheless, mortality was numerically lower and statistically similar in the SE group (3.3% for the SE group versus 9.8% for the ST group; $P=0.42$). Separate analysis of the patients with ST failure who subsequently underwent SE revealed a 41.2% mortality that was significantly higher than that of the SE or ST population ($P<0.05$).[41] Similarly, another single-institution, nonrandomized study of 80 patients with high-risk PE (28 with SE versus 52 with ST) separately analyzed 11 patients (39.3%) who failed ST and required SE.[45] The surgical cohort had more profound preoperative RV dysfunction (higher RV:LV ratios [1.67 for the SE group versus 1.43 for the ST group; $P=0.04$] and higher PA systolic pressures [72±9 mm Hg for the SE group versus 52± 25 mm Hg for the ST group; $P=0.01$]). Of note, CPR was described as a surgical indication, but the specific incidence of CPR was not reported. Although the SE cohort had more profound RV dysfunction, mortality was numerically lower and statistically similar (3.6% for the SE group versus 13.5% for

the ST group; *P*=0.25). However, separate analysis of the patients who failed ST and subsequently underwent SE demonstrated a significantly higher mortality of 26.5% (*P*=0.002) compared with those who underwent SE or ST.[45] Within the broader SE literature, many series report the incidence of patients who failed ST (4.9%–56.7%) within their SE population.[35] Although none of these studies specifically analyzed the effect of failed thrombolysis on postoperative outcomes, the authors describe postoperative bleeding complications among those with failed ST as a key contributor to postoperative morbidity and mortality.[17,35,37,38] More recent series report SE performed after failed catheter-directed therapies, but existing data are insufficient to make evidence-based conclusions on the impact on postsurgical outcomes. Because current data indicate that failure of ST is a marker of increased postoperative morbidity and mortality, future research is needed to prospectively identify patients who are likely to fail ST or to identify patients who should be referred to SE earlier to optimize outcomes.

Long-Term Outcomes

The vast majority of published research focuses on in-hospital morbidity and mortality after SE, with postdischarge outcomes being reported less frequently. Although sample sizes are relatively small, several trends are emerging. First, postdischarge mortality is mostly not related to PE, with deaths being attributed to progression of underlying disease processes such as cancer or cardiovascular disease. Second, published series do not report recurrent PE after discharge.[27,37] Third, functional status and RV function remain preserved over available follow-up times.[27,37,39,46] One study that compared objective pulmonary function parameters between 136 patients with PE treated with either SE or with ST found that among patients with high-risk PE with a median follow-up period of 30 months, SE had lower rates of residual pulmonary vascular obstruction (31% for SE versus 76% for ST; *P*=0.009) and fewer patients with pulmonary diffusion impairment (31% for SE versus 71% for ST; *P*=0.002).[47] As with other treatment modalities for PE, more structured long-term outcome studies are needed to fully understand the natural history of patients after PE treatment. It will be important to determine whether the extensive embolectomy that is achieved through surgical removal translates to a decreased incidence of chronic thromboembolic pulmonary hypertension and post-PE syndrome.

Summary

- In the current era, SE series consist of a large proportion of patients with high-risk PE, including a high proportion of patients requiring preoperative CPR.
- Despite the high acuity and high rates of preoperative CPR, morbidity and mortality after SE are low.
- Most morbidity and mortality are associated with preoperative CPR. The mortality of SE patients who do not require CPR is roughly equivalent to the average mortality associated with coronary artery bypass grafting across a wide range of patient risks.
- Most patients achieve RV recovery after SE as measured by invasive hemodynamic monitoring and transthoracic echocardiography without a need for durable RV MCS.
- Objective RV recovery is an important metric of treatment efficacy among high-risk and salvage patients and should be considered a primary outcome variable in these patient populations.
- Uniform and validated assessment of RV function is needed within the PE literature to facilitate comparative studies.
- Failure of ST is associated with compromised post-SE outcomes. Future investigation is needed to identify patients who are likely to fail ST primarily to select a more efficacious treatment modality.
- More accurate classification of the characteristics of preoperative CPR is needed in future PE research.
- Future research should attempt to determine whether extensive SE prevents chronic thromboembolic pulmonary hypertension and other post-PE syndromes.

MECHANICAL CIRCULATORY SUPPORT

VA-ECMO and MCS device use in the setting of PE functions by supporting the failing RV without direct intervention on the clot burden. The hemodynamic and myocardial support provided by VA-ECMO/MCS breaks the cycle of RV distention and ischemia, resulting in hemodynamic stability, and can be used as a bridge to RV recovery with anticoagulation alone or as a bridge to the decision to proceed with active thrombus removal strategies.

VENOARTERIAL ECMO

VA-ECMO decompresses the RV by diverting RV venous return to the ECMO circuit while augmenting perfusion by pumping oxygenated blood into the arterial system. Similar to CPB, the right side of the heart is bypassed, allowing RV and PA decompression while permitting the RV to contract in an unloaded state with minimal preload and afterload (Figures 4 and 5). Typical VA-ECMO circuits provide 4 to 6 L flow while also supporting systemic oxygenation. The ECMO circuit is mobile and can be transported directly to the patient in emergency situations both in and out of hospital.[48–50] The early days of CPB set the stage for modern VA-ECMO use for PE. Shortly after the first use of

CPB in cardiac surgery, several groups established mobile CPB systems to treat unstable patients with PE in diverse clinical settings, including the intensive care unit, ward, and emergency department.[26–28] Similar to modern practice, the patient was placed on CPB through the femoral vessels under local anesthesia, thereby stabilizing the patient and permitting transport for diagnostic testing or the operating room for definitive SE. For instance, an early series of 40 very unstable patients with PE (CPR or systolic blood pressure <55 mm Hg) placed 55% of patients on bypass in locations outside of the operating room (the majority of whom were on the regular ward).[26] Thus, mobile CPB was used much like ECMO is used today.

