American College of Radiology ACR Appropriateness Criteria® Management of Acute Pulmonary Embolism

<u>Variant 1:</u>
Adult. Extensive acute bilateral central pulmonary emboli. Sustained hypotension for more than 15 minutes. Initial therapy.

Procedure	Appropriateness Category
Anticoagulation	Usually Appropriate
Systemic thrombolysis	Usually Appropriate
Catheter-directed therapy	Usually Appropriate
Surgical embolectomy	Usually Appropriate
Extracorporeal membrane oxygenation	May Be Appropriate

<u>Variant 2:</u> Adult. Acute bilateral pulmonary emboli. RV/LV ratio greater than 0.9 on CTA. Evidence of right heart strain on echocardiogram. Elevated troponin level. No hypotension. Initial

therapy.

Procedure	Appropriateness Category
Anticoagulation	Usually Appropriate
Catheter-directed therapy	Usually Appropriate
Surgical embolectomy	May Be Appropriate (Disagreement)
Systemic thrombolysis	Usually Not Appropriate
Extracorporeal membrane oxygenation	Usually Not Appropriate

<u>Variant 3:</u> Adult. Acute bilateral pulmonary emboli. RV/LV ratio less than 0.9 on CTA. No right heart strain on echocardiogram. Normal troponin level. No hypotension. Initial therapy.

Procedure	Appropriateness Category
Anticoagulation	Usually Appropriate
Catheter-directed therapy	Usually Not Appropriate
Extracorporeal membrane oxygenation	Usually Not Appropriate
Surgical embolectomy	Usually Not Appropriate
Systemic thrombolysis	Usually Not Appropriate

<u>Variant 4:</u> Adult. Acute saddle pulmonary embolism. Normal RV/LV ratio on CTA. Normal troponin level. No hypotension. Initial therapy.

Procedure	Appropriateness Category
Anticoagulation	Usually Appropriate
Catheter-directed therapy	Usually Not Appropriate
Systemic thrombolysis	Usually Not Appropriate
Extracorporeal membrane oxygenation	Usually Not Appropriate
Surgical embolectomy	Usually Not Appropriate

Variant 5:

Adult. Acute bilateral central pulmonary emboli. Evidence of right heart failure on echocardiogram. Sustained a syncopal event with head trauma and acute intracranial hemorrhage. Initial therapy.

Procedure	Appropriateness Category
Catheter-directed therapy	Usually Appropriate
Extracorporeal membrane oxygenation	May Be Appropriate
Surgical embolectomy	May Be Appropriate (Disagreement)
Anticoagulation	May Be Appropriate
Systemic thrombolysis	Usually Not Appropriate

Variant 6:

Adult. Acute thromboembolism in transit. Thrombus in the right atrium. Sustained hypotension for more than 15 minutes. Initial therapy.

Procedure	Appropriateness Category
Anticoagulation	Usually Appropriate
Catheter-directed therapy	Usually Appropriate
Surgical embolectomy	Usually Appropriate
Systemic thrombolysis	May Be Appropriate
Extracorporeal membrane oxygenation	May Be Appropriate

MANAGEMENT OF ACUTE PULMONARY EMBOLISM

Expert Panel on Interventional Radiology: Sara Plett, MD^a; Nicholas Fidelman, MD^b; Mikhail C.S.S. Higgins, MD, MPH^c; Resmi A. Charalel, MD, MPH^d; Kavi Devulapalli, MD^c; Sanjeeva P. Kalva, MD^f; Brent Keeling, MD^g; Christopher S. King, MD^h; Yilun Koethe, MDⁱ; Sharon W. Kwan, MD, MS^j; Alexander Lam, MD^k; Rajeev Suri, MD, MBA^l; Ricky T. Tong, MD, PhD^m; Jason W. Pinchot, MD.ⁿ

Summary of Literature Review

Introduction/Background

Acute pulmonary embolism (PE) is a subclass of venous thromboembolism (VTE), in which blood clots typically formed in the deep veins of the extremities embolize to the pulmonary arterial circulation. In 2019, there were an estimated 1,036,000 documented cases of VTE in the United States, of which 393,000 involved PE [1]. Risk factors for VTE include inheritable thrombophilias, such as Factor V Leiden, or acquired risk factors, such as recent surgery, trauma, malignancy, pregnancy, hormone therapy, aging, or obesity [2]. During the COVID-19 pandemic, increased VTE and PE prevalence was reported in patients hospitalized with COVID-19 infection [3].

For a discussion of the role of imaging in the diagnosis of PE, please refer to the separate ACR Appropriateness Criteria® topic on "Suspected Pulmonary Embolism" [4]. Once a diagnosis of PE is established, risk stratification is commonly performed to help guide subsequent management. These algorithms typically distinguish 3 categories of PE severity: 1) massive or high-risk, 2) submassive or intermediate risk, and 3) low risk [5-7]. Multidisciplinary PE response teams have emerged to help streamline patient management and coordinate care [8,9].

Initial Therapy Definition

Initial therapy is defined as a first-line treatment option for the medical condition defined by the variant. More than one option can be considered usually appropriate as the initial therapy when:

• There are equivalent alternatives (ie, only one option will be planned to effectively manage the patient's care).

