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ORIGINAL PAPER

Endovascular therapy for acute severe pulmonary embolism

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Abstract
Acute pulmonary embolism (PE) is a major public health problem and accounts for 100,000–180,000 deaths per year in the United States. Current prognostic stratification separates acute PE into massive, submassive, and low-risk by the presence or absence of sustained hypotension, RV dysfunction, and myocardial necrosis. Massive, submassive and low-risk PE have mortality rates of 25–65%, 3%, and < 1%, respectively. In this review we will focus on therapies currently available to manage acute massive and submassive PE.

Keywords Pulmonary embolism · Venous thromboembolic disease · Massive pulmonary embolism · Submassive pulmonary embolism · Catheter-directed therapy · Catheterdirected thrombolysis · Thrombolysis · Embolectomy

Background

Acute pulmonary embolism (PE) is a common life-threatening condition that accounts for one-third of deaths in hospitalized patients [1]. Acute PE is responsible for 100,000–180,000 deaths per year in the United States alone [2]. Survivors of an acute PE still face potential long-term impairments such as persistent right ventricular dysfunction, impaired functional status, decreased exercise tolerance, diminished quality of life, and chronic thromboembolic pulmonary hypertension [3, 4].

Increased pulmonary vascular resistance and right ventricle (RV) load are hallmarks of acute PE. Direct physical obstruction of the pulmonary artery compounded by pulmonary arterial vasoconstriction in the face of both inflammation and hypoxemia leads to an acute increase in pressure [5]. For reasons not yet understood, the increase in pulmonary arterial pressure does not occur until obstruction of the artery exceeds 30% [6]. As the pulmonary arterial pressure rises, the increased load on the RV causes compensatory dilation and hypokinesis. RV dilation can shift the intraventricular septum, which impedes left ventricular filling. This septal shift, combined with a hypokinetic RV and pulmonary artery obstruction, may reduce left ventricular preload and cause systemic hypotension. RV ischemia due to increased wall tension and decreased coronary artery blood flow potentiates RV hypokinesis and may ultimately cause RV failure [4].

Stratification

The American heart association (AHA) classifies a PE as either massive, submassive, or low risk [7]. Massive PE has a 25–65% mortality rate; submassive PE has a 2–9% mortality rate; and low-risk PE has a < 1% mortality rate. The guidelines of PE stratification from both the AHA and the European Society of Cardiology are summarized below (See Table 1).

Massive PE is defined by prolonged hypotension (< 90 mmHg systolic blood pressure for over 15 min or the requirement of vasopressors), pulselessness, or persistent bradycardia (heart rate < 40 bpm with signs or symptoms of shock). Submassive PE is defined by RV dysfunction but a normal blood pressure [7]. RV dysfunction requires the presence of at least one of the following criteria; RV dilation (RV/LV ratio > 0.9) as seen by CT or echocardiography; RV systolic dysfunction recognized by echocardiography; elevation of Brain natriuretic peptide (> 90 pg/mL) or N-terminal pro-BNP (> 500 pm/Ml); or electrocardiographic changes such as a new complete or partial right bundle branch block, anteroseptal ST changes, or anteroseptal T-wave inversion.

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Table 1 Summary of AHA and ESC PE stratification and management guidelines

	Classification	Criteria	Management guidelines
American Heart Association	Low risk PE	No RV dysfunction and normotensive	Anticoagulation
	Submassive PE	RV dysfunction and normotensive	Anticoagulation Systemic thrombolysis (ST), catheter directed therapy (CDT), and surgical embolectomy considered in those with clinical evidence of adverse prognosis
	Massive PE	Prolonged hypotension or need for vasopressors	Systemic thrombolysis CDT and surgical embolectomy considered in those with contraindications for systemic thrombolysis or for those who remain unstable after receiving thrombolysis
European Society of Cardiology	Low risk PE	sPESI score of 0	Anticoagulation
	Intermediate-low risk PE	sPESI score $\geq$ 1, and either imaging findings of RV dysfunction, elevated biomarkers, or no such findings	Anticoagulation
	Intermediate-high risk PE	sPESI score $\geq$ 1, both evidence of RV dysfunction seen on imaging and elevated biomarkers	Anticoagulation Systemic thrombolysis considered if signs of clinical decompensation appear. CDT and Surgical embolectomy considered instead of ST in those with high bleeding risk
	High risk PE	Presence of shock or persistent hypotension	Systemic Thrombolysis If contraindications for ST or if patient remains hemodynamically unstable, CDT or Surgical embolectomy considered