Similar to CPB, access sites for ECMO cannulation have many permutations. Although the preferred sites for access are the femoral vein and femoral artery, the cannulas may be placed in a variety of different locations. Alternative venous access sites include the internal jugular and subclavian veins.[51,52] The arterial cannulas can be placed in the femoral, axillary, and, rarely, carotid arteries. Axillary and carotid arterial access has traditionally required direct surgical access. However, percutaneous axillary techniques for a variety of large-bore access procedures are growing in use.[53] The placement of an arterial cannula in the femoral artery creates a risk for ipsilateral leg ischemia, which requires vigilant attention to lower-limb perfusion. Ipsilateral leg ischemia can be avoided by inserting an antegrade perfusion catheter (5F–8F) into the femoral artery distal to the arterial cannula that is connected to the arterial ECMO limb, allowing arterial flow down the leg. It is safest to insert ECMO cannulas with the assistance of imaging modalities such as ultrasound guidance for vascular access with fluoroscopy or echocardiography for confirmation of distal cannula placement. However, in many patients, the threat of decompensation or ongoing CPR may necessitate cannula placement without additional imaging. ECMO cannulas can be placed by a variety of procedural specialists, including but not limited to interventional cardiologists, interventional radiologists, vascular surgeons, and cardiothoracic surgeons. Central ECMO is a possibility but requires a sternotomy and should be reserved for patients in whom peripheral ECMO cannot be initiated. As previously explained, intubation can be extremely hazardous for patients with PE-induced RV failure. Therefore, it is ideal to perform ECMO cannulation under local anesthesia, even when open femoral artery exposure is required.

Once VA-ECMO is initiated, patients are rapidly stabilized, affording clinicians the ability to decide the next course of PE treatment. It is important to note that other important treatments may be needed to support the RV, including (1) diuresis to optimize volume status (decrease RV), (2) anticoagulation and pulmonary vasodilators to optimize RV afterload, and (3) inotropes to augment RV function until recovery. In certain scenarios, ECMO is used as a bridge to treatment in which ECMO stabilizes the patient in preparation for other PE treatments (transcatheter or surgical). Ongoing ECMO support does not preclude concomitant transcatheter procedures, which can be performed through the contralateral femoral vein or an internal jugular vein, depending on the location of ECMO cannulation. Patients undergoing ECMO can be easily transitioned to CPB by connecting the arterial and venous ECMO lines to the corresponding CPB lines if SE is to be performed.

It is important to note that veno-veno ECMO does not treat the RV pressure-volume overload causing RV failure in the setting of PE. The RV decompression that occurs with VA-ECMO does not occur with veno-veno ECMO because the same volume that is diverted to the ECMO circuit is returned to the venous system, often at nonpulsatile pressures >100 mm Hg. Veno-veno ECMO requires sufficient RV function to generate adequate transpulmonary flow (the entire cardiac output), the ability of which is compromised with a hemodynamically significant PE. Thus, any RV dysfunction from volume pressure overload will not be relieved and, alternatively, may be exacerbated. Furthermore, veno-veno ECMO is used primarily to treat refractory hypoxia and hypercarbia, which are rarely the dominant pathophysiological derangements resulting in instability in the setting of PE except in the rare cases of a large right-to-left shunt. If a patient presents with a PE, profound hypoxia, and a functional RV, there is usually an additional cause for the hypoxia apart from the acute PE such as infection or parenchymal disease that maybe effectively treated with veno-veno ECMO.

Unless specifically contraindicated, all patients should be anticoagulated while on ECMO. Typically, patients receive a bolus of heparin before cannulation and are maintained on a heparin drip thereafter to maintain an elevated partial thromboplastin time or activated clotting time. Although general anticoagulation recommendations for VA-ECMO suggest maintaining an activated clotting time between 180 and 220 seconds, current guidelines are vague, and anticoagulation is largely left to individual operator discretion.[54] Furthermore, it is not known whether anticoagulation in the setting of PE should be altered given the hypercoagulability of the patient on presentation or the relative coagulopathy that occurs in the setting of VA-ECMO.

Although no studies have directly investigated the safety of thrombolytics in proximity to ECMO placement, recent or concomitant administration of intravenous thrombolytics is not an absolute contraindication for VA-ECMO, especially in the decompensating or arresting patient. Thrombolytics in close proximity to ECMO will undoubtedly result in increased risk of bleeding complications, but the magnitude of the risk is unknown and should be documented in future studies.

Summary

- Similar to CPB, VA-ECMO rescues the RV by decompressing the dilated and dysfunctional RV by diverting the venous return to a pump and

Table 3. VA-ECMO Use and Outcomes Among Patients With PE

Study	Study years	n	HR, n (%)	CPR before VA-ECMO, n (%)	Prior ST/CDT, n (%)	Death, n (%)*	Death+CPR, n (%)†	Death—CPR, n (%)‡	ECMO, d§	Definitive Tx, n (%)‖
Maggio et al,[61] 2007	1992–2005	21	21 (100)	8 (38.1)	6 (29)	8 (38.1)	NR	NR	4	NR
Hashiba et al,[62] 2012	1998–2010	12	12 (100)	12 (100)	0	2 (16.7)	2 (16.7)	NR	13	5 (42)
Malekan et al,[63] 2012	2005–2011	3	3 (100)	NR	0	0	NR	NR	5	3 (100)
Munakata et al,[64] 2012	1992–2008	10	10 (100)	9 (90)	100	3 (30)	3 (33.3)	0	NR	0
Swol et al,[65] 2016	2008–2014	5	5 (100)	5 (100)	3 (60)	2 (40)	2 (40)	NR	NR	3 (60)
Corsi et al,[60] 2017	2006–2015	17	17 (100)	15 (88)	9 (52.9)	9 (52.9)	7 (46.7)	0 (0)	4	NR
George et al,[66] 2018	2012–2015	30	30 (100)	16 (53.3)	5 (16.7)	15 (50)	11 (68.8)	3 (21.4)	4	0
Meneveau et al,[67] 2018	2014–2015	45	45 (100)	39 (88.6)	20 (45.5)	32 (61.5)	NR	NR	NR	18 (35)
Moon et al,[68] 2018	2010–2017	14	14 (100)	11 (78.6)	1 (7.1)	8 (57.1)	NR	NR	NR	8 (66.7)
Pasrija et al,[12] 2018	2014–2016	20	20 (100)	5 (25)	7 (35)	1 (5)	1 (20)	0 (0)	5	8 (40)
Al-Bawardy et al,[69] 2019	2012–2019	13	13 (100)	13 (100)	11 (84.6)	4 (30.8)	4 (30.8)	NR	5.5	1 (7.7)
Kjaergaard et al,[70] 2019	2004–2019	22	22 (100)	22 (100)	5 (22.7)	11 (50)	11(50)	NR	NR	NR
Oh et al,[56] 2019	2014–2018	16	16 (100)	12 (75)	2 (12.5)	7 (43.8)	5 (41.7)	2 (50)	2	3 (18.8)
Ghoreishi et al,[58] 2020	2015–2018	41	41 (100)	12 (29.3)	10 (24.4)	1 (2.4)	NR	NR	6	72.5
Goldberg et al,[10] 2020	2005–2019	27	27 (100)	10 (37)	8 (29.6)	4 (14.9)	4 (100)	0 (0)	5	88
Guliani et al,[57] 2020	2017–2019	17	17 (100)	10 (58.8)	10 (58.8)	4 (23.5)	4 (40)	0 (0)	4	77

CDT indicates catheter-directed therapy; CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; HR, high-risk pulmonary embolism; NR, not reported; PE, pulmonary embolism; ST, systemic thrombolytic; Tx, treatment; and VA-ECMO, venoarterial extracorporeal membrane oxygenation.