OR

• There are complementary therapies (ie, more than one treatment option is planned to be performed simultaneously or in sequence during the same setting, wherein the therapies provide synergistic or complementary benefits to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Adult. Extensive acute bilateral central pulmonary emboli. Sustained hypotension for more than 15 minutes. Initial therapy.

This variant depicts a patient with massive or high-risk PE. The criteria for massive/high-risk PE as established by the American Heart Association (AHA) is sustained hypotension (systolic blood pressure <90 mm Hg for at least 15 minutes) or need for vasopressor support [6]. The immediate goal of intervention is to reduce pulmonary arterial clot burden and to relieve right heart strain.

Anticoagulation

Prompt initiation of systemic anticoagulation is considered standard of care for massive/high-risk PE [10]. Although the goal of anticoagulation is to neutralize the clotting cascade and prevent the propagation of thrombus, anticoagulation does not have a direct impact on reducing the existing clot burden, which is the objective of the subsequently described therapies.

Reprint requests to: publications@acr.org

^aRadiology Partners, Houston, Texas. ^bPanel Chair, University of California San Francisco, San Francisco, California. ^cPanel Vice-Chair, Bahamas Fibroid and Interventional Clinic, Nassau, Bahamas. ^dWeill Cornell Medicine, New York, New York. ^cWest County Radiological Group, Saint Louis, Missouri. ^fMassachusetts General Hospital, Boston, Massachusetts. ^gEmory University, Atlanta, Georgia; American Association for Thoracic Surgery. ^hInova Fairfax Hospital, Falls Church, Virginia; American College of Chest Physicians. ⁱTRG Imaging, Portland, Oregon. ⁱColorado Permanente Medical Group, Denver, Colorado. ^kUniversity of California San Francisco, San Francisco, California. ^lUT Health San Antonio, San Antonio, Texas. ^mMain Line Health, Bryn Mawr, Pennsylvania. ⁿSpecialty Chair, University of Wisconsin, Madison, Wisconsin.

The American College of Radiology seeks and encourages collaboration with other organizations on the development of the ACR Appropriateness Criteria through representation of such organizations on expert panels. Participation on the expert panel does not necessarily imply endorsement of the final document by individual contributors or their respective organization.

Catheter-Directed Therapy

Catheter-directed therapy (CDT) can involve a combination of mechanical and/or pharmacologic endovascular techniques targeted at reducing the existing PE burden. Many of the published clinical trials evaluating the use of CDT have focused on intermediate/submassive risk PE and are discussed to greater detail in the subsequent variant. Although fewer in number, trials including high-risk PE do support the use of catheter-directed techniques in appropriately selected patients within this cohort. The Pulmonary Embolism Response to Fragmentation, Embolectomy, and Catheter Thrombolysis (PERFECT) multicenter registry [11] and the Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism (SEATTLE II) trial [12] included patients with high-risk or intermediate-risk pulmonary emboli. These trials published data supporting the use of catheter-directed delivery of thrombolytic agents directly into the pulmonary arterial system, with the SEATTLE II trial demonstrating a decrease in thrombus burden, improvement in right heart strain, and reduced pulmonary hypertension [12]. The FlowTriever All-Comer Registry for Patient Safety and Hemodynamics (FLASH) registry, a multinational, multicenter registry of patients with highand intermediate-risk PE treated with the FlowTriever mechanical thrombectomy system, has reported a 7.6 mm Hg mean drop in mean pulmonary artery pressure (-23.0%; P < .0001) and decreased right ventricular (RV)/left ventricular (LV) ratio (1.23-0.98; P < .0001) at 48 hours posttreatment, with a favorable adverse event risk profile [13]. The Higher-Risk Pulmonary Embolism Thrombolysis (HI-PEITHO) multinational multicenter randomized control trial, targeted to complete patient enrollment in December 2023, will evaluate the clinical benefits of ultrasound (US)-facilitated catheter-directed thrombolysis with anticoagulation versus anticoagulation alone in high- to intermediate-risk PE, including primary outcome PE-related mortality as well as quality of life indicators and functional status over a 12-month follow-up period [14].

Extracorporeal Membrane Oxygenation

In high-risk PE with hemodynamic instability, mechanical circulatory support via venoarterial extracorporeal membrane oxygenation (ECMO) is an emerging therapy that is gaining traction in the management of these critically ill patients. This may be considered as a rescue therapy in patients with refractory cardiogenic shock despite previous treatment with thrombectomy or thrombolysis [15].

Treatment with ECMO may also serve a role as a primary or standalone therapy in highly unstable patients presenting with profound shock and/or requirement for cardiopulmonary resuscitation. In an institutional retrospective review of 17 patients over a 2-year duration, 77% of survivors of high-risk PE received ECMO and anticoagulation alone [16]. Furthermore, a separate retrospective review of 83 patients did not demonstrate a statistically significant difference in survival to discharge for patients receiving systemic thrombolysis before ECMO versus those receiving ECMO alone (88.9% versus 84.6%; P = .94) [17].

