State of the Art: Contemporary Management of Acute Pulmonary Embolism

Corinne W. Tan MD , Sujana Balla MBBS , Ravi K. Ghanta MD , Aditya M. Sharma MD , Subhasis Chatterjee MD

PII: S1043-0679(20)30111-8
DOI: https://doi.org/10.1053/j.semtcvs.2020.04.002
Reference: YSTCS 1487

To appear in: *Seminars in Thoracic and Cardiovascular Surgery*

Please cite this article as: Corinne W. Tan MD , Sujana Balla MBBS , Ravi K. Ghanta MD , Aditya M. Sharma MD , Subhasis Chatterjee MD , State of the Art: Contemporary Management of Acute Pulmonary Embolism, *Seminars in Thoracic and Cardiovascular Surgery* (2020), doi: https://doi.org/10.1053/j.semtcvs.2020.04.002

State of the Art: Contemporary Management of Acute Pulmonary Embolism

Corinne W. Tan[a], MD, Sujana Balla[a], MBBS, Ravi K. Ghanta[a], MD, Aditya M. Sharma[b], MD, and Subhasis Chatterjee,[a c d] MD

[a]Michael E. DeBakey Department of Surgery, Baylor College of Medicine, 1 Baylor Plaza, MC 390, Houston, Texas 77030

[b]Department of Medicine, University of Virginia, PO Box 800793, Health Sciences Center, Charlottesville, Virginia 22908

[c]Department of Cardiovascular Surgery, CHI St Luke's Health—Baylor St Luke's Medical Center, MC 3-116, PO Box 20345, Houston, Texas 77225-0345

[d]Department of Cardiovascular Surgery, Texas Heart Institute, MC 3-116, PO Box 20345, Houston, Texas 77225-0345

Conflict of interest: None of the authors has any conflict of interest to disclose.

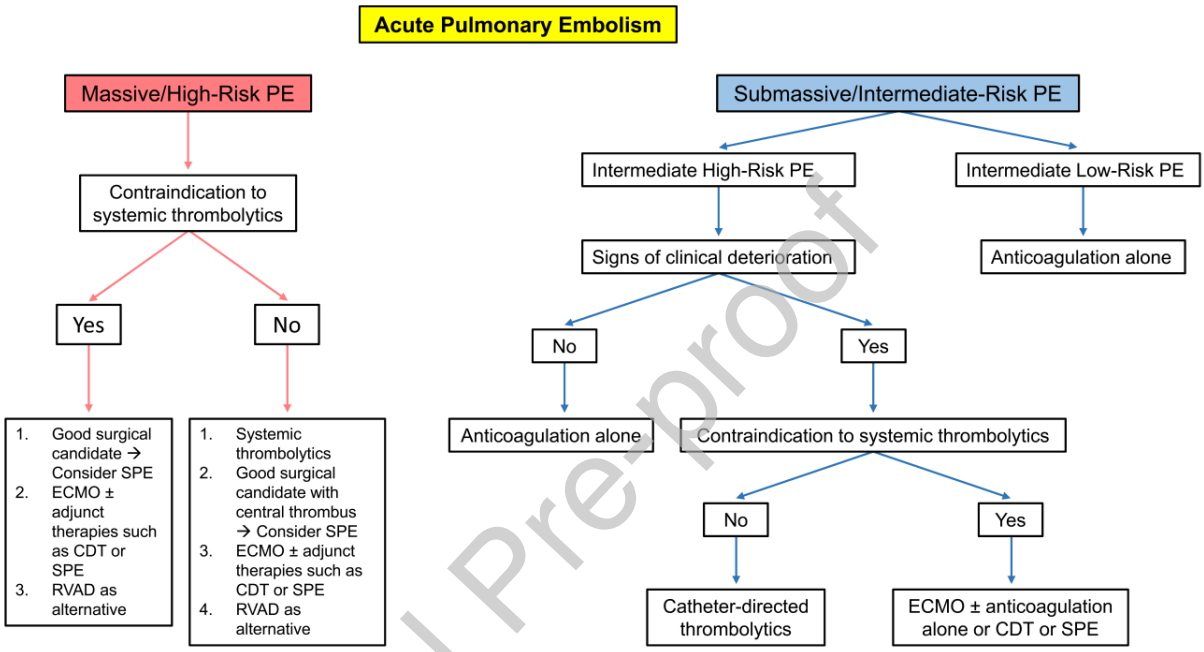
Funding statement: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Address reprints to Subhasis Chatterjee, MD, FACS, FACC, FCCP, Michael E. DeBakey Department of Surgery, Baylor College of Medicine, One Baylor Plaza, MC 390, Houston, TX 77030. Phone: 713-798-8051; fax: 713-798-2744; e-mail: Subhasis.Chatterjee@bcm.edu

Word count: 3337

Central Message

Multiple therapeutic strategies currently exist for massive and submassive pulmonary embolism. Surgical management with embolectomy and extracorporeal life support remain important options.



Central Picture Legend

Management algorithm for higher-risk acute pulmonary embolism to individualize treatment.

ABSTRACT

Multiple treatment options beyond anticoagulation exist for massive and submassive pulmonary embolism to reduce mortality. For some patients, systemic thrombolytics and catheter-directed thrombolysis are appropriate interventions. For others, surgical pulmonary embolectomy can be life-saving. Extracorporeal life support and right ventricular assist devices can provide hemodynamic support in challenging cases. We propose a management algorithm for the treatment of massive and submassive pulmonary embolism, in conjunction with a multidisciplinary pulmonary embolism response team, to guide clinicians in individualizing treatment for patients in a timely manner.

Keywords: pulmonary embolism, extracorporeal membrane oxygenation, surgical embolectomy, thrombolysis

INTRODUCTION

Pulmonary embolism (PE) has long been a scourge of clinical medicine, incurring high morbidity, mortality, and cost.[1,2] While the mainstay of treatment for most PE is anticoagulation (AC), advanced therapies such as systemic thrombolysis, catheter-directed therapies, mechanical circulatory support such as extracorporeal membrane oxygenation (ECMO) and right ventricular assist devices, and surgical pulmonary embolectomy (SPE) have well-established benefits in preventing PE-related morbidity and mortality for patients with higher-risk PE. Cardiac surgeons play an important role in multidisciplinary teams that treat these higher-risk patients and should be familiar with the therapeutic options available. This review outlines a contemporary approach to PE, focusing on the role of SPE and mechanical circulatory support.