Myocardial necrosis is indicated by an elevated Troponin I (> 0.4 ng/mL) or Troponin T (> 0.1 ng/Ml) [7]. An RV/LV ratio of greater than 0.9 has a 92% sensitivity for RV dysfunction and suggests up to a 7.4-fold increase in short term mortality in PE patients [8, 9]. Elevated levels of serum troponin and brain natriuretic peptide are also indicative of cardiac muscle damage and can be associated with a four to eight-fold increase [10] and six-fold increase [11] in short term mortality, respectively. Additional clinical features such as age, gender, blood pressure, and pre-existing cancer have also been identified as contributing factors to short term mortality risk. Finally, a low risk PE is defined as an acute PE with no RV dysfunction or systemic hypotension.

The ESC guidelines released in 2014 classify an acute PE as either high risk, intermediate risk, or low risk [12]. High risk is equivalent to the AHA Massive PE classification. They incorporate the simplified PESI score (sPESI) to distinguish between low risk and intermediate risk [12]. The PE Severity Index (PESI) created in 2000 allows practitioners to estimate the 30 day mortality risk based on 11 parameters [13]. In 2010 the PESI scale was simplified, only assigning one point to each of the following; an age greater than 80, the presence of heart failure or pulmonary disease, a heart rate greater than 110 beats per minute, a systolic blood pressure less than 100 mmHg, and an oxygen saturation on room air less than 90%. Having a score of zero suggests an excellent prognosis (mortality < 1%) with mortality risk increasing after each added point [14]. An sPESI score of one or greater places the patient in the intermediate risk category, whereas a patient presenting with an sPESI score of less than one is considered low risk, regardless of evidence of right heart strain on imaging or elevated biomarkers (troponin/BNP). The ESC guidelines recognize the complexity and range of presentations within the intermediate risk category and thus further distinguish between intermediate high risk and intermediate low risk groups [12]. Intermediate high-risk patients have both elevated biomarkers and CT or echocardiography findings suggestive of RV dilation/dysfunction, while intermediate low risk patients have only one or neither of these features. Patients presenting with a low risk PE will have a sPESI score of zero, no elevated biomarkers, and no evidence of RV dysfunction/dilation.

Management

In the presence of an acute pulmonary embolism, anticoagulation (AC) should be administered immediately regardless of the severity, unless its use is contraindicated. Anticoagulants serve to allow the natural fibrinolytic system to function unopposed, ultimately decreasing the thromboembolic burden [2]. Low risk acute PE is associated with an excellent prognosis (< 1% mortality) and can adequately be managed with therapeutic anticoagulation alone [15]. Therapeutic anticoagulation should also be given during diagnostic workup of patients with intermediate or high clinical probability of PE and no contraindications to anticoagulation so as to not delay management [7].

In massive PE, treatment is aimed at rapidly removing clot to improve RV dysfunction and restoring pulmonary perfusion [16, 17] to prevent death. Treatment is escalated beyond anticoagulation and depending on the risk of bleeding, may include systemic thrombolysis, surgical embolectomy, or catheter directed therapy. Because right ventricular hypokinesis and dysfunction have been associated with increased mortality [18–20] treatment escalation in patients with submassive (intermediate risk) PE is considered in select patients. Overall such interventions, while not proven [21], are considered in the hope of reducing short-term morbidity and mortality and/or preserving long-term exercise tolerance and quality of life.

Systemic thrombolysis

Systemic thrombolysis (ST) refers to the administration of a fibrinolytic drug via a peripheral intravenous line. For massive PE, the FDA approved regimen is 100 mg of alteplase (tissue plasminogen activator [tPA]; Genentech, South San Francisco, California) as a continuous infusion over 2 h [7]. A large meta-analysis [22] of 16 randomly controlled trials (RCTs) found that systemic thrombolysis lowered all-cause mortality in patients with massive PE versus AC alone. However, ST is also associated with increased major and intracranial bleeding [22].