Surgical Embolectomy

Although surgical embolectomy has traditionally been considered a salvage therapy in the setting of failed attempts at the management of high-risk/massive PE, modern surgical techniques to promptly remove the thrombus have been demonstrated to be associated with a lower rate of bleeding complications as compared with thrombolysis [18]. Furthermore, a meta-analysis review of 17 studies comparing mechanical reperfusion strategies (of which 85.9% was surgical embolectomy) to other strategies, including systemic thrombolysis, CDT, or standalone ECMO, found a significant reduction in mortality in the mechanical reperfusion group compared with other strategies (22.6% versus 41.8%; odds ratio [OR], 0.439; 95% confidence interval [CI], 0.237-0.816; P = .009) [19]. Although reported in-hospital mortality rates for surgical embolectomy remain higher than for systemic thrombolysis or CDTs (20% versus 16% versus 7%, P < .01) [20], this may reflect a selection bias with physicians opting toward surgical thrombectomy or systemic thrombolysis over CDT for higher severity PE.

Systemic Thrombolysis

A meta-analysis review of 15 clinical trials concluded that although systemic thrombolytic therapy was associated with a significant reduction of overall mortality compared with anticoagulation alone (OR, 0.59; 95% CI, 0.36-0.96), it was also associated with an increased risk of fatal, intracranial, or major hemorrhage [21]. Another meta-analysis of 33 studies also demonstrated a reduction in overall mortality in patients treated with thrombolysis compared with anticoagulation alone (2.29% versus 4.03%; OR, 0.57; 95% CI, 0.35-0.92) but with increased risk of major bleeding events (9.46% versus 3.75%; OR, 2.70; 95% CI, 1.83-3.97) [22].

Variant 2: Adult. Acute bilateral pulmonary emboli. RV/LV ratio greater than 0.9 on CTA. Evidence of right heart strain on echocardiogram. Elevated troponin level. No hypotension. Initial therapy.

This variant describes a patient with submassive or intermediate-risk PE. The criteria for submassive/intermediate-risk PE as outlined by the AHA is RV strain without hypotension [6]. RV strain can be demonstrated by echocardiography or CT angiography of the pulmonary arteries (measured RV/LV ratio >0.9). Alternatively, RV strain can be demonstrated by an elevation in cardiac biomarkers (troponin, brain natriuretic peptide). The goal of intervention is to improve patient outcome by reducing clot burden and relieving right heart strain.

Anticoagulation

Prompt initiation of systemic anticoagulation is considered the standard of care for submassive/intermediate-risk PE [10].

Catheter-Directed Therapy

Given that intermediate-risk/submassive PE is associated with right heart strain, CDTs facilitate a targeted approach to attempt to reduce the clot burden, thereby relieving the elevated right heart pressure effectively and expediently.

Data supporting the use of pharmacological CDT in high-risk/massive PE detailed previously also extends to the use of these techniques for intermediate-risk/submassive PE. The Ultrasound Accelerated Thrombolysis of Pulmonary Embolism (ULTIMA) trial concluded that CDT was superior to anticoagulation alone in reversing RV dilation at 24 hours in patients with intermediate-risk/submassive PE [23]. In 2015, the PERFECT multicenter registry [11] and the SEATTLE II trial [12] were published supporting the use of catheter-directed delivery of thrombolytic agents directly into the pulmonary arterial system, with the latter demonstrating a decrease in thrombus burden, improvement in right heart strain and reduced pulmonary hypertension [12]. The Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism (OPTALYSE PE) trial demonstrated that CDT can be performed safely with lower-dose thrombolytics and for shorter durations than previously used [24].

Because the market for catheter infusion systems expanded, the Standard Versus Ultrasound-Assisted Thrombolysis for Submassive Pulmonary Embolism (SUNSET sPE) multicenter randomized clinical trial was commenced to evaluate conventional multiside-hole lysis catheters versus US-assisted delivery systems and found them to be comparable in their efficacy in the reduction of thrombus burden at 48 hours posttreatment [25]. The HI-PEITHO multinational multicenter randomized control trial, targeted to complete patient enrollment in December 2023, will evaluate the clinical benefits of US-facilitated catheter-directed thrombolysis with anticoagulation versus anticoagulation alone in high- to intermediate-risk PE, including primary outcome PE-related mortality as well as quality of life indicators and functional status over a 12-month follow-up period [14].

Catheter-directed mechanical thrombectomy has also demonstrated efficacity in the treatment of PE. The FlowTriever Pulmonary Embolectomy Clinical Study (FLARE) trial evaluated the effectiveness of large bore catheter aspiration thrombectomy in intermediate-risk/submassive PE and demonstrated a statistically significant 25% reduction in RV/LV ratio at 48 hours postprocedure [26]. The EXTRACT-PE (A Prospective Multicenter Trial to Evaluate the Safety and Efficacy of the Indigo Aspiration System in Acute Pulmonary Embolism) trial, a prospective multicenter study of a commercially available small bore catheter—based aspiration system, showed a significant reduction in RV/LV ratio and a low major adverse event rate while avoiding the use of intraprocedural thrombolytic agents in 98.3% of treated patients [27]. In addition, the FLASH registry, a multinational, multicenter registry of patients with high- and intermediate-risk PE treated with the FlowTriever mechanical thrombectomy system, has reported a 7.6 mm Hg mean drop in mean pulmonary artery pressure (-23.0%; P < .0001) and decreased RV/LV ratio (1.23-0.98, P < .0001) at 48 hours posttreatment, with a favorable adverse event risk profile [13].