*In-hospital mortality.

†Mortality among patients who underwent preoperative CPR.

‡Mortality among patients who did not require preoperative CPR.

§Average number of days of VA-ECMO support.

‖Right ventricular recovery achieved with ECMO and anticoagulation alone without additional pharmacological or extirpative therapy.

oxygenator, allowing the RV to beat in a decompressed state with minimal preload and afterload while augmenting systemic perfusion.

- VA-ECMO is mobile and can be initiated by a variety of clinicians in a variety of settings.

VA-ECMO OUTCOMES

The vast majority of ECMO literature on patients with PE is limited to nonrandomized, single-center case series and observational studies.[55] In addition, each study reflects the treatment algorithm of the institution. For instance, some institutions use ECMO as a salvage platform, whereas other series report ECMO use as an upfront bridge to recovery or definitive reperfusion therapy (SE, catheter-directed therapy).[12,32,55–58] Similar to the SE literature, further heterogeneity arises in the presentation of patients, including variability in hemodynamics and CPR and failure of other treatment modalities. It comes as no surprise that series report increased mortality with increased duration of CPR before ECMO and ongoing CPR at the time of ECMO insertion.[56,59] For instance, a recent meta-analysis reported a 7-fold increase in mortality when ECMO is placed during ongoing CPR compared with after return of spontaneous circulation (odds ratio, 6.84 [95% CI, 1.53–30.58]; P=0.01).[59] Furthermore, failure of systemic thrombolytic therapy or use of systemic thrombolytics after ECMO insertion has been associated with increased mortality and bleeding complications.[56,60] This tremendous variability inevitably affects postoperative outcomes and makes comparison between studies challenging.

Nevertheless, several trends in the VA-ECMO literature are readily apparent (Table 3). First, virtually all patients with PE treated with VA-ECMO have high-risk or fulminant PE. Second, the incidence of pre-ECMO CPR is high at ≈70%, with many series reporting that 100% of patients undergoing ECMO receive pre-ECMO CPR. Third, even with a high incidence of CPR, survival is excellent with an overall mortality of ≈30%, which compares favorably with ECMO mortality rates after cardiac arrest resulting from acute MI (83.3%).[62] As with SE, much of the mortality is associated with preoperative CPR (41% mortality in those who received pre-ECMO CPR versus 9% in those who did not; Table 3). Fourth, VA-ECMO is effective at reversing cardiogenic shock and systemic malperfusion, as evidenced by rapid improvement of acidosis and weaning of vasopressors and inotropes.[12,56,57,60,62] Fifth, although VA-ECMO in and of itself is not extirpative therapy, it is definitive therapy in ≈45% of patients. A substantial proportion of patients may achieve RV recovery with VA-ECMO and anticoagulation alone without additional reperfusion therapy such as catheter-directed therapy or SE after a mean of 5

days of ECMO support. As with SE, critics of ECMO use in PE express concern about persistent RV failure requiring durable RVAD. This is not supported by the current literature because durable RVAD use is rare.[8]

Survival is an imperfect metric of VA-ECMO success and other similar procedures used to treat patients with fulminant PE because it is confounded by numerous exposures before the institution of ECMO such as CPR, failure of other treatment modalities, and underlying medical conditions that adversely affect survival. As a result of the frequency of pre-ECMO CPR, a common cause of mortality among the ECMO population is anoxic brain injury. Series report numerous cases in which the RV recovers, the patient is successfully weaned from ECMO, yet death occurs as a result of the sequelae of their anoxic brain injury.[10,12,57,71] A poignant example is a patient who was placed on VA-ECMO after sustained cardiac arrest resulting from a PE. The patient was diagnosed with brain death from anoxic brain injury and was made an organ donor. After 5 days of ECMO support, the RV had fully recovered, and the heart was successfully transplanted.[71] Furthermore, the frequency of RV recovery is likely underestimated in patients with anoxic brain injury because care is often withdrawn before evaluation of RV recovery.[10,12,57,60,62,71] Rather than survival, clinical and echocardiographic metrics of RV function may be better indicators of RV rescue efficacy, with carefully adjudicated ECMO-specific complications perhaps being the best metrics for safety.

The current published data largely lack the granularity to make an accurate assessment of RV recovery because most studies use survival as a proxy for RV recovery, which underestimates the efficacy of ECMO. It is also often difficult to differentiate whether post-ECMO complications such as stroke, renal failure, and bleeding are the result of the treatment or the severity of the patient's condition at presentation. Furthermore, because the vast majority of published data consist of small uncontrolled case series with high variability and heterogeneity, it is difficult to ascertain the true morbidity burden associated with ECMO in the setting of PE. A recent meta-analysis including 533 high-risk PEs from 16 uncontrolled case series found that in-hospital survival with good neurological outcomes, defined as a Cerebral Performance Category score of 1 to 2, occurred in 50% to 95% of cases, lower-limb ischemia occurred in 8% (95% CI, 3%–15%), and ischemic or hemorrhagic stroke occurred in 11% (95% CI, 3%–23%). More systematic research is needed to reliably document and report ECMO outcomes in the setting of PE.

Summary

- The vast majority of patients with acute PE receiving VA-ECMO are high risk, with a high proportion of patients requiring preoperative CPR.
- Relative to the severity of illness at presentation, survival and RV recovery are excellent.
- As with SE, morbidity and mortality in patients with PE receiving VA-ECMO are associated with preoperative CPR or failed ST.
- Given the high acuity of patients receiving VA-ECMO and the high proportion of salvage patients, RV recovery may be a better metric of treatment success than survival.
- Analysis of the impact of the heterogeneity of treatment patterns and clinical presentation of patients is needed to better risk-stratify patients and to determine comparative treatment modality efficacy.