The use of ST in submassive PE patients was most rigorously studied in the PEITHO randomized double-blind trial. The PEITHO investigators compared tenecteplase (tPA) plus heparin to a placebo plus heparin in intermediate risk PE patients. Although no significant decrease in 30 day mortality was seen, systemic thrombolysis decreased the probability of hemodynamic deterioration. ST was also associated with increased major bleeding and intracranial hemorrhage [23]. A meta-analysis conducted by Chatterjee et al. included 1499 intermediate risk patients and showed that ST was associated with lower overall mortality than anticoagulation alone. There was also an increased risk of major bleeding in the ST cohort (9.2% vs. 3.4%) [22]. Another meta-analysis conducted by Nakamura et al. found no significant difference in mortality between submassive PE patients who were given ST and those who were given AC alone [24]. However, the authors did find that systemic thrombolysis decreased the risk of clinical deterioration but increased the incidence of intracranial bleeding.

Surgical embolectomy

Surgical embolectomy has historically been reserved as an emergency treatment for massive PE, and high procedural mortality rates in the past have limited its use. However, in the past two decades, improved techniques and patient selection have increased survival (20% mortality from 1985 to 2005 compared with 32% before 1985) [25]. As expected, the fatality rates of pulmonary embolectomy are lower in hemodynamically stable patients compared to massive PE patients [26]. A retrospective study in 2014 of 115 patients examined the use of surgical embolectomy in both submassive and massive PE cases. Surgical mortality rates for massive and submassive PE patients were 10.2% and 3.6% respectively, and 1 year survival rates were 65.8% and 80.4% [27].

Catheter directed therapy in massive PE

Although systemic thrombolysis is currently the first line treatment for acute massive PE, many patients cannot receive systemic thrombolysis due to contraindications. As mentioned earlier even with proper screening for contraindications, systemic thrombolysis has a 9.2% associated rate of major bleeding and 1.5% rate of intracranial bleeding [22]. It is among these patients that catheter directed therapy (CDT) and surgical embolectomy are considered. CDT encompasses various endovascular techniques to remove, macerate, and/or dissolve acute PEs (see Fig. 1). CDT provides