In a matched retrospective cohort analysis of 470 patients with submassive PE, patients receiving anticoagulation plus CDT (thrombolysis or aspiration thrombectomy) demonstrated lower mortality at 1 year (7.6% versus 9.8%; P = .004) and no difference in bleeding complications at 30 days (2.9% versus 1.6%, P = .28) or development of chronic thromboembolic pulmonary hypertension (10.6% versus 9.5%, P = .44) [28].

Extracorporeal Membrane Oxygenation

There is no relevant literature to support ECMO as the primary treatment for hemodynamically stable patients with intermediate-risk/submassive PE.

Surgical Embolectomy

Although surgical embolectomy has traditionally been considered as a treatment option for hemodynamically unstable patients with massive PE, the literature also lends support to the surgical management of intermediaterisk/submassive central PE in patients with increased bleeding risk from thrombolysis [29]. A retrospective review of 133 patients with submassive PE undergoing either surgical embolectomy or catheter-directed treatment demonstrated reduced incidence of bleeding complications in the surgical patients compared with those receiving endovascular therapy (1.4% versus 9.7%, P < .05) [30].

Systemic Thrombolysis

The use of systemic thrombolytics in the patient with intermediate-risk/submassive PE is controversial. The multicenter PEITHO randomized control trial evaluated the use of systemic thrombolysis with standard anticoagulation versus standard anticoagulation alone in patients with intermediate-risk PE [31]. Whereas the systemic thrombolysis group did demonstrate a reduced incidence of death or hemodynamic compromise compared with the anticoagulation group alone (2.6% versus 5.6%; OR, 0.44; 95% CI, 0.23-0.87; P = .02), thrombolytic therapy was associated with a high rate of major adverse events including hemorrhagic stroke (2.0% versus 0.2%; P = .003) and major extracranial hemorrhage (6.3% versus 1.2%; P < .001). Subsequent meta-analysis reviews, although demonstrating an overall reduction in mortality for systemic thrombolysis over anticoagulation alone when both high- and intermediate-risk PE cases were included, found that this benefit disappeared when high-risk PE cases were excluded [21,22]. This would imply that the risk of major bleeding adverse events with systemic thrombolysis would outweigh the mortality benefit for patients with hemodynamically stable intermediate-risk/submassive PE.

Long-term follow-up of patients in the PEITHO trial after a period of at least 24 months (median 37.8 months) from thrombolysis versus placebo for intermediate-risk PE failed to demonstrate a significant difference in mortality rate (20.3% versus 18.0%; P = .43), functional limitation (36.0% versus 30.1%; P = .23), or chronic thromboembolic pulmonary hypertension detected at echocardiography (2.1% versus 3.2%; P = .79) [32].

Variant 3: Adult. Acute bilateral pulmonary emboli. RV/LV ratio less than 0.9 on CTA. No right heart strain on echocardiogram. Normal troponin level. No hypotension. Initial therapy.

This variant illustrates a patient with low-risk PE, defined by the AHA as not meeting high- or intermediate-risk categories [6].

The goal of intervention is to provide appropriate treatment of acute low-risk PE. Appropriate intervention improves patient outcome by recognizing low-risk clot burden and providing clinical management to prevent escalation to a higher-risk category.

Anticoagulation

Anticoagulation is typically considered the standard of care for low-risk PE [10]. In patients with low-risk isolated subsegmental PE, a meta-analysis of pooled data fails to demonstrate clear harm or benefit for anticoagulation, suggesting that the decision of whether to commence anticoagulation may be determined by a case-by-case clinical judgment [33].

Catheter-Directed Therapy

There is no relevant literature to support CDT as the primary treatment for patients with low-risk PE.

Extracorporeal Membrane Oxygenation

There is no relevant literature to support ECMO as the primary treatment for patients with low-risk PE.

Surgical Embolectomy

The literature does not support surgical embolectomy as the primary treatment for patients with low-risk PE. A single-center review including 779 patients with central or peripheral PE presented an algorithm for appropriate surgical management for patients with PE [34]. In this algorithm, patients with peripheral PE were not surgical candidates because of unfavorable anatomic accessibility and were recommended for medical therapy. Patients with central PE and without hemodynamic compromise or evidence of RV dysfunction (low-risk per AHA classification) were also recommended for medical therapy.

Systemic Thrombolysis

There is no relevant literature to support systemic thrombolysis as the primary treatment for patients with low-risk PE.

Variant 4: Adult. Acute saddle pulmonary embolism. Normal RV/LV ratio on CTA. Normal troponin level. No hypotension. Initial therapy.

This variant describes a patient with low-risk central PE. The literature evaluating the implications of central versus peripheral PE distribution is controversial. Although a central distribution of PE may be more likely to be associated with RV strain [35], central PE does not appear to be an independent predictor of mortality [36]. In fact, in a single-center retrospective review of 174 patients with central PE that was either saddle or nonsaddle in distribution, the nonsaddle PE had greater clinical RV dysfunction [37]. Thus, the management of saddle PE should be guided by appropriate risk stratification rather than appearance on imaging [38].