RISK STRATIFICATION OF ACUTE PULMONARY EMBOLISM

Tailoring treatment options to the patient requires methods of identifying patients with acute PE who are at higher risk of adverse outcomes, such as the pulmonary embolism severity index (PESI) classification system (Table 1).[3] Two of the most widely used guidelines come from the American Heart Association (AHA)[4] and the European Society of Cardiology (ESC)[5] (Fig. 1). In this review, we use the AHA classifications of massive, submassive, and nonmassive to describe PEs rather than the ESC categorization of high, intermediate, and low risk.[4,5] Risk stratification of patients with PE uses hemodynamics, imaging, and laboratory parameters to identify "higher-risk" patients with massive and submassive PEs.

Massive PE (MPE) is defined as acute PE with sustained hypotension (systolic blood pressure <90 mmHg, or 40 mmHg below baseline) for at least 15 minutes or necessitating inotropic support. The International Cooperative Pulmonary Embolism Registry of 2392 patients

showed that at 90 days, mortality rates were much higher for the 5% of patients who presented with MPE than for the 95% with nonmassive PE (52% vs 15%).[6] Therefore, simple AC alone is insufficient in most patients with MPE, who are likely to benefit from therapies used in addition to AC.

Submassive PE (SMPE) is characterized by normotension with right ventricular (RV) dysfunction or elevated cardiac biomarkers. Criteria for RV dysfunction include 1) echocardiographic RV dilation (RVdiameter / LVdiameter > 0.9); 2) RV systolic dysfunction (RV systolic pressure >40 mmHg); 3) elevation of brain natriuretic peptide (BNP) level to >90 pg/mL or elevation of the N-terminal pro-BNP level to >500 pg/mL; and 4) characteristic electrocardiographic findings. Myocardial necrosis is defined by an elevated troponin level (troponin I >0.4 ng/mL or troponin T >0.1 ng/mL).[4] The short-term mortality among SMPE patients ranges from 3% to 15%, and identifying those patients who may benefit from therapies beyond AC is important to improving survival. Thus, patients suspected to have or diagnosed with PE should have an echocardiogram, an electrocardiogram, and appropriate laboratory tests for proper risk stratification to determine whether management beyond AC alone is needed.

ROLE OF THE MULTIDISCIPLINARY TEAM

The complex task of selecting treatment options benefits from a multidisciplinary approach; consequently, the PE response team (PERT) was developed.[7] Analogous to rapid response teams for ST elevated myocardial infarction (STEMI), the PERT expeditiously coordinates medical (vascular medicine, cardiology, critical care), interventional (interventional radiology/cardiology/vascular surgery), and surgical arms (cardiothoracic and/or vascular surgery) (Fig. 1). In cases of acute MPE or SMPE, this multidisciplinary team is activated to

rapidly create an individualized treatment plan. In addition, the PERT includes a monitoring group consisting of a quality management team, a research and outcomes team, and a safety reporting team, which provides valuable feedback to the program. By understanding local institutional capabilities, the PERT at different centers may treat similar patients in slightly different ways.

Many tertiary centers have established multidisciplinary PERTs. At the University of Virginia, the PERT consists of vascular medicine, cardiac surgery, pulmonary critical care, interventional radiology, emergency medicine, pharmacy, hematology, a clinical research and outcomes team, and diagnostic radiology. Decision-making is guided by evidence-based protocols. Data from their initial 111 patients showed an overall 30-day mortality rate of 12.6% (SMPE: 11.4%; MPE: 25%), which is lower than the 30-day mortality rate of 19% reported in historical data.[7] Similarly, experiences from the Massachusetts General Hospital with using a PERT team showed a 12% 30-day mortality rate,[8] and the Cleveland Clinic showed a near halving of mortality in both the overall (8.5% vs 4.7%) and higher-risk PE cohorts (10.0% vs 5.3%).[9] The collaborative effort produces both better results and greater provider satisfaction because the treatment options are jointly selected.

TREATMENT OPTIONS

Figure 2 summarizes primary treatment recommendations from 3 clinical guidelines: ACC/AHA,[4] ESC,[5] and CHEST.[10] We will discuss the role of the multidisciplinary team and the therapeutic options available to clinicians.

Anticoagulation

Early therapeutic AC can reduce mortality and recurrent venous thromboembolism (VTE) rates and is the sole therapeutic intervention required for most patients.[4,5,10] Previously, AC was limited to unfractionated heparin followed by warfarin; however, with the development of direct oral anticoagulants (DOACs), alternative strategies are available. Choice of AC therapy depends on patient comorbidities, concurrent medications, PE characteristics, bleeding risk, need for additional therapies, patient preferences, and cost. Unfractionated heparin is recommended if primary reperfusion is being considered, or if the patient is obese (weight >120 kg) or has a creatinine clearance of less than 30 mL/min. In other scenarios, low-molecular-weight heparin (LMWH) or DOACs can be considered as first-line therapies. Although 3 months is generally accepted as an adequate duration of long-term oral AC, certain clinical circumstances, such as "unprovoked" PE (ie, PE in patients without any risk factors), those with persistent risk factors, PE in cancer patients, and recurrent PE, may justify extended AC for 3-6 months on an individualized basis.[4,5,10] Depending on the severity and circumstances of the initial PE, AC beyond 3 months is common.

Systemic Thrombolysis

Systemic thrombolysis (ST) is an AHA Class IIa and ESC Class Ib recommendation for MPE (Table 2).[4,5] Agents used for ST, such as tissue plasminogen activator (tPA), tenecteplase, and alteplase, lyse thrombus and reestablish hemodynamic stability by restoring pulmonary arterial blood flow and reducing RV strain. In a large epidemiologic study, ST was associated with significantly lower all-cause mortality in MPE patients than AC alone (15% vs 47%, $P<.0001$).[11] Despite ST being recommended as a first-line therapy, a sizable proportion of MPE

patients have ST contraindications such as recent surgery, stroke, and gastrointestinal bleeding, limiting ST use. Thus, similar to acute stroke management, evaluating higher-risk PE involves expeditiously determining a patient's candidacy for ST or whether alternative therapies beyond ST are necessary.

For SMPE, evidence for the use of ST is less clear. In the Pulmonary Embolism Thrombolysis (PEITHO)[12] study—the largest randomized controlled trial of ST, involving 1005 SMPE patients—ST with tenecteplase was associated with a lower rate of the composite endpoint of 30-day mortality or hemodynamic decompensation than AC alone (2.6% vs 5.6%, P=0.02), although mortality was comparable (1.2% vs 1.8%, P=0.42). However, ST resulted in more major extracranial bleeding (6.3% vs 1.2%, P<0.001) and stroke (2.4% vs 0.2%, P=0.003). A meta-analysis by Chatterjee et al[13] of 8 randomized trials that included 1775 SMPE patients showed less mortality in patients receiving ST versus AC alone (1.4% vs 2.9%; P=0.03), but ST recipients had more major bleeding events (7.7% vs 2.3%; P<0.001). Given the risk of significant bleeding with ST, some investigators have tried using a lower dose of ST (50 instead of 100 mg of tPA), which showed similar efficacy and is a reasonable consideration in high-bleeding-risk patients.[14] In addition, if the decision is made to proceed with full-dose ST, then heparin should be discontinued because concomitant use with ST increases hemorrhagic risk.