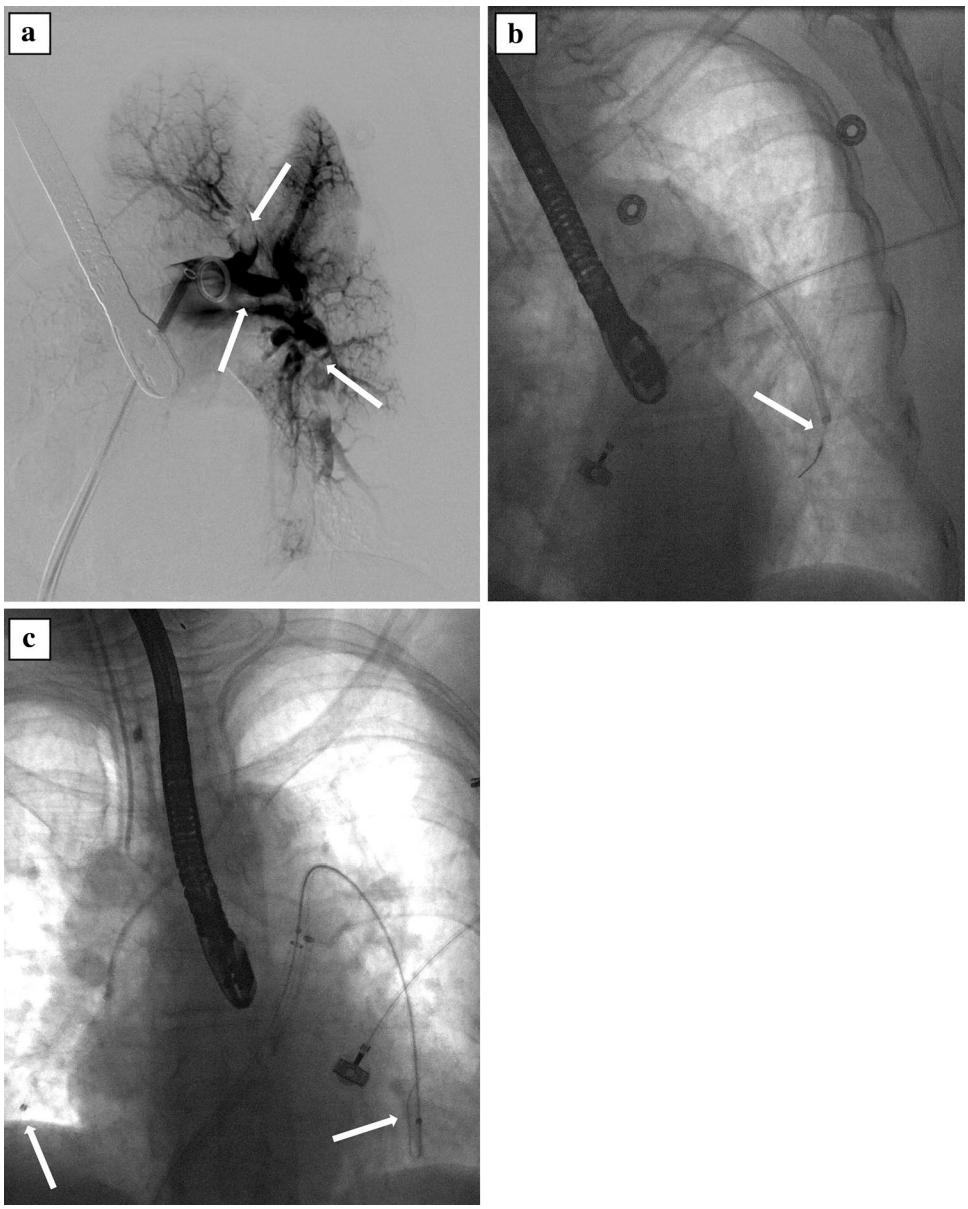

Fig. 1 Representative case of catheter directed therapy. **a** Left pulmonary angiogram in a 78 year old woman with massive PE demonstrates occlusive thrombi and poor perfusion. **b** Placement of CAT eight aspiration device (Penumbra, Alameda, Calif) in the left lower lobe pulmonary artery. **c** Successful placement of bilateral infusion catheters for catheter directed thrombolysis, (0.5 tPA per hour for 8 h)

patients with high risk of bleeding the option of an endovascular intervention with low dose or no tPA.

According to the American college of chest physicians, CDT should be considered in patients with massive PE who either have contraindications to thrombolysis, have failed thrombolysis, or are in shock that is likely to cause death before systemic thrombolysis may take effect [15]. The goal of CDT in massive PE management is rapid debulking of central occlusive thrombus to relieve life-threatening heart strain and improve pulmonary perfusion and oxygenation [28]. Although many CDT techniques have proven to be effective in massive PE management (see Table 2), the most widely used is rotating pigtail fragmentation [29]. Any standard 5F pigtail can be used to manually debulk the clot. A wire is used to guide the catheter across the embolic occlusion. The catheter now at the distal end of the clot is rotated back and forth while being retracted proximally through the thrombus with multiple passes [30]. This easily available and cost-effective method can be combined with mechanical thrombectomy, mechanical aspiration, local thrombolytic drug infusion, and balloon angioplasty. Although such additional techniques have undetermined safety and efficacy and are thus not specifically indicated for acute PE, they may be useful in rescuing a patient from hemodynamic collapse.

Like other forms of treatment, catheter directed therapy in the setting of acute massive PE is not supported by high level evidence. The rarity of massive PE and its high rate of mortality make randomized studies for therapy beyond anticoagulation difficult both ethically and logistically. Many of the studies assessing the use of CDT in acute massive PE are therefore small and retrospective in nature. A systematic review and meta-analysis conducted by Kuo et al. assessed the use of modern CDT techniques in 594 patients with an acute massive PE. Modern CDT techniques was defined as the use of 10-F or smaller catheters, catheter-based fragmentation and/or aspiration, and fibrinolytic infusion through a multi side-hole catheter spanning the thrombus [29]. Clinical success (stabilization of hemodynamics, survival to discharge, and resolution of hypoxia) was seen in 86.5% of cases, with a 2.4% rate of major procedural complications [29]. CDT was used as the first adjunct therapy following anticoagulation in 96% of the cases, and in 33% of the cases mechanical thrombectomy alone was used (no local thrombolytic infusion). Although the statistics are encouraging, the meta-analysis is limited by its basis in retrospective studies and consequently its lack of randomized trials. The SEATTLE II [32] study and the PERFECT registry [31] are two prospective CDT studies that enrolled some patients