The goal of intervention is to provide appropriate treatment of appropriately risk stratified PE, by understanding that clinical parameters have greater weight in determining risk classification than imaging findings alone. Appropriate intervention improves patient outcome by providing appropriate risk stratified care and preventing escalation to a higher-risk category.

Anticoagulation

Anticoagulation is considered the standard of care for central PE [10].

Catheter-Directed Therapy

There is no relevant literature to support the use of CDT as the primary treatment for patients with low-risk central PE without hypotension or clinical or imaging evidence of right heart strain.

Extracorporeal Membrane Oxygenation

There is no relevant literature to support the use of ECMO as the primary treatment for patients with low-risk central PE without hypotension or clinical or imaging evidence of right heart strain.

Surgical Embolectomy

The literature does not support the use of surgical embolectomy as the primary treatment for patients with low-risk central PE without hypotension or clinical or imaging evidence of right heart strain. A single-center review including 103 patients with central PE, defined as involving the main, primary, or both branch pulmonary arteries, presented an algorithm for appropriate surgical management for patients with central PE [34]. Although RV dysfunction was demonstrated in the majority of patients with central PE who underwent echocardiography (28 of 47; 60%), there was a subset of patients who had central PE and normal RV function and thus would be classified according to the AHA as "low-risk." In this algorithm, patients with central PE and without hemodynamic compromise or evidence of RV dysfunction were recommended for treatment with medical therapy.

Systemic Thrombolysis

There is no relevant literature to support the use of systemic thrombolysis as the primary treatment for patients with low-risk central PE without hypotension or clinical or imaging evidence of right heart strain.

Variant 5: Adult. Acute bilateral central pulmonary emboli. Evidence of right heart failure on echocardiogram. Sustained a syncopal event with head trauma and acute intracranial hemorrhage. Initial therapy.

Major bleeding events are a significant contributor to morbidity and mortality of patients receiving thrombolytics for the treatment of acute PE. A risk stratification score, the PE-CH score, was designed to stratify the risk of intracranial hemorrhage in patients receiving thrombolytics, and includes 4 independent prognostic factors: 1) preexisting peripheral vascular disease, 2) age >65 years, 3) prior stroke with residual deficit, and 4) prior myocardial infarction [39].

The goal of intervention is to provide appropriate treatment of appropriately risk stratified PE, in the setting of contraindication to anticoagulation or thrombolysis. Appropriate intervention improves patient outcome by providing alternative therapies to reduce clot burden and improve right heart strain in the context of increased risk of adverse bleeding events.

Anticoagulation

The use and timing of anticoagulation as well as the selection of an anticoagulant agent following a recent intracranial bleeding event is controversial and often depends on case-by-case assessment. Although case studies have documented the use of heparin and oral anticoagulants for VTE and PE in patients with intracranial hemorrhage [40,41], there currently exist no large randomized clinical trials evaluating the use of anticoagulation for PE in the context of recent intracranial hemorrhage.

Catheter-Directed Therapy

Optimal pharmacochemical therapy is suggested to improve outcomes while minimizing risk of bleeding [42]. Although the SEATTLE II and ULTIMA trials evaluating US-assisted catheter-directed thrombolysis excluded patients deemed high risk for thrombolytic therapy, subsequent studies have evaluated the safety profile of localized thrombolysis in this patient population. Lee et al [43] performed an institutional retrospective review of 91 patients undergoing treatment for PE, of whom 17 were deemed high risk for thrombolysis because of such variables as surgery, hemorrhage, or cardiac arrest. There was a total of 7 major bleeding events, including 3 within the high-risk cohort. Conversely, mechanical thrombectomy techniques without the use of adjunctive systemic or locally delivered thrombolytics have been demonstrated as effective in reducing RV/LV ratio with a minimized bleeding risk profile [27].

Extracorporeal Membrane Oxygenation

Whether used as a salvage therapy in the setting of failed thrombolysis or thrombectomy, as a bridge to surgical embolectomy, or as a standalone therapy, ECMO is emerging as a therapeutic option in patients with a high risk of bleeding [44]. ECMO does require full anticoagulation to maintain patency of the system, thereby warranting careful patient selection.

Surgical Embolectomy

Although surgical embolectomy may be considered as a treatment option for massive or high-risk central PE in a subset of patients with increased bleeding risk, in the particular setting of acute intracranial hemorrhage, the necessary use of intraoperative high-dose systemic anticoagulation has been associated with risks of further bleeding and neurologic deterioration [45].

Systemic Thrombolysis

Intracranial hemorrhage is an absolute contraindication to the use of systemic thrombolysis.

Variant 6: Adult. Acute thromboembolism in transit. Thrombus in the right atrium. Sustained hypotension for more than 15 minutes. Initial therapy.