EMERGING MODALITIES OF RV SUPPORT

In general, RV MCS or RVAD entails placement of a surgically implanted or percutaneously inserted pump that augments the work required of the failing RV. RVADs used in the setting of acute PE are peripherally inserted and function by circumventing the RV by pumping RV preload into the pulmonary circulation. There are a couple of conceptual problems with RVAD support in the setting of PE. First, most pumps are afterload sensitive. Thus, downstream occlusion from the embolus may limit the amount of support the RVAD can provide. Second, the PA embolus can physically interfere with the function of the device. Neither ECMO or RVAD directly extirpates the obstructing embolism. Third and most important, RVAD support may not facilitate optimal RV recovery. Nonpulsatile RVADs subject a failing RV to constant afterload by diverting RV preload into the pulmonary circulation, thereby increasing RV afterload. The constant pressure in the PAs generated by an RVAD requires more RV work, which may inhibit RV ejection and decompression. This is a known mechanism of failure to rescue RV function with RVAD support in non-PE conditions.[72] RV myocardial wall tension, dilation, and failure may persist because the RV may not be able to adequately empty against the persistent afterload. Especially in the setting of PE, in which there are a significant component of PA obstruction and acute RV afterload to begin with, PA pressure and RV afterload may become high enough to result in pulmonic valve insufficiency, which would further exacerbate RV distention. In contrast, VA-ECMO decompresses both RV preload and RV afterload as it diverts the RV venous return to the ECMO circuit and returns the blood to the systemic arterial system. Any residual RV preload can be ejected with little work as the PA system is decompressed. All that being said, isolated RVADs decompress the RV at least partially through direct removal of RV preload and have the potential to augment overall cardiac output through an overall increase in right-sided flow rates. In addition, percutaneous RVADs may avoid the need for and

potential complications associated with a large-bore arterial cannula. The balance between the benefits of percutaneous RVADs and theoretical harm to the RV from afterload-inducing effects on RV ejection is unclear. Further investigation is needed to justify the use of percutaneous RVADs in the setting of PE because there are currently few studies investigating their use, with both the physiological effects and clinical results of the devices remaining unclear.

There are differing strata of RVAD support, including selective RV support devices with and without oxygenation. The Impella RP (Abiomed, Danvers, MA) is a percutaneous RVAD system that can be placed through the femoral veins with a 23F sheath. The Impella RP is then guided into the left PA over a wire under fluoroscopic guidance. The inflow port lies in the inferior vena cava, and the outflow port is situated in the left PA. The device can provide up to 4 L flow per minute.[73] Experience with the Impella RP is limited to several case reports. Although it is a promising technology, the experience and data are insufficient to draw any meaningful conclusions about its safety and efficacy in the setting of acute PE.[74–78]

The Protek Duo system (LivaNova, London, UK) is inserted through the right internal jugular vein and into the right PA under fluoroscopic guidance with the proximal portion of the device measuring 29F or 31F. The proximal port is located in the right atria and the distal port in the right PA. This device is then attached to an extracorporeal pump and has the ability to also use an oxygenator. At present, this is the only percutaneous RVAD that has the ability to oxygenate. As with the Impella RP, experience with the Protek Duo is limited to case reports, and more research is needed to draw meaningful conclusions about its safety and efficacy in the setting of acute PE.[79] It is important to note that the Impella RP and Protek Duo require fluoroscopy for placement, limiting their applicability in emergency situations in which transport to a catheterization laboratory may not be possible.

Summary

- Emerging percutaneous RV MCS with or without an associated oxygenator can be used to support a failing RV.
- Data on their efficacy in the setting of PE are limited.

CONCLUSIONS AND CALL TO ACTION

The surgical and MCS literature represents the most robust data on the high-risk PE population because the vast majority of catheter-directed therapy and systemic thrombolytic research has thus far focused on the intermediate-risk PE population. Referral patterns based on historical practice and current guidelines have largely relegated SE and MCS as salvage treatments. Nevertheless, as described in the previous sections, modern SE and VA-ECMO demonstrate favorable safety and efficacy profiles when we account for the baseline level of illness of the populations in whom they are used. Among patients who do not require preoperative CPR, mortality rates of SE are <3%. Even among those who require CPR, survival is ≈75%. Although VA-ECMO treats the sickest of the high-risk population, with preoperative CPR needed in the majority of patients, reported short-term survival rates are ≈70% (38.5%–100%). Despite this, SE and VA-ECMO are infrequently used and, when used, it is frequently later in the disease process after other treatment modalities have failed.[80,81] On the basis of the outcome data described previously, expansion of the use of SE and MCS may provide additional survival benefit in a population in whom the current treatment paradigms continue to be associated with exceedingly high mortality.

There are numerous limitations to the data presented, related largely to the lack of large multi-institution registries and trials, which prevents rigorous analysis and comparison of techniques and strategies. The current literature represents a heterogeneous mix of single-institution experiences, techniques, and patient selection algorithms, making comparisons difficult. In the next section, the authors identify several areas on which the PE treatment community should focus to improve our understanding of surgical treatment strategies, the high-risk PE population, and ultimately patient outcomes.

Call to Action

High-Risk PE Registries/Trials

It is imperative that current and future PE registries include patients with high-risk and fulminant PE. Prior clinical and industry registry and trial data have almost exclusively focused on intermediate-risk patients, with guidance and recommendations for high-risk patients being extrapolated from their analysis. Given the wide spectrum of hemodynamic status within the high-risk population and the rapid progression from intermediate risk to high risk in some patients with PE, data are needed to understand the natural history of high-risk PE in the modern era and to compare different treatment strategies and modalities. Furthermore, trials including patients with high-risk PE should include an SE/VA-ECMO cohort for comparative-effectiveness analyses. Results of the FLAME study (FlowTriever for Acute Massive Pulmonary Embolism; NCT04795167) are anticipated and will include a broad range of patients with high-risk PE treated with large-bore catheter–based embolectomy, MCS, SE, systemic thrombolysis, and other modalities. The National Pulmonary Embolism Response Team Consortium is also

assembling data in a large, prospective registry that may allow more information to be gained on management strategies and clinical outcomes in high-risk patients. To have an accurate understanding of the safety and efficacy of SE and VA-ECMO in the high-risk population, it is imperative that their use be analyzed before salvage situations. Analysis of their use in context of the clinical presentation will help control for the selection bias affecting the reported outcomes in the past and current literature.

Refined Definition of High-Risk PE

A wide and clinically significant spectrum of hemodynamic status exists within the high-risk population. A patient who is classified as high risk on the basis of a 40–mm Hg drop in baseline blood pressure is different from a patient who is defined as high risk because of ongoing CPR. To better risk-stratify patients, compare treatment modalities, and risk-adjust outcomes, more precise strata reflecting patients' hemodynamic and clinical status are necessary to separate the population with salvage/fulminant PE from the high-risk population. For instance, CPR should no longer be defined as a dichotomous variable with attempts to further define CPR timing (eg, out of hospital, in hospital, after anesthesia induction) and duration. In addition, neurological status at the time of intervention influences survival and may be important in further risk-stratifying the high-risk PE population.