Table 2 Current catheter directed therapy devices and techniques as seen in recent clinical trials and studies

Technique	Device	Use in massive PE	Use in submassive PE	Major findings
Standard CDT thrombolysis	Unifuse (AngioDynamics)	PERFECT registry [31]	PERFECT registry [31]	In this study, CDT was successfully used as first-line therapy for acute massive or submassive PE, and overall, CDT improved clinical outcomes while minimizing the risk of major bleeding [31]
	Cragg-McNamara (Medtronic)	PERFECT registry [31]	PERFECT registry [31]	
Ultrasound assisted thrombolysis (USAT)	EkoSonic (EKOS)	SEATTLE II study [32]	SEATTLE II study [32], ULTIMA trial [33], OPTALYSE PE trial [34]	Only EKOS catheter used in all three trials. All three trials show promising results using CDT to treat acute PE
Aspiration	FlowTriever (Inari)	Weinberg at al [35]	FLARE trial [36]	Findings of FLARE trial yet to be published
	Indigo CAT 8 (Penumbra)	Ciampo-Dopazo et al. [37]	EXTRACT-PE trial [38]	Findings of Extract-PE trial yet to be published
	Angiovac (AngioDynamics)	RAPID registry, Pasha et al. [39]	D'ayala et al. [40]	Findings of RAPID registry yet to be published
Fragmentation/maceration	Cleaner (Argon Medical)	Barjaktarevic et al. [43]		Case report
	Balloon non-specific	Kuo et al. [29]		Kuo et al. concluded modern CDT is a relatively safe and effective treatment for acute massive PE. 11 patients included in analysis that underwent Balloon fragmentation along with pigtail fragmentation

with massive PE. These studies showed a statistically significant reduction in pulmonary artery pressures (PAPs) and improvement in RV function and pulmonary blood flow following CDT.

It is important to note that the meta-analysis conducted by Kuo et al. on CDT usage in patients with massive PE saw major procedural complications occur in 25 patients [29]. The highest complication rates were seen in patients that received CDT with the AngioJet (Boston Scientific) Rheolytic thrombectomy device. Complications observed included bradyarrhythmia, heart block, hemoglobinuria, renal insufficiency, major hemoptysis, and procedure-related death. Interestingly, AngioJet was used in only 68 (11%) of the patients evaluated but accounted for 76% (19 of 25) of the major procedural complications. Of the 68 cases involving AngioJet, 27 minor complications (40%) and 19 major complications (28%) occurred [29]. Consequently, the food and drug administration (FDA) issued a black box warning for its use in PE. However, there are still publications supporting its use, suggesting that further study should be conducted to determine its efficacy and safety.

Catheter directed therapy in submassive PE

CDT has garnered much interest for its potential use as a first line therapy in submassive PE because of the limitations and risks of systemic thrombolysis. Table 3 shown below summarizes the author's approach to escalating therapy with CDT in submassive PE. Mechanical debulking as performed for massive PE is unproven and potentially risky for intermediate-risk PE because clot fragmentation can lead to distal embolization and elevated pulmonary pressure [28, 42], though several catheter-based thrombus removal devices are being investigated in prospective trials. Instead, the current practice standard is to place a multisidehole catheter into the pulmonary artery through which a fibrinolytic drug is administered at a low rate (e.g. 1 mg alteplase /hour). CDT as a therapy for submassive PE is intended to have similar efficacy to systemic thrombolysis but decrease the rate of major bleeding complications by decreasing the dosage of thrombolytic drug. CDT administers the fibrinolytic drug over a 12–24 h period of time (approx. 20–24 mg alteplase compared with 100 mg administered systemically) [28].