Catheter-directed Therapies

Because thrombolytics alone have limitations and may not be suitable for all patients with higher-risk PE, alternative strategies have been developed. Catheter-directed therapies (CDTs) have gained momentum in the treatment of MPE and SMPE at centers experienced with these devices and techniques. Catheter-directed thrombolysis (CDL), in which a thrombolytic

agent is injected directly into the pulmonary arterial vasculature, is the most frequently used CDT for higher-risk PE. Because the infusion is localized, CDL requires 75% less thrombolytic agent than ST alone, resulting in a lower bleeding risk. In a meta-analysis[15] of 16 studies in which 860 patients with acute MPE and SMPE received CDL (22% MPE and 78% SMPE), the rates of major bleeding (4.65%) and hemorrhagic stroke (0.35%) were substantially lower than those observed in the ST arm of the PEITHO trial.[12]

Alternative CDT techniques include thrombectomy approaches such as thrombus fragmentation with and without aspiration (Amplatz thrombectomy device; Bard-Microvena, White Bear Lake, MN), rheolytic thrombectomy and aspiration suction devices (AngioJet; Boston Scientific, Marlborough, MA), suction embolectomy (Argon Medical Devices, Athens, TX), and rotational thrombectomy (Aspirex; Straub Medical, Wangs, Switzerland).[16] A more recent invention, the FlowTriever system (Inari Medical, Irvine, CA), was evaluated as a suction thrombectomy device in the FlowTriever Pulmonary Embolectomy Clinical Study (FLARE): a multicenter, single-arm trial of suction thrombectomy with the FlowTriever system in 106 patients with SMPE.[17] Suction thrombectomy resulted in a mean reduction of the RV/LV ratio from 1.53 at baseline to 1.15 at 48 hours after the procedure, a difference of 0.38 ($P < .0001$), and a 3.8% rate of major adverse events.

In a systematic review and meta-analysis of CDT for MPE, which included 594 patients from 35 studies, the reported clinical success rate was 86.5%, and the rates of minor and major procedural complications were 7.9% and 2.4%, respectively.[18] The AHA[4] and ESC[5] guidelines have a Class IIa recommendation for CDT for MPE patients with a contraindication to or failed full-dose ST and a Class IIb recommendation for CDT in SMPE patients if the bleeding risk from ST is high (Table 2).[5] At our centers, CDT is used selectively in appropriate candidates.

Surgical Pulmonary Embolectomy

Surgical pulmonary embolectomy (SPE) was first described by Trendelenburg in 1908 and inspired Gibbon to develop the heart-lung machine. It continues to be an effective strategy in patients for whom ST has failed or who have ST contraindications, including recent major surgery or trauma. In patients with MPE or SMPE with RV dysfunction, SPE may be a primary option.[19-21] Other scenarios in which SPE may be the primary option include right atrial thrombus, thrombus-in-transit, and extensive intracardiac and pulmonary artery (PA) clot burden.[20] Optimal surgical candidates have large clot limited to central PA branches.[21] The current AHA and ESC clinical guidelines recommend SPE for MPE patients with absolute contraindication to ST, with failed ST, or at imminent risk of hemodynamic deterioration (Table 2).[4,5] While there are few, if any, absolute contraindications to SPE, there may be relative contraindications such as a "hostile chest" from previous sternotomies or local inexperience.

Relative contraindications to SPE include out-of-hospital cardiac arrest and prolonged, unsuccessful cardiopulmonary resuscitation. For patients with active malignant disease, we avoid SPE in those with an estimated survival of less than 1 year. In pregnant women, SPE may be able to save both mother and fetus. Saeed et al[22] identified 13 reported cases of SPE in pregnant women, with a 77% (10/13) rate of maternal survival.

In an analysis of more than 174,000 patients with acute PE in the New York State registry, Lee et al[23] found that among 2111 patients treated with either ST (88%) or SPE (12%), there was no difference in 30-day mortality or 5-year survival. However, the ST group had higher rates of stroke (odds ratio 4.7), reintervention (odds ratio 7.2), and readmission for recurrent PE (hazard ratio 3.4). In addition, SPE has been associated with greater improvement

in RV function, lower PA pressure, and less bleeding than thrombolysis alone.[24] As a result, with continued improvements in outcomes, SPE is increasingly being considered for patients with SMPE, proximal clot burden, and RV dysfunction.[21,25]

Surgical Technique of SPE

We perform SPE through a median sternotomy under normothermic cardiopulmonary bypass (CPB), using aortic and bicaval cannulation.[20,21] The main PA trunk extending into the left PA, as well as the right PA between the superior vena cava and aorta, are incised longitudinally (Fig. 3).[20] After polypropylene stay sutures are placed, aiding visualization, clots are removed under direct vision from the main, right, and left PA. Thrombus is also removed from the segmental level with gallbladder stone forceps and suction.[21] Copious irrigation with saline is helpful. One must be careful to avoid blind instrumentation of distal vasculature and limit extraction to visible clots to prevent mechanical injury to the PA wall that can cause parenchymal and endobronchial bleeding. Some groups have used retrograde pulmonary perfusion or videoscopic inspection of the segmental arteries to remove as much residual thrombus as possible.[26,27] Use of a Fogarty catheter is controversial because of concerns about injuring the PA branches.[20,27] Manual compression of the lungs is also discouraged because of the risk of pulmonary injury. The right atrium and ventricle may be explored; they are found to contain thrombi in 20-30% of cases.[26,27] Aortic cross-clamping and cardioplegic arrest can and should be avoided to keep from exacerbating RV strain, except in patients with a patent foramen ovale or atrial septal defect, or for inadequate visualization; typically, temporary reductions in CPB flows are all that is necessary to allow clot visualization.[20,21] Because of the RV dysfunction, patients may require a prolonged period of CPB and weaning.[2] We resume systemic

AC 6 hours postoperatively, assuming there is no evidence of ongoing coagulopathy or excessive mediastinal bleeding. Consistent with guidelines,[4,5,10] we do not routinely place inferior vena caval filters.