Metrics of Treatment Efficacy

In comparisons of outcomes in hemodynamically unstable patients, survival may not be the optimal measure of the efficacy of a particular treatment modality. In addition to survival, universal measures of RV recovery should be reported such as RV:LV ratio, RV fractional area change, and tricuspid annular plane systolic excursion because these are more specific metrics of RV function.

Increased Education and Awareness

Surgical and interventional societies should educate their members about the techniques and risk/benefit profile of using SE and MCS in the setting of PE. Currently, most centers and surgeons have minimal experience with SE. When performed at low-volume centers, these modalities tend to be used for unique indications or in salvage situations and are not part of a standard treatment algorithm, which can lead to suboptimal outcomes. Increased programmatic experience with both surgical and anesthetic management is a necessary prerequisite for well-designed, controlled trials to truly evaluate the optimal management of patients with high-risk PE. Furthermore, broader use of surgical strategies will enable comparison of different techniques and management strategies such as the conduct of CPB (timing of cannulation, temperature management) and surgical timing and technique. In addition, cardiac surgeons should be involved in PE response teams, especially in the evaluation of intermediate- and high-risk PEs.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

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*Modest.

†Significant.

REFERENCES

1. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). *Lancet.* 1999;353:1386–1389. doi: 10.1016/s0140-6736(98)07534-5
2. Virani SS, Alonso A, Aparicio HJ, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Cheng S, Delling FN, et al; on behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics–2021 update: a report from the American Heart Association. *Circulation.* 2021;143:e254–e743. doi: 10.1161/CIR.0000000000000950
3. Centers for Disease Control and Prevention (CDC). Venous thromboembolism in adult hospitalizations–United States, 2007-2009. *MMWR Morb Mortal Wkly Rep.* 2012;61:401–404.
4. Kabrhel C, Rosovsky R, Channick R, Jaff MR, Weinberg I, Sundt T, Dudzinski DM, Rodriguez-Lopez J, Parry BA, Harshbarger S, et al. A multidisciplinary pulmonary embolism response team: initial 30-month experience with a novel approach to delivery of care to patients with submassive and massive pulmonary embolism. *Chest.* 2016;150:384–393. doi: 10.1016/j.chest.2016.03.011
5. Secemsky E, Chang Y, Jain CC, Beckman JA, Giri J, Jaff MR, Rosenfield K, Rosovsky R, Kabrhel C, Weinberg I. Contemporary management and outcomes of patients with massive and submassive pulmonary embolism. *Am J Med.* 2018;131:1506–1514.e0. doi: 10.1016/j.amjmed.2018.07.035
6. Rosovsky R, Chang Y, Rosenfield K, Channick R, Jaff MR, Weinberg I, Sundt T, Witkin A, Rodriguez-Lopez J, Parry BA, et al. Changes in treatment and outcomes after creation of a pulmonary embolism response team (PERT), a 10-year analysis. *J Thromb Thrombolysis.* 2019;47:31–40. doi: 10.1007/s11239-018-1737-8
7. Giri J, Sista AK, Weinberg I, Kearon C, Kumbhani DJ, Desai ND, Piazza G, Gladwin MT, Chatterjee S, Kobayashi T, et al. Interventional therapies for acute pulmonary embolism: current status and principles for the development of novel evidence: a scientific statement from the American Heart Association. *Circulation.* 2019;140:e774–e801. doi: 10.1161/CIR.0000000000000707
8. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, Huisman MV, Humbert M, Jennings CS, Jiménez D, et al; Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). 2019 ESC guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). *Eur Respir J.* 2019;54:1901647. doi: 10.1183/13993003.01647-2019
9. Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, Jenkins JS, Kline JA, Michaels AD, Thistlethwaite P, et al; on behalf of the American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; American Heart Association Council on Peripheral Vascular Disease; American Heart Association Council on Arteriosclerosis, Thrombosis and Vascular Biology. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association [published corrections appear in *Circulation.* 2012;125:e495 and *Circulation.* 2012;126:e104]. *Circulation.* 2011;123:1788–1830. doi: 10.1161/CIR.0b013e318214914f
10. Goldberg JB, Spevack DM, Ahsan S, Rochlani Y, Dutta T, Ohira S, Kai M, Spielvogel D, Lansman S, Malekan R. Survival and right ventricular function after surgical management of acute pulmonary embolism. *J Am Coll Cardiol.* 2020;76:903–911. doi: 10.1016/j.jacc.2020.06.065
11. Hartman AR, Manetta F, Lessen R, Pekmezaris R, Kozikowski A, Jahn L, Akerman M, Lesser ML, Glassman LR, Graver M, et al. Acute surgical pulmonary embolectomy: a 9-year retrospective analysis. *Tex Heart Inst J.* 2015;42:25–29. doi: 10.14503/THIJ-13-3877
12. Pasrija C, Kronfli A, George P, Raithel M, Boulos F, Herr DL, Gammie JS, Pham SM, Griffith BP, Kon ZN. Utilization of veno-arterial extracorporeal membrane oxygenation for massive pulmonary embolism. *Ann Thorac Surg.* 2018;105:498–504. doi: 10.1016/j.athoracsur.2017.08.033
13. Keeling WB, Sundt T, Leacche M, Okita Y, Binongo J, Lasajanak Y, Aklog L, Lattouf OM; SPEAR Working Group. Outcomes after surgical pulmonary embolectomy for acute pulmonary embolus: a multi-institutional study. *Ann Thorac Surg.* 2016;102:1498–1502. doi: 10.1016/j.athoracsur.2016.05.004
14. Panchal AR, Bartos JA, Cabañas JG, Donnino MW, Drennan IR, Hirsch KG, Kudenchuk PJ, Kurz MC, Lavonas EJ, Morley PT, et al; on behalf of the Adult Basic and Advanced Life Support Writing Group. Part 3: adult basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation.* 2020;142(suppl 2):S366–S468. doi: 10.1161/CIR.0000000000000916
15. Takahashi H, Okada K, Matsumori M, Kano H, Kitagawa A, Okita Y. Aggressive surgical treatment of acute pulmonary embolism with circulatory collapse. *Ann Thorac Surg.* 2012;94:785–791. doi: 10.1016/j.athoracsur.2012.03.101
16. Zarrabi K, Zolghadrasli A, Ali Ostovan M, Azimifar A, Malekmakan L. Residual pulmonary hypertension after retrograde pulmonary embolectomy: long-term follow-up of 30 patients with massive and submassive pulmonary embolism. *Interact Cardiovasc Thorac Surg.* 2013;17:242–246. doi: 10.1093/icvts/ivt210
17. Ahmed P, Khan AA, Smith A, Pagala M, Abrol S, Cunningham JN Jr, Vaynblat M. Expedient pulmonary embolectomy for acute pulmonary embolism: improved outcomes. *Interact Cardiovasc Thorac Surg.* 2008;7:591–594. doi: 10.1510/icvts.2008.176735
18. Edelman JJ, Okiwelu N, Anvardeen K, Joshi P, Murphy B, Sanders LH, Newman MA, Passage J. Surgical pulmonary embolectomy: experience in a series of 37 consecutive cases. *Heart Lung Circ.* 2016;25:1240–1244. doi: 10.1016/j.hlc.2016.03.010
19. Burrowes KS, Clark AR, Wilsher ML, Milne DG, Tawhai MH. Hypoxic pulmonary vasoconstriction as a contributor to response in acute pulmonary embolism. *Ann Biomed Eng.* 2014;42:1631–1643. doi: 10.1007/s10439-014-1011-y
20. Smulders YM. Pathophysiology and treatment of haemodynamic instability in acute pulmonary embolism: the pivotal role of pulmonary vasoconstriction. *Cardiovasc Res.* 2000;48:23–33. doi: 10.1016/s0008-6363(00)00168-1
21. Burrowes KS, Clark AR, Tawhai MH. Blood flow redistribution and ventilation-perfusion mismatch during embolic pulmonary arterial occlusion. *Pulm Circ.* 2011;1:365–376. doi: 10.4103/2045-8932.87302
22. McFadden PM, Ochsner JL. Aggressive approach to pulmonary embolectomy for massive acute pulmonary embolism: a historical and contemporary perspective. *Mayo Clin Proc.* 2010;85:782–784. doi: 10.4065/mcp.2010.0481
23. Cross FS, Mowlem A. A survey of the current status of pulmonary embolectomy for massive pulmonary embolism. *Circulation.* 1967;35(suppl):I86–I91. doi: 10.1161/01.cir.35.4s1.i-86