Thrombus from the deep veins of the lower extremities, once mobilized, may temporarily lodge in the right-sided cardiac chambers as it transits toward the pulmonary arterial circulation. This is termed "clot-in-transit" and represents an unstable variant of VTE, which is prone to distal embolization. Right-sided cardiac thrombus has been associated with a higher mortality, approaching 20%, as compared with controls [46].

The goal of intervention is to provide appropriate treatment of acute thrombus-in-transit within the right heart. Appropriate surgical or nonsurgical intervention improves patient outcome by reducing clot burden and minimizing the risk of significant distal clot embolization with resultant right heart strain.

Anticoagulation

Standard anticoagulation is a mainstay in the treatment of PE, including PE with right heart thrombus, or "clot-in-transit." However, the role of anticoagulation as a standalone treatment for right heart thrombus is controversial. Right heart thrombus is associated with a higher-risk for clinical deterioration due to its propensity for clot migration leading to hemodynamic compromise, and thus more advanced therapies may be warranted.

A retrospective review of 325 patients with PE and right heart thrombi failed to demonstrate a lower risk of all-cause death or PE-rated mortality for reperfusion treatment versus anticoagulation alone (6.2% versus 14%; P = .15; 4.7% versus 7.8%; P = .47) [47]. Multiple additional retrospective reviews, in contrast, demonstrate an improved mortality for treatment with either thrombolysis or surgical embolectomy compared with anticoagulation alone [48-51].

Catheter-Directed Therapy

There are limited data in the literature to evaluate the use of CDTs in the management of right heart clot-in-transit. Case reports have described the use of CDTs in the management of right heart thrombus [52].

Extracorporeal Membrane Oxygenation

There are limited data in the literature to evaluate the use of ECMO in the management of right heart clot-in-transit. Given the propensity of right heart thrombus for distal migration leading to cardiogenic shock, ECMO may be considered as a treatment strategy in hemodynamically unstable patients.

Surgical Embolectomy

Given the high risk of clinical deterioration, surgical thrombectomy has been employed as a treatment option for patients with high- and intermediate-risk PE and right heart thrombus [53]. A particular advantage to surgical embolectomy for the management of clot-in-transit is that the surgeon can address both the intracardiac clot and the frequently associated central PE concurrently.

Systemic Thrombolysis

The use of systemic thrombolysis has been described as a treatment option for right heart thrombus-in-transit, with favorable mortality compared with no treatment or anticoagulation alone [48-51].

Summary of Highlights

This is a summary of the key recommendations from the variant tables. Refer to the complete narrative document for more information.

- Variant 1: For massive or high-risk PE, there are a variety of first-line treatment options available. Anticoagulation, systemic thrombolysis, CDTs, and surgical embolectomy are all considered usually appropriate techniques to reduce clot burden and relieve right heart strain, with management strategy typically determined based on patient factors and local expertise.
- Variant 2: For submassive or intermediate-risk PE, anticoagulation and CDTs are considered usually appropriate management techniques.
- Variants 3 and 4: For patients presenting with low-risk PE, without hypotension or clinical or imaging evidence of right heart strain, anticoagulation alone is considered the usually appropriate management technique. This applies to both central and peripheral pulmonary emboli because management should be guided by appropriate risk stratification rather than appearance on imaging.
- Variant 5: For patients with acute high- or intermediate-risk PE necessitating treatment but with a contraindication to thrombolysis, catheter-directed techniques using mechanical thrombectomy without pharmacologic thrombolytics is considered usually appropriate, provided the thrombus is in a distribution accessible to catheter techniques.
- Variant 6: For acute right atrial thrombus-in-transit, first-line management with anticoagulation, CDTs, or surgical embolectomy are considered usually appropriate techniques to reduce clot burden and minimize risk of distal embolization causing right heart strain.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, click here.

Gender Equality and Inclusivity Clause

The ACR acknowledges the limitations in applying inclusive language when citing research studies that predates the use of the current understanding of language inclusive of diversity in sex, intersex, gender, and gender-diverse people. The data variables regarding sex and gender used in the cited literature will not be changed. However, this guideline will use the terminology and definitions as proposed by the National Institutes of Health [54].

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

References

- 1. Tsao CW, Aday AW, Almarzooq ZI, et al. Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. Circulation 2023;147:e93-e621.
- 2. Turetz M, Sideris AT, Friedman OA, Triphathi N, Horowitz JM. Epidemiology, Pathophysiology, and Natural History of Pulmonary Embolism. Semin Intervent Radiol 2018;35:92-98.
- 3. Porfidia A, Valeriani E, Pola R, Porreca E, Rutjes AWS, Di Nisio M. Venous thromboembolism in patients with COVID-19: Systematic review and meta-analysis. Thromb Res 2020;196:67-74.
- 4. Kirsch J, Wu CC, Bolen MA, et al. ACR Appropriateness Criteria® Suspected Pulmonary Embolism: 2022 Update. J Am Coll Radiol 2022;19:S488-S501.
- 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): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). Eur Respir J 2019;54.
- 6. Giri J, Sista AK, Weinberg I, 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.
- 7. Triantafyllou GA, O'Corragain O, Rivera-Lebron B, Rali P. Risk Stratification in Acute Pulmonary Embolism: The Latest Algorithms. Semin Respir Crit Care Med 2021;42:183-98.
- 8. Chopard R, Campia U, Morin L, et al. Trends in management and outcomes of pulmonary embolism with a multidisciplinary response team. J Thromb Thrombolysis 2022;54:449-60.
- 9. Hussein EA, Semaan DB, Phillips AR, et al. Pulmonary embolism response team for hospitalized patients with submassive and massive pulmonary embolism: A single-center experience. J Vasc Surg Venous Lymphat Disord 2023;11:741-47 e2.
- 10. Stevens SM, Woller SC, Baumann Kreuziger L, et al. Executive Summary: Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel Report. Chest 2021;160:2247-59.
- 11. Kuo WT, Banerjee A, Kim PS, et al. Pulmonary Embolism Response to Fragmentation, Embolectomy, and Catheter Thrombolysis (PERFECT): Initial Results From a Prospective Multicenter Registry. Chest 2015;148:667-73.
- 12. Piazza G, Hohlfelder B, Jaff MR, et al. A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Catheter-Directed, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: The SEATTLE II Study. JACC Cardiovasc Interv 2015;8:1382-92.