Outcomes of SPE

The mortality rate after SPE has decreased from 50-60% in the 1960s to 20-30% in the 1990s to 10-15% in the 2010s.[21,27,28] Not unexpectedly, mortality is as high as 60% in patients with cardiac arrest before SPE; a recent systematic review found that the mortality rates of surgical series are almost directly correlated with the proportion of patients with preoperative cardiac arrest included in the series.[29] Causes of early death include recurrent PE (in about 5% of cases), RV failure, persistent pulmonary hypertension, pulmonary edema, massive parenchymal or intrabronchial hemorrhage, intraoperative complications (eg, dissection during cannulation), intracerebral hemorrhage, and cardiac arrest.[21,27]

Unexpectedly, Kilic and colleagues' analysis of data from 2709 patients in the Nationwide Inpatient Sample (1999-2008) who underwent SPE found that neither surgeon nor hospital SPE volume correlated with mortality in a multivariate model.[25] This suggests that SPE may be better done sooner at a local, lower-volume center, because waiting for transfer to a higher-volume center can delay SPE by several hours. The overall mortality rate was 27%, with approximately 10% of SPE patients having a previous, failed ST.

Treating certain subsets of patients poses a unique challenge and opportunity for SPE. In 12,441 patients studied from the Computerized Registry of Patients with Venous Thromboembolism (RIETE), right heart thrombi (RHT) or thrombus-in-transit had a 2.6% incidence among all PE patients and was associated with greater all-cause mortality than not

having not having either condition (8.6% vs 2.9%, $P<0.001$).[30] Other predictors of mortality include younger age, prior bleeding, congestive heart failure, syncope, cancer, systolic blood pressure <100 mmHg, and arterial oxygen saturation <90%. In a pooled analysis, RHT were associated with an in-hospital mortality of 23.2%.[31] Comparing treatment strategies for RHT showed that the odds ratio for survival was 4.83 (95% confidence interval [CI] 1.51-15.36) with thrombolysis and 2.61 (95% CI 0.90-7.58) with SPE compared with AC alone.[31]

Right Ventricular Assist Devices

Right ventricular assist devices (RVADs) can be used to support RV function in the perioperative period, sometimes in conjunction with nonsurgical strategies such as CDT. However, the most commonly reported use of RVADs is to support patients who cannot be weaned off CPB after SPE.[19,32] Using an RVAD allows RV preload reduction and a chance for the patient's RV to recover over the next 24-72 hours as evidenced by echocardiography and PA pressures.[19,32] Compared with ECMO support, RVAD implantation after embolectomy has the advantage of providing continuous pulmonary blood flow, thereby minimizing stasis in the PAs. In addition, if the patient develops hypoxemia secondary to reperfusion injury after embolectomy, an oxygenator can be used with the RVAD.[32] Our practice is to initiate early RVAD support with a CentriMag (Thoratec Corp., Pleasanton, CA) via direct right atrial and PA cannulation in patients with RV failure (Fig. 4).[33]

Extracorporeal Membrane Oxygenation (ECMO) Support

Cooley first described ECMO support for PE in 1961.[34] Peripheral percutaneous venoarterial ECMO support can be used with AC alone, as an adjunct to ST, or as a bridge to

SPE or CDT in patients with MPE and impending or ongoing circulatory collapse.[20,35] In addition, it can be used for patients unable to wean from CPB after SPE, usually secondary to RV dysfunction, although in our practice, we often favor using a temporary RVAD in this situation. Other indications for ECMO include hypoxemic respiratory failure (venovenous ECMO), cardiopulmonary arrest, metabolic acidosis with end-organ hypoperfusion, and severe RV failure.[34] ECMO bypasses the right heart and the entire pulmonary circulation and allows time for RV recovery. Arterial cannulation is most commonly done in the femoral or axillary vessels. ECMO flow rates range from 2 to 4 L/min with pump speeds of ~3000-4000 rpm; the pump speed is adjusted to optimize flow and maintain adequate arterial saturation, cardiac output, pulsatility, and some pulmonary blood flow to allow thrombus fibrinolysis. Another advantage of ECMO is that patients can be extubated and even ambulatory while receiving prolonged ECMO support.

A meta-analysis[35] of 19 papers reporting ECMO use in MPE found 70% survival among 78 patients treated between 1995 and 2014; this rate is comparable to those associated with other treatment modalities. However, 11 of these papers were single case reports, and of the remaining 8 case series, only 3 contained at least 10 patients. It should be noted that half of the patients received ECMO as part of cardiopulmonary resuscitation (55.1%), and half of these patients actually survived (51.2%). The University of Maryland protocol uses ECMO support for all patients with MPE as an initial triage and bridge-to-decision strategy.[36] The ECMO protocol group (n=29) was compared with a historical control group of 27 patients with MPE. One-year survival was higher in the ECMO protocol group than in the historical group (96% vs 73%; *P*=0.02). In a similar study, Ain et al[37] reported the ECMO experience with acute PE at Massachusetts General Hospital. They identified 2 eras of PE management: pre-ECMO, in which

none of the 31 patients received ECMO, and post-ECMO, in which 13/29 (44.8%) patients received it. The 30-day survival rate was higher in the post-ECMO era (41.4% vs 17.2%; *P*=0.043). Notably, there was also an increase in the use of CDT (24.1% vs 3.2%; *P*=0.024) and SPE (31% vs 12.5%; *P*=0.12) in the post-ECMO era. It is likely that the combination and coordination of different treatment modalities under the PERT team contributed to the improved outcomes.

Various small series have reported mean durations of ECMO support between 2 and 16 days, with a 30-day mortality rate of up to 75%.[2,34,35] Meanwhile, Pasrija and colleagues' in-hospital and 90-day survival was favorable at 95%,[38] probably because their series was not limited to emergency cannulations. Identifying patients for whom ECMO would be futile is difficult. Interestingly, George et al[39] found that among patients supported by ECMO for MPE, a lactic acid level ≤6 mmol/L had an 82.4% sensitivity and 84.6% specificity for predicting survival to discharge. Mortality rates for patients who have cardiac arrest secondary to PE are as high as 60%,[36] and ECMO initiation more than 30 minutes after arrest has been associated with survival rates of less than 10%.[39]

CONCLUSIONS

For patients with PE, clinicians can select from a range of treatment options with different degrees of risk and invasiveness according to each patient's risk classification. While nonsurgical treatments are evolving and many new CDT are available besides AC and ST, outcomes of SPE have been encouraging with improved patient selection and suggest that earlier intervention is beneficial, especially for SMPE patients. Improved outcomes are also evident with appropriate use of circulatory support systems such as RVADs and ECMO. We have

proposed an up-to-date algorithm for treating intermediate- and high-risk PE (Fig. 2). The advent of multidisciplinary PERT teams to guide clinicians through a high-stakes and urgent clinical situation is poised to improve the care of patients with SMPE and MPE.