23a. Johnson SL. *The History of Cardiac Surgery, 1896-1955.* Johns Hopkins Press; 1970.

24. Clarke DB. Pulmonary embolectomy re-evaluated. *Ann R Coll Surg Engl.* 1981;63:18–24.
25. Steenburg RW, Warren R, Wilson RE, Rudolf LE. A new look at pulmonary embolectomy. *Surg Gynecol Obstet.* 1958;107:214–220.
26. Mattox KL, Feldtman RW, Beall AC Jr, DeBakey ME. Pulmonary embolectomy for acute massive pulmonary embolism. *Ann Surg.* 1982;195:726–731. doi: 10.1097/00000658-198206000-00008
27. Meyer G, Tamisier D, Sors H, Stern M, Vouhé P, Makowski S, Neveux JY, Leca F, Even P. Pulmonary embolectomy: a 20-year experience at one center. *Ann Thorac Surg.* 1991;51:232–236. doi: 10.1016/0003-4975(91)90792-o
28. Glassford DM Jr, Alford WC Jr, Burrus GR, Stoney WS, Thomas CS Jr. Pulmonary embolectomy. *Ann Thorac Surg.* 1981;32:28–32. doi: 10.1016/s0003-4975(10)61369-0
29. Reul GJ, Beall AC Jr. Emergency pulmonary embolectomy for massive pulmonary embolism. *Circulation.* 1974;50(suppl):II236–II241.
30. Sharp EH. Pulmonary embolectomy: successful removal of a massive pulmonary embolus with the support of cardiopulmonary bypass: case report. *Ann Surg.* 1962;156:1–4. doi: 10.1097/00000658-196207000-00001
31. Rosenberger P, Shernan SK, Shekar PS, Tuli JK, Weissmüller T, Aranki SF, Eltzschig HK. Acute hemodynamic collapse after induction of general anesthesia for emergent pulmonary embolectomy. *Anesth Analg.* 2006;102:1311–1315. doi: 10.1213/01.ane.0000208970.14762.7f
32. Goldberg JB, Spevack DM, Ahsan S, Rochlani Y, Ohira S, Spencer P, Kai M, Malekan R, Spielvogel D, Lansman S. Comparison of surgical embolectomy and veno-arterial extracorporeal membrane oxygenation for massive pulmonary embolism. *Semin Thorac Cardiovasc Surg.* 2022;34:934–942. doi: 10.1053/j.semtcvs.2021.06.011
33. Leacche M, Unic D, Goldhaber SZ, Rawn JD, Aranki SF, Couper GS, Mihaljevic T, Rizzo RJ, Cohn LH, Aklog L, 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.* 2005;129:1018–1023. doi: 10.1016/j.jtcvs.2004.10.023