CDT as a primary adjunct therapy for intermediate risk PE is still considered exploratory due to the lack of evidence supporting its efficacy and safety [43]. Three clinical studies have suggested that CDT lyses pulmonary arterial thrombi, improves pulmonary blood flow at 48 h, and restores RV function [31–33]. The ULTIMA study [33] was a randomized trial involving 59 patients with acute intermediate PE who received either ultrasound assisted CDT or AC alone. The CDT group had more rapid (24 h) normalization of the RV/LV than the AC group. RV dysfunction was also significantly more common in the heparin-only group than in the CDT group at 90 days. There were no major bleeding complications in either of the treatment arms. SEATTLE II [32] was a single-arm prospective multicenter study that enrolled 150 patients, 119 of whom had submassive PE. CDT was associated with a decrease in the RV/LV ratio and pulmonary artery pressures at 48 h. There was an 11% major bleeding complication rate (one severe bleed and sixteen moderate bleeds). No intracranial bleeds were observed. The PERFECT registry [31], which also lacked a control arm, was a prospective registry including 101 patients with either massive or submassive PE. Clinical success was achieved in 86% of massive cases and 96% of submassive PE cases. CDT was found to improve pulmonary artery pressure and right heart strain without any major procedure related complications or bleeds. While these results are promising, they cannot be used to routinely recommend CDT over systemic thrombolysis or anticoagulation alone for submassive PE patients [43], as they are insufficiently powered to define CDT's safety, and were not designed to evaluate clinical outcomes such as death, hemodynamic deterioration, and long-term exercise intolerance [43].

Catheter directed therapy procedure outline

Access to the venous system is often achieved by ultrasonography-guided femoral or jugular puncture. Internal jugular access may be preferred if extensive thrombus is seen in the inferior vena cava (IVC), iliac, or femoral vein. If dual

Table 3 When do I escalate therapy in submassive PE?

PE classification	Parameters	CDT escalation	Notes
High risk submassive	High risk submassive bordering on massive PE. Signs of imminent decomposition, organ hypoperfusion or severe RV dysfunction	Almost always	Consider systemic lysis or surgical embolectomy depending on local expertise
	sPESI score ≥ 1, both evidence of RV dysfunction seen on imaging and elevated biomarkers	Possibly	CDT used in those with low bleeding risk or with a central thrombus
Low risk submassive	sPESI score ≥ 1, and either imaging findings of RV dysfunction, elevated biomarkers, or no such findings	Rare	CDT used in those that are young and active with a lot of clot burden, have low bleeding risk, or are concerned for long term pulmonary disability

catheter infusion is required, a second access may be used in the same vein. 5–7 Fr introducer sheaths are sufficient to secure access once achieved. It should be noted that an electrocardiogram should be routinely examined for the presence of left bundle-branch block (LBBB) prior to treatment. Catheterization of the right heart can potentially induce a new right bundle-branch block, which if in the presence of a preexisting LBBB can lead to complete heart block [44].

Several catheters have been described to access the pulmonary circulation, including a straight or angled pigtail catheter, balloon catheter, or cobra catheter. The catheter is advanced over guidewire and manipulated through the right atrium (RA) and right ventricle (RV) and into the main PA. Once accessed, the pulmonary arterial pressure (PAP) should be measured using a multisidehole catheter to establish baseline pressure readings and to determine contrast injection rate for pulmonary angiography. Although not commonly recorded, RA and right ventricular RV pressures can be measured to further understand the hemodynamic state. Normal RA and RV pressures are 0–5 mmHg and 20–25 mmHg, respectively. Normal PA pressures range from 20 to 25 mmHg systolic to 10–15 mmHg diastolic, with mean pressure of 9–18 mmHg. The ECG should be continuously monitored to detect induced cardiac arrhythmias.

Detailed arteriography is often unnecessary given the diagnostic CT findings and the need for rapid and safe intervention. The rate of contrast injection is determined using the estimated rate of blood flow in the pulmonary vessels via a test injection. An injection rate of 15–20 mL/s, for a total volume of 30–40 mL is common. For severe pulmonary hypertension, injection rates may be reduced to 10–15 mL/s for a total volume of 20–30 mL. The injection should be recorded at 4–6 frames per second. After the thrombus has been identified, the guidewire can be exchanged for a stiff wire (Rosen or Ampaltz) to stabilize the introduction of a long vascular sheath. Longer sheaths improve delivery of thrombectomy catheters/devices to the PA and better secure infusion catheters during thrombolysis.