Acknowledgments/Disclosures

We appreciate the editorial support provided by Stephen N. Palmer, PhD, ELS, of the Texas Heart Institute's Department of Scientific Publications. In addition, we thank Scott A. Weldon, MA, CMI, FAMI, for the illustrations.

FIGURE LEGENDS

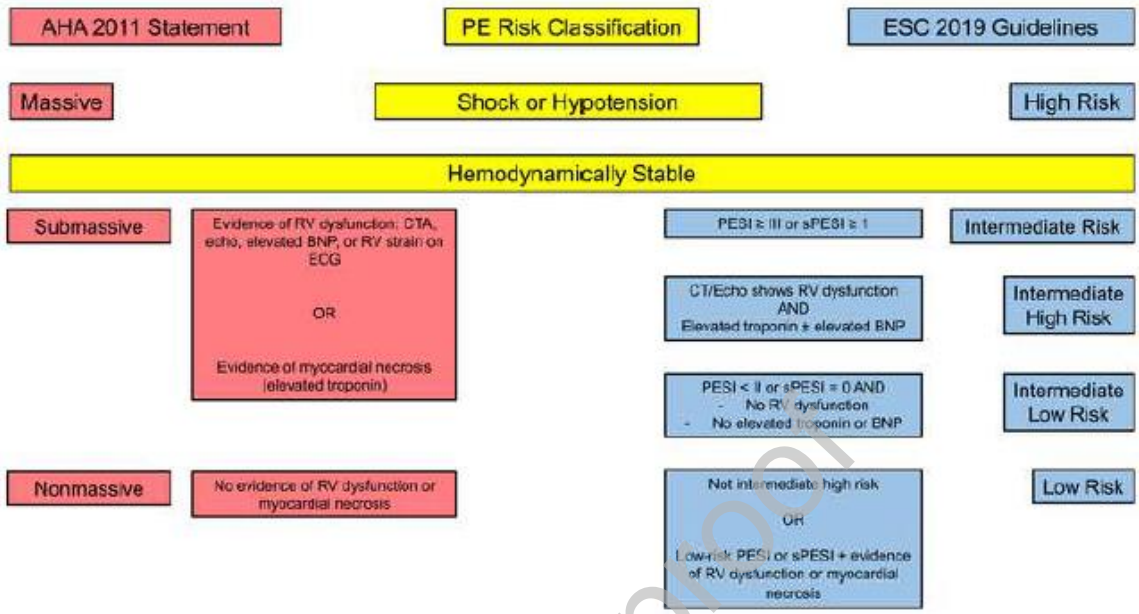


Figure 1. A comparison of the American Heart Association (AHA) and European Society of Cardiologists (ESC) pulmonary embolism (PE) risk-stratification systems. Shock or hypotension was defined as the need for vasopressors. BNP, brain natriuretic peptide; CT, computed tomography; CTA, computed tomographic angiography; ECG, electrocardiogram; PE, pulmonary embolism; PESI, pulmonary embolism severity index; RV, right ventricular; sPESI simplified pulmonary embolism severity index.

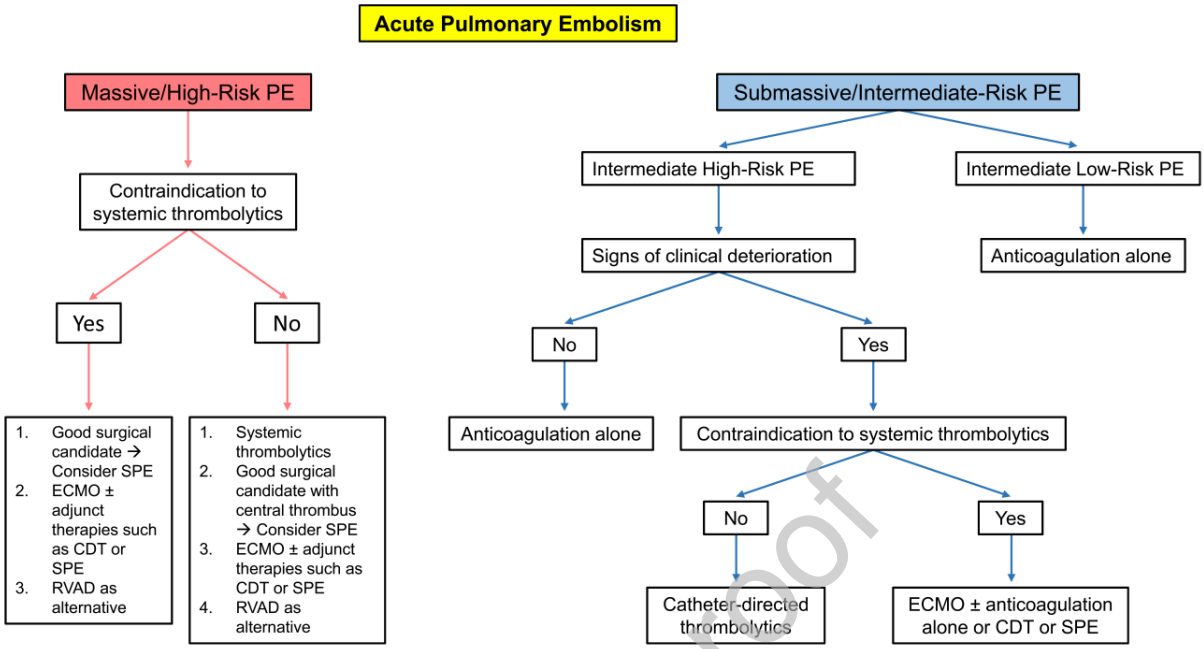
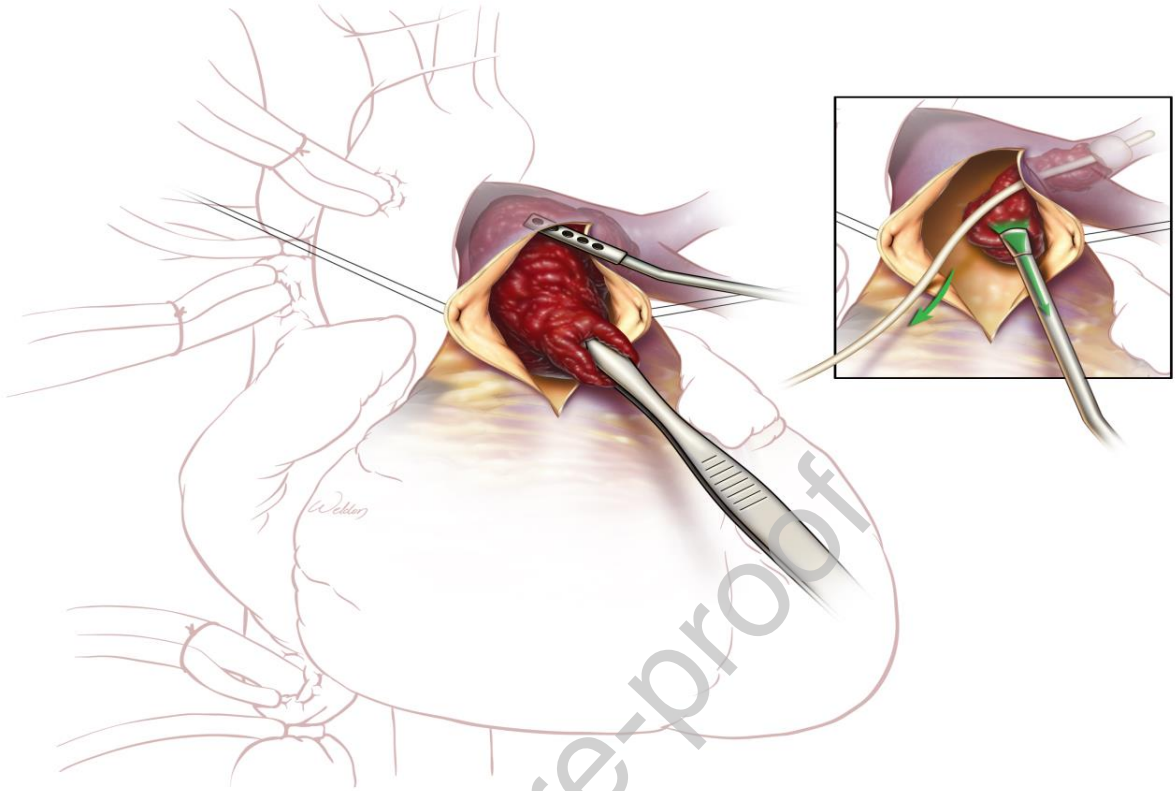