34. Pasrija C, Kronfli A, Rouse M, Raithel M, Bittle GJ, Pousatis S, Ghoreishi M, Gammie JS, Griffith BP, Sanchez PG, et al. Outcomes after surgical pulmonary embolectomy for acute submassive and massive pulmonary embolism: a single-center experience. *J Thorac Cardiovasc Surg.* 2018;155:1095–1106.e2. doi: 10.1016/j.jtcvs.2017.10.139
35. QiMin W, LiangWan C, DaoZhong C, HanFan Q, ZhongYao H, XiaoFu D, XueShan H, Feng L, HuaBin C. Clinical outcomes of acute pulmonary embolectomy as the first-line treatment for massive and submassive pulmonary embolism: a single-centre study in China. *J Cardiothorac Surg.* 2020;15:321. doi: 10.1186/s13019-020-01364-z
36. Kadner A, Schmidli J, Schönhoff F, Krähenbühl E, Immer F, Carrel T, Eckstein F. Excellent outcome after surgical treatment of massive pulmonary embolism in critically ill patients. *J Thorac Cardiovasc Surg.* 2008;136:448–451. doi: 10.1016/j.jtcvs.2007.11.021
37. Fukuda I, Taniguchi S, Fukui K, Minakawa M, Daitoku K, Suzuki Y. Improved outcome of surgical pulmonary embolectomy by aggressive intervention for critically ill patients. *Ann Thorac Surg.* 2011;91:728–732. doi: 10.1016/j.athoracsur.2010.10.086
38. Neely RC, Byrne JG, Gosev I, Cohn LH, Javed Q, Rawn JD, Goldhaber SZ, Piazza G, Aranki SF, Shekar PS, et al. Surgical embolectomy for acute massive and submassive pulmonary embolism in a series of 115 patients. *Ann Thorac Surg.* 2015;100:1245–1251. doi: 10.1016/j.athoracsur.2015.03.111
39. Keeling WB, Leshnower BG, Lasajanak Y, Binongo J, Guyton RA, Halkos ME, Thourani VH, Lattouf OM. Midterm benefits of surgical pulmonary embolectomy for acute pulmonary embolus on right ventricular function. *J Thorac Cardiovasc Surg.* 2016;152:872–878. doi: 10.1016/j.jtcvs.2015.11.042
40. D'Agostino RS, Jacobs JP, Badhwar V, Fernandez FG, Paone G, Wormuth DW, Shahian DM. The Society of Thoracic Surgeons Adult Cardiac Surgery Database: 2018 update on outcomes and quality. *Ann Thorac Surg.* 2018;105:15–23. doi: 10.1016/j.athoracsur.2017.10.035
41. Azari A, Beheshti AT, Moravvej Z, Bigdelu L, Salehi M. Surgical embolectomy versus thrombolytic therapy in the management of acute massive pulmonary embolism: short and long-term prognosis. *Heart Lung.* 2015;44:335–339. doi: 10.1016/j.hrtlng.2015.04.008
42. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, Gibbs JS, Huisman MV, Humbert M, Kucher N, et al; Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J.* 2014;35:3033–3069, 3069a. doi: 10.1093/eurheartj/ehu283
43. Bennett-Guerrero E, Zhao Y, O'Brien SM, Ferguson TB Jr, Peterson ED, Gammie JS, Song HK. Variation in use of blood transfusion in coronary artery bypass graft surgery. *JAMA.* 2010;304:1568–1575. doi: 10.1001/jama.2010.1406
44. Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounameaux H, Huisman M, King CS, Morris TA, Sood N, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. *Chest.* 2016;149:315–352. doi: 10.1016/j.chest.2015.11.026
45. Aymard T, Kadner A, Widmer A, Basciani R, Tevaearai H, Weber A, Schmidli J, Carrel T. Massive pulmonary embolism: surgical embolectomy versus thrombolytic therapy: should surgical indications be revisited? *Eur J Cardiothorac Surg.* 2013;43:90–94. doi: 10.1093/ejcts/ezs123
46. Doerge HC, Schoendube FA, Loeser H, Walter M, Messmer BJ. Pulmonary embolectomy: review of a 15-year experience and role in the age of thrombolytic therapy. *Eur J Cardiothorac Surg.* 1996;10:952–957. doi: 10.1016/s1010-7940(96)80396-4
47. Lehnert P, Møller CH, Mortensen J, Kjaergaard J, Olsen PS, Carlsen J. Surgical embolectomy compared to thrombolysis in acute pulmonary embolism: morbidity and mortality. *Eur J Cardiothorac Surg.* 2017;51:354–361. doi: 10.1093/ejcts/ezw297
48. Krzak AM, Fowles JA, Vuylsteke A. Mobile extracorporeal membrane oxygenation service for severe acute respiratory failure: a review of five years of experience. *J Intensive Care Soc.* 2020;21:134–139. doi: 10.1177/1751143719855207
49. Corno AF, Faulkner GM, Harvey C. Mobile extracorporeal membrane oxygenation. *ASAIO J.* 2021;67:594–600. doi: 10.1097/MAT.0000000000001286
50. Vaja R, Chauhan I, Joshi V, Salmasi Y, Porter R, Faulkner G, Harvey C. Five-year experience with mobile adult extracorporeal membrane oxygenation in a tertiary referral center. *J Crit Care.* 2015;30:1195–1198. doi: 10.1016/j.jcrc.2015.07.032
51. Chaves RCF, Rabello Filho R, Timenetsky KT, Moreira FT, Vilanova LCDS, Bravim BA, Serpa Neto A, Corrêa TD. Extracorporeal membrane oxygenation: a literature review. *Rev Bras Ter Intensiva.* 2019;31:410–424. doi: 10.5935/0103-507X.20190063
52. Chan EG, Chan PG, Harano T, Sanchez PG. Transition of femoral-jugular to dual-stage left subclavian without discontinuation of extracorporeal membrane oxygenation. *J Card Surg.* 2020;35:2794–2797. doi: 10.1111/jocs.14881
53. Cui CQ, Cook BS, Cauchi MP, Foerst JR. A case series: alternative access for refractory shock during cardiac arrest. *Eur Heart J Case Rep.* 2019;3:ytz101. doi: 10.1093/ehjcr/ytz101
54. Extracorporeal Life Support Organization. ELSO anticoagulation guideline. Accessed December 31, 2021. https://www.elso.org/portals/0/files/elso-anticoagulationguideline8-2014-table-contents.pdf
55. Pozzi M, Metge A, Martelin A, Giroudon C, Lanier Demma J, Koffel C, Fornier W, Chiari P, Fellahi JL, Obadia JF, et al. Efficacy and safety of extracorporeal membrane oxygenation for high-risk pulmonary embolism: a systematic review and meta-analysis. *Vasc Med.* 2020;25:460–467. doi: 10.1177/1358863X20944469
56. Oh YN, Oh DK, Koh Y, Lim CM, Huh JW, Lee JS, Jung SH, Kang PJ, Hong SB. Use of extracorporeal membrane oxygenation in patients with acute high-risk pulmonary embolism: a case series with literature review. *Acute Crit Care.* 2019;34:148–154. doi: 10.4266/acc.2019.00500
57. Guliani S, Das Gupta J, Osofsky R, Kraai EP, Mitchell JA, Dettmer TS, Wray TC, Tawil I, Rana MA, Marinaro J. Venoarterial extracorporeal membrane oxygenation is an effective management strategy for massive pulmonary embolism patients. *J Vasc Surg Venous Lymphat Disord.* 2021;9:307–314. doi: 10.1016/j.jvsv.2020.04.033
58. Ghoreishi M, DiChiacchio L, Pasrija C, Ghazi A, Deatrick KB, Jeudy J, Griffith BP, Kon ZN. Predictors of recovery in patients supported with venoarterial extracorporeal membrane oxygenation for acute massive pulmonary embolism. *Ann Thorac Surg.* 2020;110:70–75. doi: 10.1016/j.athoracsur.2019.10.053
59. Scott JH, Gordon M, Vender R, Pettigrew S, Desai P, Marchetti N, Mamary AJ, Panaro J, Cohen G, Bashir R, et al. Venoarterial extracorporeal membrane oxygenation in massive pulmonary embolism-related cardiac arrest: a systematic review. *Crit Care Med.* 2021;49:760–769. doi: 10.1097/CCM.0000000000004828
60. Corsi F, Lebreton G, Bréchot N, Hekimian G, Nieszkowska A, Trouillet JL, Luyt CE, Leprince P, Chastre J, Combes A, et al. Life-threatening massive pulmonary embolism rescued by venoarterial-extracorporeal membrane oxygenation. *Crit Care.* 2017;21:76. doi: 10.1186/s13054-017-1655-8
61. Maggio P, Hemmila M, Haft J, Bartlett R. Extracorporeal life support for massive pulmonary embolism. *J Trauma.* 2007;62:570–576. doi: 10.1097/TA.0b013e318031cd0c
62. Hashiba K, Okuda J, Maejima N, Iwahashi N, Tsukahara K, Tahara Y, Hibi K, Kosuge M, Ebina T, Endo T, et al. Percutaneous cardiopulmonary support in pulmonary embolism with cardiac arrest. *Resuscitation.* 2012;83:183–187. doi: 10.1016/j.resuscitation.2011.10.019
63. Malekan R, Saunders PC, Yu CJ, Brown KA, Gass AL, Spielvogel D, Lansman SL. Peripheral extracorporeal membrane oxygenation: comprehensive therapy for high-risk massive pulmonary embolism. *Ann Thorac Surg.* 2012;94:104–108. doi: 10.1016/j.athoracsur.2012.03.052
64. Munakata R, Yamamoto T, Hosokawa Y, Tokita Y, Akutsu K, Sato N, Murata S, Tajima H, Mizuno K, Tanaka K. Massive pulmonary embolism requiring extracorporeal life support treated with catheter-based interventions. *Int Heart J.* 2012;53:370–374. doi: 10.1536/ihj.53.370
65. Swol J, Buchwald D, Strauch J, Schildhauer TA. Extracorporeal life support (ECLS) for cardiopulmonary resuscitation (CPR) with pulmonary embolism in surgical patients: a case series. *Perfusion.* 2016;31:54–59. doi: 10.1177/0267659115583682
66. George B, Parazino M, Omar HR, Davis G, Guglin M, Gurley J, Smyth S. A retrospective comparison of survivors and non-survivors of massive pulmonary embolism receiving veno-arterial extracorporeal membrane oxygenation support. *Resuscitation.* 2018;122:1–5. doi: 10.1016/j.resuscitation.2017.11.034
67. Meneveau N, Guillon B, Planquette B, Piton G, Kimmoun A, Gaide-Chevronnay L, Aissaoui N, Neuschwander A, Zogheib E, Dupont H, et al. Outcomes after extracorporeal membrane oxygenation for the treatment of high-risk pulmonary embolism: a multicentre series of 52 cases. *Eur Heart J.* 2018;39:4196–4204. doi: 10.1093/eurheartj/ehy464
68. Moon D, Lee SN, Yoo KD, Jo MS. Extracorporeal membrane oxygenation improved survival in patients with massive pulmonary embolism. *Ann Saudi Med.* 2018;38:174–180. doi: 10.5144/0256-4947.2018.174
69. Al-Bawardy R, Rosenfield K, Borges J, Young MN, Albaghdadi M, Rosovsky R, Kabrhel C. Extracorporeal membrane oxygenation in acute massive pulmonary embolism: a case series and review of the literature. *Perfusion.* 2019;34:22–28. doi: 10.1177/0267659118786830

