Chapter 6
Right Heart Failure from Pulmonary Embolism

Peeyush Grover, Alireza Vaziri, and Lawrence A. Garcia

Case 1

A 76-year-old female after total knee replacement surgery, presented with sudden onset shortness of breath and pleuritic chest pain. She was noted to have worsening right lower extremity swelling for 3 days prior to presentation. Her initial vital signs included blood pressure of 90/60 mmHg, heart rate of 110 beats per minute (bpm) and an O2 saturation of 90% on room air. She had no personal or family history of venous thromboembolic events (VTE). A computed tomographic pulmonary angiogram (CTPA) demonstrated a saddle pulmonary embolism (PE) with extension into both the right and the left main pulmonary arteries (PA) (Fig. 6.1). The right ventricle (RV) at its largest cross-sectional diameter was 1.8 times the size of the left ventricle. Transthoracic echocardiogram (TTE) demonstrated a dilated RV with reduced right ventricular systolic function and septal flattening consistent with acute elevation of PA systolic pressure.

P. Grover · A. Vaziri · L. A. Garcia (✉)
Steward St Elizabeth's Medical Center, Tufts University School of Medicine, Boston, MA, USA
e-mail: Lawrence.garcia@steward.org

L. Tsao, M. E. Afari (eds.), *Clinical Cases in Right Heart Failure*, Clinical Cases in Cardiology,
https://doi.org/10.1007/978-3-030-38662-7_6

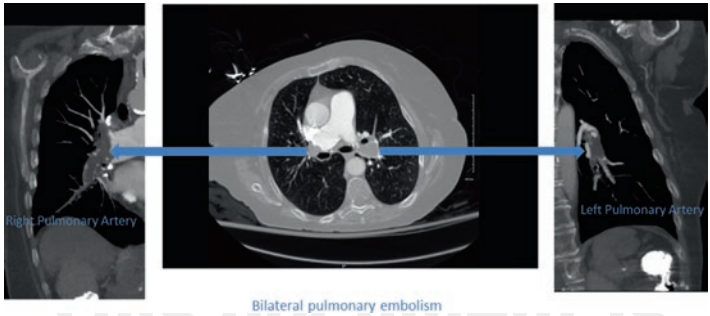

FIGURE 6.1 A computed tomographic pulmonary angiogram demonstrating a saddle pulmonary embolism. The blue arrows show the extension of the clot into bilateral pulmonary arteries

Case 2

A 56-year-old male patient with prior history of alcohol abuse, was found unconscious at home in a disheveled state. Emergency responders reported the patient to be hypotensive (80/50 mmHg) and in atrial fibrillation with rapid ventricular response (>140 bpm). In the hospital, initial resuscitation was performed with intravenous fluids and vasopressor support. An early diagnosis of alcohol intoxication was made. He was also noted to have bilateral lower extremity swelling on physical examination. TTE showed a serpiginous mass extending from the inferior vena cava (IVC) into the right atrium and across the tricuspid valve into the RV (Fig. 6.2). CTPA confirmed the diagnosis of acute PE and also demonstrated a massive thrombus in the left main PA, along with sub segmental thrombus in the right PA branches.

Case 3

A 65-year-old male with past medical history of diabetes mellitus and essential hypertension presented with sudden onset chest pain and shortness of breath at rest. He had no known past medical history of VTE or abnormal bleeding. When initially assessed in the emergency room, he had normal vital

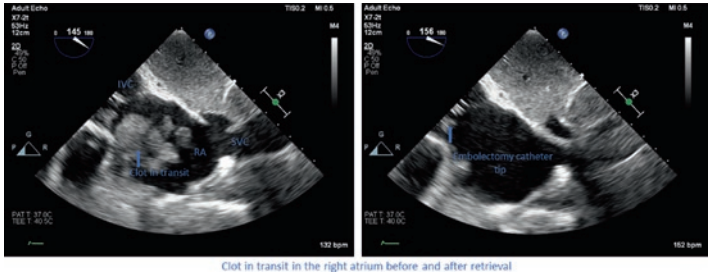

Figure 6.2 Transthoracic Echocardiogram showing a clot in transit. The clot extends from the IVC into the right atrium across the tricuspid valve and into the right ventricle