The local fibrinolytic therapy is primarily delivered through a standard 5 Fr multisidehole infusion catheter (10–15 cm infusion length) that is advanced over wire and embedded into the thrombus. Once the catheter is in place a bolus of fibrinolytic drug (1–4 mg) may be given after which infusion begins. Infusion rate protocols have been generally shaped by the ULTIMA study and the SEATTLE II study. The ULTIMA study infused between 0.5 and 1 mg tPA per hour for a total of 20 ± 1 mg [33]. In the SEATTLE II trial, patients were given 1 mg tPA per hour for a total infusion of 24 mg tPA [32]. The consensus guidelines suggest an infusion rate between 0.5 mg and 2 mg tPA per hour for a total infusion of no more than 24 mg. If bilateral catheters are used, a common strategy is to infuse 0.5 mg to 1 mg tPA per catheter per hour.

After catheter placement, patients should be transferred to monitored beds with vascular sheaths and catheters secured by sutures and dressings. During infusion, anticoagulation with heparin is also continued at a subtherapeutic dose (eg, 400–600 U/h) to maintain an activated partial thromboplastin time between 40 and 60 s. Postintervention PAP measurements can be obtained through the long vascular sheath during the monitoring period. Infusion catheters typically remain in place for 12–24 h. Most providers remove catheters at the bedside. A minority will bring the patient back to the interventional suite to perform pulmonary angiography and pressure measurement. Infusion should be stopped if the patient has clinically significant bleeding or if there is imaging or clinical and hemodynamic evidence of cardiopulmonary improvement. Such endpoints would include diminished dyspnea, improved systemic blood pressure, reduced PAP, improved pulmonary blood flow seen on angiography, or improved RV function seen on ECG. Figure 2 (below) depicts a case to demonstrate the classification and management strategies when approaching a pulmonary embolism.

Inferior vena cava filters

The routine use of periprocedural Inferior vena cava (IVC) filters remains a point of disagreement. A hospital discharge analysis found that unstable PE patients who received an IVC filter had a lower in-hospital case fatality rate [45]. It is proposed that the filter may reduce recurrent PE. While the data is limited, IVC filter insertion may be beneficial in the setting of massive PE. On the other hand, there is no convincing evidence to support routine placement of IVC filters in submassive PE if the patient may be anticoagulated [46]. If femoral access is used for CDT in conjunction with IVC filter placement, caution should be used while passing catheters and sheaths past the newly placed filter. In our specific practice IVC filters are not routinely placed for submassive PE and the jugular approach for CDT is more often performed.

Follow up care

Close follow-up care intended to reduce the rate of recurrent PE and the development of post-PE syndrome is recommended for months to years after the embolic event. The type and length of postprocedural anticoagulation treatment should be periodically assessed and adjusted according to the patient's thrombotic risk. Keen attention should be paid to complaints of exercise intolerance and chronic dyspnea. Important diagnostic studies may include echocardiography, ventilation-perfusion scintigraphy, and cardiopulmonary exercise assessments. Furthermore, if a retrievable IVC filter