Figure 2. Approach to treatment of massive and submassive pulmonary embolism. CDT, catheter-directed therapies; ECMO, extracorporeal membrane oxygenation; RVAD, right ventricular assist device; SPE, surgical pulmonary embolectomy.



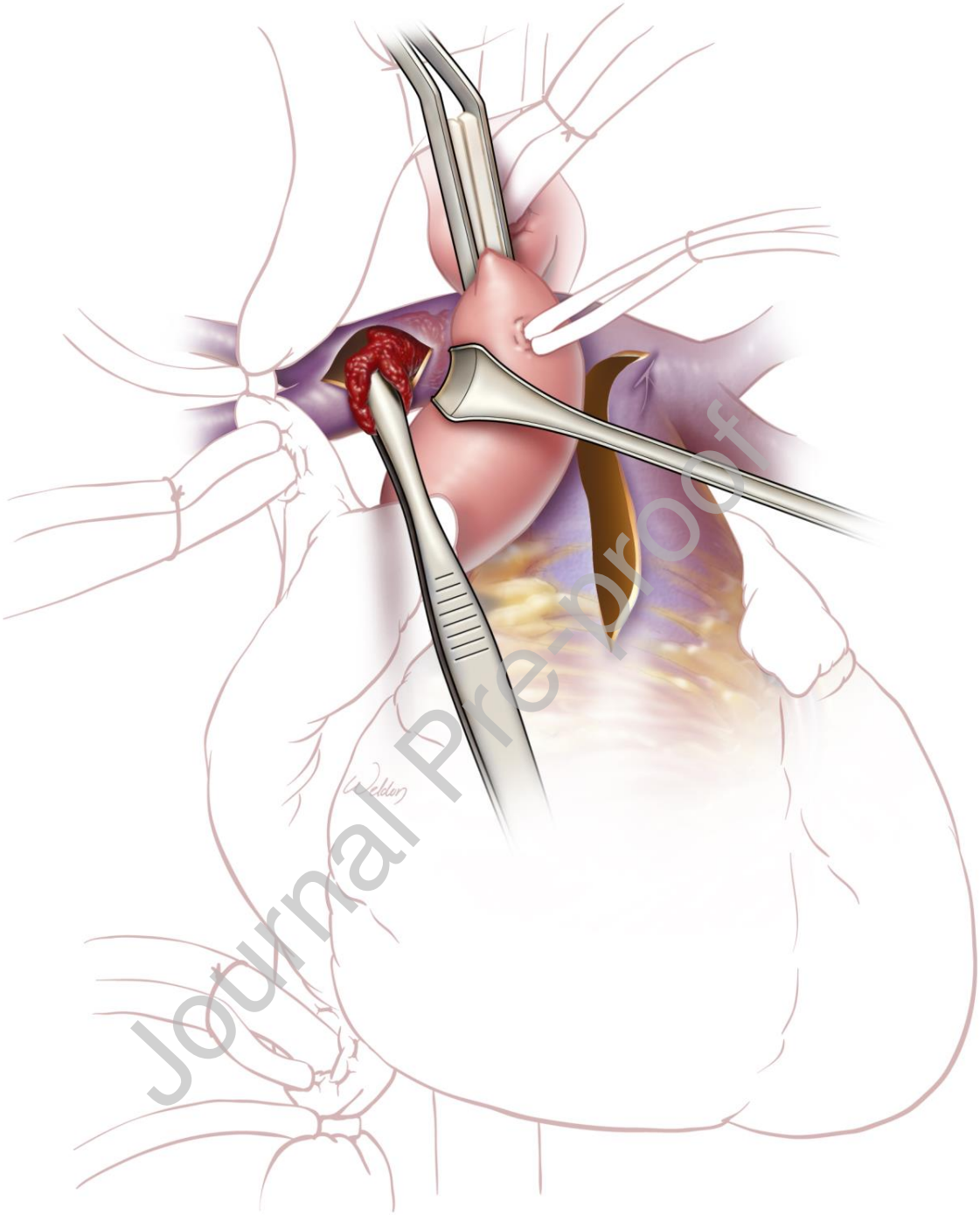


Figure 3. Illustration of surgical pulmonary embolectomy. Thrombus is removed from (a) main pulmonary artery and (b) left pulmonary artery. Inspired by Saxena et al.[20]