70. Kjaergaard B, Kristensen JH, Sindby JE, de Neergaard S, Rasmussen BS. Extracorporeal membrane oxygenation in life-threatening massive pulmonary embolism. *Perfusion*. 2019;34:467–474. doi: 10.1177/0267659119830014
71. Goldberg JB, Levine A, Ohira S, Spielvogel D, Kai M. Successful heart transplantation recovered from a brain-dead donor on veno-arterial extracorporeal membrane oxygenation support. *ASAIO J*. 2022;68:e64–e65. doi: 10.1097/MAT.0000000000001437
72. Kai M, Tang GH, Malekan R, Lansman SL, Spielvogel D. Venoarterial extracorporeal membrane oxygenation for right heart failure complicating left ventricular assist device use. *J Thorac Cardiovasc Surg*. 2014;147:e31–e33. doi: 10.1016/j.jtcvs.2013.10.040
73. Abiomed. *Impella RP With the Automated Impella Controller: Instructions for Use and Clinical Reference Manual*. Accessed October 20, 2021. https://www.accessdata.fda.gov/cdrh_docs/pdf14/H140001d.pdf
74. Shokr M, Rashed A, Mostafa A, Mohamad T, Schreiber T, Elder M, Kaki A. Impella RP support and catheter-directed thrombolysis to treat right ventricular failure caused by pulmonary embolism in 2 patients. *Tex Heart Inst J*. 2018;45:182–185. doi: 10.14503/THIJ-17-6316
75. Kumar Bhatia N, Dickert NW, Samady H, Babaliaros V. The use of hemodynamic support in massive pulmonary embolism. *Catheter Cardiovasc Interv*. 2017;90:516–520. doi: 10.1002/ccd.26872
76. Lashin H, Spiritoso R. Impella RP as rescue measure for pulmonary embolism with hemodynamic compromise. *JACC Case Rep*. 2019;1:626–627. doi: 10.1016/j.jaccas.2019.10.031
77. Zuin M, Rigatelli G, Daggubati R, Nguyen T, Roncon L. Impella RP in hemodynamically unstable patients with acute pulmonary embolism. *J Artif Organs*. 2020;23:105–112. doi: 10.1007/s10047-019-01149-9
78. Shekiladze N, Condado JF, Sandesara PB, Kim JH, Devireddy C, McDaniel M, Babaliaros V, Samady H, Kumar G, Jaber WA. A single healthcare experience with Impella RP. *Catheter Cardiovasc Interv*. 2021;97:E161–E167. doi: 10.1002/ccd.28986
79. Oliveros E, Collado FM, Poulin MF, Seder CW, March R, Kavinsky CJ. Percutaneous right ventricular assist device using the TandemHeart ProtekDuo: real-world experience. *J Invasive Cardiol*. 2021;33:E407–E411.
80. Lee T, Itagaki S, Chiang YP, Egorova NN, Adams DH, Chikwe J. Survival and recurrence after acute pulmonary embolism treated with pulmonary embolectomy or thrombolysis in New York State, 1999 to 2013. *J Thorac Cardiovasc Surg*. 2018;155:1084–1090.e1012. doi: 10.1016/j.jtcvs.2017.07.074
81. Percy ED, Shah R, Hirji S, Tartarini RJ, Yazdchi F, Harloff M, Kaneko T, Pelletier MP. National outcomes of surgical embolectomy for acute pulmonary embolism. *Ann Thorac Surg*. 2020;110:441–447. doi: 10.1016/j.athoracsur.2020.02.024