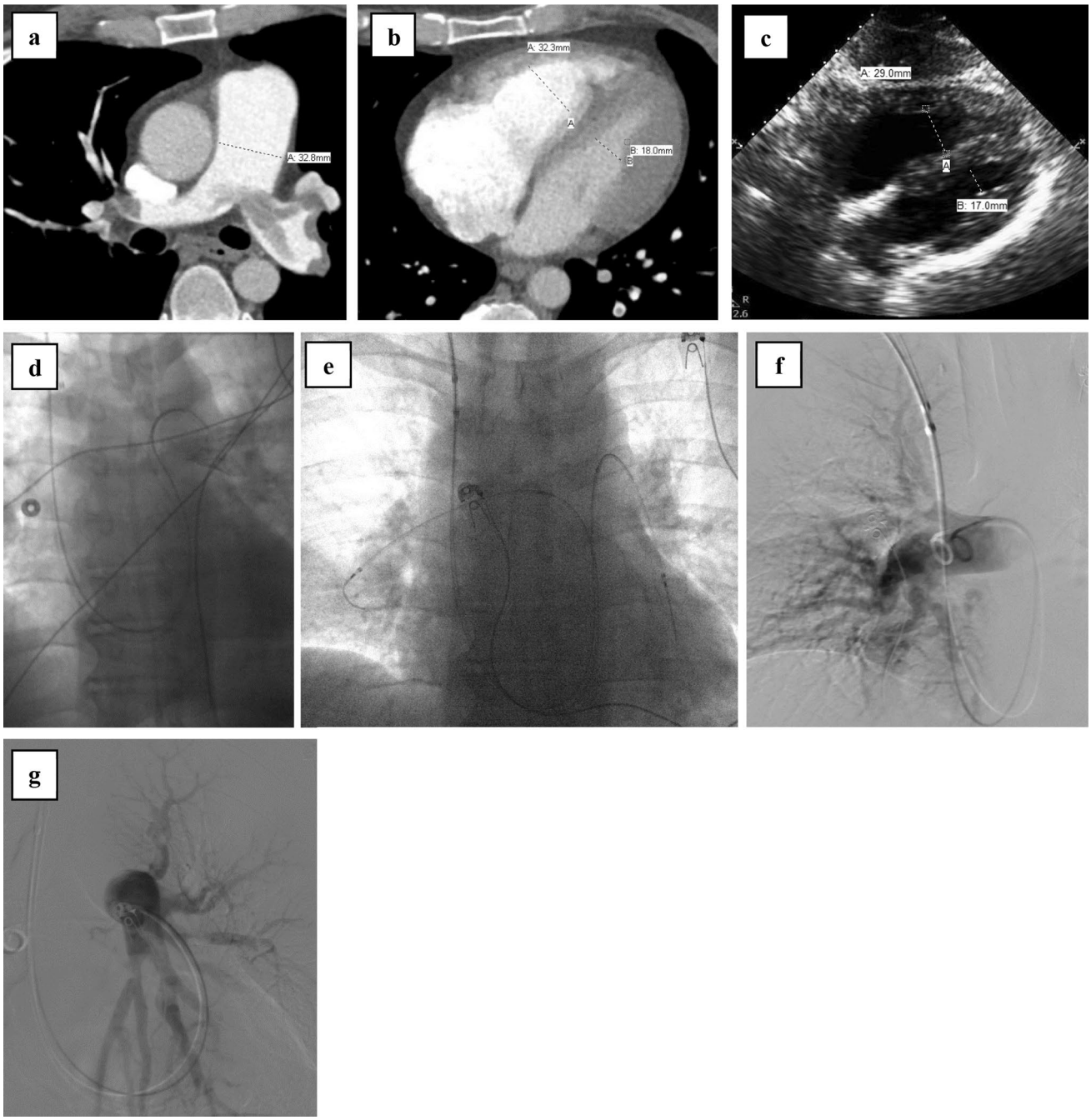

Fig. 2 Summary case of submassive pulmonary embolism year old female status post left robotic nephrectomy with post op respiratory distress and anemia. **a**, **b** CT pulmonary angiography shows extensive pulmonary emboli including saddle embolism and evidence of right heart enlargement/dysfunction. **c** Electrocardiogram demonstrates paradoxical septal motion, mild right atrial dilatation, and right ventricular dilatation and hypokinesis (RA/LA diameter ~ 1.7). Patient is normotensive and tachycardic with a sPESI score: 1; Troponin: 0.05 (normal 0.0–0.08 ng/ml), NT ProBNP = 2410 (normal < 300 pg/ml), Venous lactate = 2.99 (normal 0.90–1.7 nnol L). Labs and imaging findings suggest high-intermediate risk pulmonary embolism (ESC). Catheter directed therapy administered due to PE classification and persistent tachycardia and dyspnea. **d** Cobra catheter used to select PAs. PA pressure 83/30 (mean 56) mmHg measured prior to therapy administration. **e** Infusion of tPA through 2 5 Fr 90 cm with 10 cm infusion length UniFuse devices, at a rate of 0.5 mg/catheter/hour tPA (10 mg/1000 cc = 100 cc/hr). **f**, **g** Post CDT angiography of both right and left lungs after ~ 18 hours tPA infusion. Post intervention PA Pressure 53/23 (33) mmHg- mean PA pressure improved (56–33)

was placed, the patient should be monitored and evaluated for removal.

Future direction

Future research on acute PE treatment should focus on randomized trials with clinically relevant short-term and long-term outcomes to assess the clinical utility of CDT in patients with intermediate-risk PE. Further studies are needed to assess the impact of low-dose CDT on long term RV function, exercise tolerance, and risk of chronic thromboembolic pulmonary hypertension. Additionally, more data is required to standardize thrombolytic doses and to refine PE treatment protocols to determine the ideal method of thrombolytic administration.

Compliance with Ethical Standards

Conflict of interest Authors declare no conflicts of interest.

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