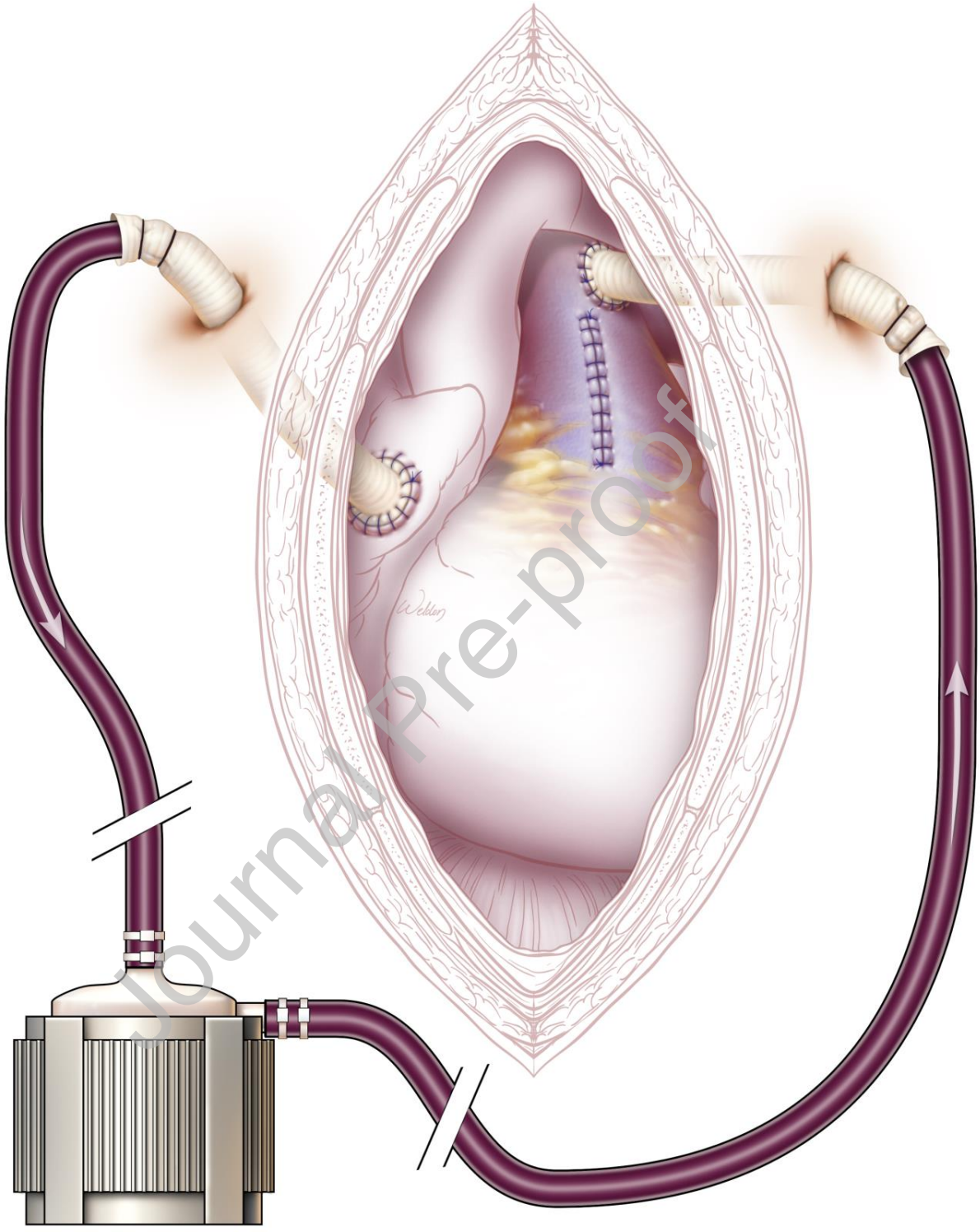


Figure 4. Illustration of right ventricular assist device. Inspired by Chancellor et al.[33]

Table 1. Original and Simplified Pulmonary Embolism Severity Index Scores

Parameter	**Original PESI**	**Simplified PESI**
Age	Age in years	1 point (if age >80 y)
Male sex	+10 points	-
History of cancer	+30 points	1 point
Chronic heart failure	+10 points	-
Chronic pulmonary disease	+10 points	1 point
Pulse rate ≥110 bpm	+20 points	1 point
Systolic blood pressure <100 mmHg	+30 points	1 point
Respiratory rate >30 breaths per min	+20 points	-
Temperature <36 °C	+20 points	-
Altered mental status	+60 points	-
Arterial oxyhemoglobin saturation <90%	+20 points	1 point
	Risk strata (based on sum of points)	
	Class I: ≤65 points	0 points = 30-day mortality risk
	Very low 30-day mortality risk (0-	1.0% (95% CI 0.0%-2.1%)

	1.6%)	≥1 point(s) = 30-day mortality
	Class II: 66-85 points	risk 10.9% (95% CI 8.5%-13.2%)
	Low mortality risk (1.7%-3.5%)	
	Class III: 86-105 points	
	Moderate mortality risk (3.2-7.1%)	
	Class IV: 106-125 points	
	High mortality risk (4.0-11.4%)	
	Class V: >125 points	
	Very high mortality risk (10.0-	
	24.5%)	

PESI, pulmonary embolism severity index.

Table 2. Clinical Guidelines and Scientific Statements for Management of Massive and Submassive Pulmonary Embolism

Guidelines and scientific statements	Risk stratification	Recommended management	Level of evidence
ACC / AHA scientific statement[4]	Massive PE	ST	IIa B
	Massive PE with CI to fibrinolysis	CDT	IIa C
	Submassive PE	ST	IIb C
ESC clinical guidelines[5]	High-risk PE	ST	I B
	High-risk PE with CI to ST	CDT	IIa C
	High-risk PE with CI to ST	SPE	I C
	Intermediate/high-risk PE	N/A	I B
	Intermediate/high-risk PE	Close monitoring for hemodynamic decompensation	IIa B
	Intermediate/high-risk PE with CI to ST	CDT	IIb B
	Intermediate/high-risk PE with CI to ST	SPE	IIb C
CHEST 2016[10]	PE with hypotension	Systemic thrombolysis	II B
	PE with clinical deterioration on anticoagulation	ST	II C
	PE with hypotension and CI to ST	CDT	II C

ACC, American College of Cardiology; AHA, American Heart Association; CDT, catheter-directed therapies; CI, contraindications; ESC, European Society of Cardiology; N/A, not available; PE, pulmonary embolism; SPE, surgical pulmonary embolectomy; ST, systemic thrombolysis.