- 13. Toma C, Jaber WA, Weinberg MD, et al. Acute outcomes for the full US cohort of the FLASH mechanical thrombectomy registry in pulmonary embolism. EuroIntervention 2023;18:1201-12.
- 14. Klok FA, Piazza G, Sharp ASP, et al. Ultrasound-facilitated, catheter-directed thrombolysis vs anticoagulation alone for acute intermediate-high-risk pulmonary embolism: Rationale and design of the HI-PEITHO study. Am Heart J 2022;251:43-53.
- 15. Kaese S, Lebiedz P. Extracorporeal life support after failure of thrombolysis in pulmonary embolism. Adv Respir Med 2020;88:13-17.
- 16. Guliani S, Das Gupta J, Osofsky R, et al. Venoarterial extracorporeal membrane oxygenation is an effective management strategy for massive pulmonary embolism patients. J Vasc Surg Venous Lymphat Disord 2021;9:307-14.
- 17. Prasad NK, Boyajian G, Tran D, et al. Veno-Arterial Extracorporeal Membrane Oxygenation for Pulmonary Embolism after Systemic Thrombolysis. Semin Thorac Cardiovasc Surg 2022;34:549-57.
- 18. 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;44:335-9.
- 19. Chopard R, Nielsen P, Ius F, et al. Optimal reperfusion strategy in acute high-risk pulmonary embolism requiring extracorporeal membrane oxygenation support: a systematic review and meta-analysis. Eur Respir J 2022;60.
- 20. Percy ED, Shah R, Hirji S, et al. National Outcomes of Surgical Embolectomy for Acute Pulmonary Embolism. Ann Thorac Surg 2020;110:441-47.
- 21. Marti C, John G, Konstantinides S, et al. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. Eur Heart J 2015;36:605-14.
- 22. Wang TF, Squizzato A, Dentali F, Ageno W. The role of thrombolytic therapy in pulmonary embolism. Blood 2015;125:2191-9.
- 23. Kucher N, Boekstegers P, Muller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation 2014;129:479-86.
- 24. Tapson VF, Sterling K, Jones N, et al. A Randomized Trial of the Optimum Duration of Acoustic Pulse Thrombolysis Procedure in Acute Intermediate-Risk Pulmonary Embolism: The OPTALYSE PE Trial. JACC Cardiovasc Interv 2018;11:1401-10.
- 25. Avgerinos ED, Jaber W, Lacomis J, et al. Randomized Trial Comparing Standard Versus Ultrasound-Assisted Thrombolysis for Submassive Pulmonary Embolism: The SUNSET sPE Trial. JACC Cardiovasc Interv 2021;14:1364-73.
- 26. 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 2019;12:859-69.
- 27. Sista AK, Horowitz JM, Tapson VF, et al. Indigo Aspiration System for Treatment of Pulmonary Embolism: Results of the EXTRACT-PE Trial. JACC Cardiovasc Interv 2021;14:319-29.
- 28. Semaan DB, Phillips AR, Reitz K, et al. Improved long-term outcomes with catheter-directed therapies over medical management in patients with submassive pulmonary embolism-a retrospective matched cohort study. J Vasc Surg Venous Lymphat Disord 2023;11:70-81.
- 29. Neely RC, Byrne JG, Gosev I, et al. Surgical Embolectomy for Acute Massive and Submassive Pulmonary Embolism in a Series of 115 Patients. Ann Thorac Surg 2015;100:1245-51; discussion 51-2.
- 30. Kolkailah AA, Hirji S, Piazza G, et al. Surgical pulmonary embolectomy and catheter-directed thrombolysis for treatment of submassive pulmonary embolism. J Card Surg 2018;33:252-59.
- 31. Meyer G, Vicaut E, Danays T, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med 2014;370:1402-11.
- 32. Konstantinides SV, Vicaut E, Danays T, et al. Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism. J Am Coll Cardiol 2017;69:1536-44.
- 33. Bariteau A, Stewart LK, Emmett TW, Kline JA. Systematic Review and Meta-analysis of Outcomes of Patients With Subsegmental Pulmonary Embolism With and Without Anticoagulation Treatment. Acad Emerg Med 2018;25:828-35.
- 34. Greelish JP, Leacche M, Solenkova NS, Ahmad RM, Byrne JG. Improved midterm outcomes for type A (central) pulmonary emboli treated surgically. J Thorac Cardiovasc Surg 2011;142:1423-9.
- 35. Jain CC, Chang Y, Kabrhel C, et al. Impact of Pulmonary Arterial Clot Location on Pulmonary Embolism Treatment and Outcomes (90 Days). Am J Cardiol 2017;119:802-07.