REFERENCES

1. Grosse SD, Nelson RE, Nyarko KA, et al: The economic burden of incident venous thromboembolism in the United States: A review of estimated attributable healthcare costs. Thromb Res 137:3-10, 2016
2. Yamamoto T: Management of patients with high-risk pulmonary embolism: a narrative review. J Intensive Care 6:16, 2018
3. Donze J, Le Gal G, Fine MJ, et al: Prospective validation of the Pulmonary Embolism Severity Index. A clinical prognostic model for pulmonary embolism. Thromb Haemost 100:943-948, 2008
4. Jaff MR, McMurtry MS, Archer SL, et al: Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. Circulation 123:1788-1830, 2011
5. Konstantinides SV, Meyer G, Becattini C, et al: 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 41:543-603, 2020
6. Kucher N, Rossi E, De Rosa M, et al: Massive pulmonary embolism. Circulation 113:577-582, 2006
7. Pal K, Solanki J, Kadl A, et al: The use of a pulmonary embolism response team (PERT) at University of Virginia Medical Center to improve patient outcomes. Am J Respir Crit Care Med 197:A3780, 2018

8. Kabrhel C, Rosovsky R, Channick R, 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 150:384-393, 2016

9. Chaudhury P, Gadre S, Schneider E, et al: Impact of multidisciplinary pulmonary embolism response team availability on management and outcomes. Am J Cardiol 124:1465-1469, 2019

10. Kearon C, Akl EA, Ornelas J, et al: Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest 149:315-352, 2016

11. Stein PD, Matta F: Thrombolytic therapy in unstable patients with acute pulmonary embolism: saves lives but underused. Am J Med 125:465-470, 2012

12. Meyer G, Vicaut E, Danays T, et al: Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med 370:1402-1411, 2014

13. Chatterjee S, Chakraborty A, Weinberg I, et al: Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis. JAMA 311:2414-2421, 2014

14. Sharifi M, Bay C, Skrocki L, et al: Moderate pulmonary embolism treated with thrombolysis (from the "MOPETT" Trial). Am J Cardiol 111:273-277, 2013

15. Bloomer TL, El-Hayek GE, McDaniel MC, et al: Safety of catheter-directed thrombolysis for massive and submassive pulmonary embolism: Results of a multicenter registry and meta-analysis. Catheter Cardiovasc Interv 89:754-760, 2017

16. Engelberger RP, Kucher N: Catheter-based reperfusion treatment of pulmonary embolism. Circulation 124:2139-2144, 2011

17. Tu T, Toma C, Tapson VF, et al: A prospective, single-arm, multicenter trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism: The FLARE study. JACC Cardiovasc Interv 12:859-869, 2019

18. Kuo WT, Gould MK, Louie JD, et al: Catheter-directed therapy for the treatment of massive pulmonary embolism: systematic review and meta-analysis of modern techniques. J Vasc Interv Radiol 20:1431-1440, 2009

19. Salsano A, Sportelli E, Olivieri GM, et al: RVAD support in the setting of submassive pulmonary embolism. J Extra Corpor Technol 49:304-306, 2017

20. Saxena P, Smail H, McGiffin DC: Surgical techniques of pulmonary embolectomy for acute pulmonary embolism. Op Tech Thorac Cardiovasc Surg 21:80-88, 2016

21. Leacche M, Unic D, Goldhaber SZ, et al: Modern surgical treatment of massive pulmonary embolism: results in 47 consecutive patients after rapid diagnosis and aggressive surgical approach. J Thorac Cardiovasc Surg 129:1018-1023, 2005

22. Saeed G, Moller M, Neuzner J, et al: Emergent surgical pulmonary embolectomy in a pregnant woman: case report and literature review. Tex Heart Inst J 41:188-194, 2014

23. Lee T, Itagaki S, Chiang YP, et al: Survival and recurrence after acute pulmonary embolism treated with pulmonary embolectomy or thrombolysis in New York State, 1999 to 2013. J Thorac Cardiovasc Surg 155:1084-1090, 1090.e1-1090.e12, 2018

24. de Perrot M: Timing of surgery for pulmonary embolism: An evolving paradigm. J Thorac Cardiovasc Surg 155:1091-1092, 2018

25. Kilic A, Shah AS, Conte JV, et al: Nationwide outcomes of surgical embolectomy for acute pulmonary embolism. J Thorac Cardiovasc Surg 145:373-377, 2013

26. Spagnolo S, Grasso MA, Tesler UF: Retrograde pulmonary perfusion improves results in pulmonary embolectomy for massive pulmonary embolism. Tex Heart Inst J 33:473-476, 2006

27. Kadner A, Schmidli J, Schonhoff F, et al: Excellent outcome after surgical treatment of massive pulmonary embolism in critically ill patients. J Thorac Cardiovasc Surg 136:448-451, 2008

28. He C, Von Segesser LK, Kappetein PA, et al: Acute pulmonary embolectomy. Eur J Cardiothorac Surg 43:1087-1095, 2013

29. Kalra R, Bajaj NS, Arora P, et al: Surgical embolectomy for acute pulmonary embolism: Systematic review and comprehensive meta-analyses. Ann Thorac Surg 103:982-990, 2017

30. Barrios D, Rosa-Salazar V, Jimenez D, et al: Right heart thrombi in pulmonary embolism. Eur Respir J 48:1377-1385, 2016

31. Athappan G, Sengodan P, Chacko P, et al: Comparative efficacy of different modalities for treatment of right heart thrombi in transit: a pooled analysis. Vasc Med 20:131-138, 2015

32. Lango R, Kowalik MM, Klajbor K, et al: Circulatory support with right ventricular assist device and intra-aortic balloon counterpulsation in patient with right ventricle failure after pulmonary embolectomy. Interact Cardiovasc Thorac Surg 7:643-645, 2008

33. Chancellor WZ, Tribble C, Ghanta R, et al: Novel cannulation technique for temporary right ventricular assist device after LVAD placement. Op Tech Thorac Cardiovasc Surg 23:90-100, 2018

34. Dolmatova EV, Moazzami K, Cocke TP, et al: Extracorporeal membrane oxygenation in massive pulmonary embolism. Heart Lung 46:106-109, 2017

35. Yusuff HO, Zochios V, Vuylsteke A: Extracorporeal membrane oxygenation in acute massive pulmonary embolism: a systematic review. Perfusion 30:611-616, 2015

36. Pasrija C, Shah A, George P, et al: Triage and optimization: A new paradigm in the treatment of massive pulmonary embolism. J Thorac Cardiovasc Surg 156:672-681, 2018

37. Ain DL, Albaghdadi M, Giri J, et al: Extra-corporeal membrane oxygenation and outcomes in massive pulmonary embolism: Two eras at an urban tertiary care hospital. Vasc Med 23:60-64, 2018

38. Pasrija C, Kronfli A, George P, et al: Utilization of veno-arterial extracorporeal membrane oxygenation for massive pulmonary embolism. Ann Thorac Surg 105:498-504, 2018

39. George B, Parazino M, Omar HR, et al: A retrospective comparison of survivors and non-survivors of massive pulmonary embolism receiving veno-arterial extracorporeal membrane oxygenation support. Resuscitation 122:1-5, 2018