- 36. Senturk A, Ozsu S, Duru S, et al. Prognostic importance of central thrombus in hemodynamically stable patients with pulmonary embolism. Cardiol J 2017;24:508-14.
- 37. Isath A, Shah R, Bandyopadhyay D, et al. Dispelling the Saddle Pulmonary Embolism Myth (from a Comparison of Saddle Versus Non-Saddle Pulmonary Embolism). Am J Cardiol 2023;201:341-48.
- 38. Ata F, Ibrahim WH, Choudry H, et al. Optimal management, prevalence, and clinical behavior of saddle pulmonary embolism: A systematic review and meta-analysis. Thromb Res 2022;217:86-95.
- 39. Chatterjee S, Weinberg I, Yeh RW, et al. Risk factors for intracranial haemorrhage in patients with pulmonary embolism treated with thrombolytic therapy Development of the PE-CH Score. Thromb Haemost 2017;117:246-51.
- 40. Oneglia C, Gualeni A. Pulmonary embolism after brain hemorrhage in a hypertensive patient: the therapeutic dilemma. J Thromb Thrombolysis 2008;25:231-4.
- 41. Lee WC, Fang HY. Management of pulmonary embolism after recent intracranial hemorrhage: A case report. Medicine (Baltimore) 2018;97:e0479.
- 42. Meng Y, Zhang J, Ma Q, et al. Pulmonary Interventional Therapy for Acute Massive and Submassive Pulmonary Embolism in Cases Where Thrombolysis Is Contraindicated. Ann Vasc Surg 2020;64:169-74.
- 43. Lee KA, Cha A, Kumar MH, Rezayat C, Sales CM. Catheter-directed, ultrasound-assisted thrombolysis is a safe and effective treatment for pulmonary embolism, even in high-risk patients. J Vasc Surg Venous Lymphat Disord 2017;5:165-70.
- 44. Gangaraju R, Klok FA. Advanced therapies and extracorporeal membrane oxygenation for the management of high-risk pulmonary embolism. Hematology Am Soc Hematol Educ Program 2020;2020:195-200.
- 45. Musleh R, Schlattmann P, Caldonazo T, et al. Surgical Timing in Patients With Infective Endocarditis and With Intracranial Hemorrhage: A Systematic Review and Meta-Analysis. J Am Heart Assoc 2022;11:e024401.
- 46. Koc M, Kostrubiec M, Elikowski W, et al. Outcome of patients with right heart thrombi: the Right Heart Thrombi European Registry. Eur Respir J 2016;47:869-75.
- 47. Barrios D, Chavant J, Jimenez D, et al. Treatment of Right Heart Thrombi Associated with Acute Pulmonary Embolism. Am J Med 2017;130:588-95.
- 48. Athappan G, Sengodan P, Chacko P, Gandhi S. Comparative efficacy of different modalities for treatment of right heart thrombi in transit: a pooled analysis. Vasc Med 2015;20:131-8.
- 49. Burgos LM, Costabel JP, Galizia Brito V, et al. Floating right heart thrombi: A pooled analysis of cases reported over the past 10years. Am J Emerg Med 2018;36:911-15.
- 50. Islam M, Nesheim D, Acquah S, et al. Right Heart Thrombi: Patient Outcomes by Treatment Modality and Predictors of Mortality: A Pooled Analysis. J Intensive Care Med 2019;34:930-37.
- 51. Ibrahim WH, Ata F, Choudry H, et al. Prevalence, Outcome, and Optimal Management of Free-Floating Right Heart Thrombi in the Context of Pulmonary Embolism, a Systematic Review and Meta-Analysis. Clin Appl Thromb Hemost 2022;28:10760296221140114.
- 52. Chen G, Zhang X, Wang Q, et al. The removal of floating right heart thrombi and pulmonary embolus using AngioJet device and venoarterial extracorporeal membrane oxygenation: a case report. Ann Transl Med 2022;10:612.
- 53. Zielinski D, Zygier M, Dyk W, et al. Acute pulmonary embolism with coexisting right heart thrombi in transit-surgical treatment of 20 consecutive patients. Eur J Cardiothorac Surg 2023;63.
- 54. National Academies of Sciences, Engineering, and Medicine; Division of Behavioral and Social Sciences and Education; Committee on National Statistics; Committee on Measuring Sex, Gender Identity, and Sexual Orientation. In: Becker T, Chin M, Bates N, eds. *Measuring Sex, Gender Identity, and Sexual Orientation*. Washington (DC): National Academies Press (US) Copyright 2022 by the National Academy of Sciences. All rights reserved.; 2022.

The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.