signs. Initial work-up including ECG and serum troponin levels ruled out cardiac etiologies of chest pain. He was then noted to become progressively tachypneic and tachycardic. Arterial Blood Gas (ABG) analysis demonstrated a pH of 7.6 with PaO2 of 65 mmHg on 4 L of inhaled oxygen by nasal cannula and increased A-a gradient. CTPA demonstrated a right ventricle/ left ventricle (RV/LV) cross sectional diameter ratio of >2:1. PE was involved in both the right and left PAs. TTE demonstrated the presence of McConnell's sign. He was started on anticoagulation with IV unfractionated heparin. His hypoxemia continued to worsen over the next few hours, warranting urgent intubation and vasopressor support.

6.1 Introduction

Acute PE is a major cause of acute RHF. VTE occurs when thrombi commonly arising from the proximal lower extremity deep veins, pelvic veins or less commonly the gonadal or renal veins, travel through the inferior vena cava (IVC) to the RV via the right atrium and tricuspid valve to eventually lodge in the PA. Acute PE originating from the upper extremities or thoracic veins, is rare and usually not large enough to cause hemodynamic derangement. Acute PE follows the

same etiologic classification as VTE. It is considered a provoked event if it is due to the presence of an identifiable risk factor within the last 6–12 weeks prior to the event and is unprovoked in the absence of such. The risk factors for acute PE are similar to the risk factors for VTE.

Common presenting symptoms range from a subclinical asymptomatic condition to shortness of breath and/or chest pain that is typically pleuritic in nature [1]. Less common symptoms of acute PE include cough, wheezing or syncope. Syncope indicates a more serious form of acute PE with high clot burden causing hypotension. Less commonly, a massive PE can also present as obstructive shock or sudden cardiac death [2].

PE is classified into massive, submassive, or low risk [3]. The European Society of Cardiology classifies sub-massive PE into *intermediate high risk* or *intermediate low risk* based on the presence of one/none or both of the following indicators: (a) imaging evidence of RV dysfunction; (b) cardiac biomarkers of RV strain [4].

Untreated massive PE has a high mortality rate of 25–30% [5]. A Hemodynamically Unstable presentation of PE is found in 10–12% of patients with underlying saddle pulmonary emboli [6, 7]. Adequately treated hemodynamically unstable PE carries a mortality rate of approximately 5%. A clot-in-transit has been reported to be associated with a mortality rate as high as 40% [7]. This type of clot is often identified on an echocardiogram and is located either in the RV or in the IVC (Fig. 6.2), [6]. Anatomy and pattern of lodgment of the embolus plays a role in hemodynamic derangement. For example, a saddle PE would typically lodge at the bifurcation of the right and left main PA and is more often associated with hemodynamically unstable PE.

Right ventricular failure is defined as the inability of the RV to maintain adequate pulmonary arterial blood flow in spite of normal central venous pressures [8]. Acute right ventricular pressure overload is the main pathophysiologic event during massive PE which results in acute RHF. Ultimately, obstructive shock occurs. The pathophysi-

ology of acute RHF in PE differs from chronic RHF as seen in pulmonary hypertension (Chap. 7).

The RV, as discussed in Chap. 1; Introduction to the Right Heart, is composed of a thin crescent shaped free wall which ejects nearly the same volume of blood as the LV into a high compliance, low resistive pulmonary arterial system with only 1/6 of the energy expenditure of the LV. RV end systolic and end diastolic pressures are 15–28/0–8 mm Hg respectively. The vascular resistance of the pulmonary arterial system is 123 ± 54 dyne s cm^{-5} m^2. In contrast, systemic LV vascular resistance is 10–20 times greater at 2130 ± 450 dyne s cm^{-5} m^2. The pulmonary vascular system has a large buffer of partially collapsed or unused vascular beds, and proximal PA vascular tone is very low [9]. RV geometry is suitable to adapt to large increases in venous return but is incapable of generating systolic pressures >40 mmHg in an acute setting [5].

6.2 What Is the Pathophysiology of Acute Right Heart Failure in Pulmonary Embolism?

The right ventricular response to pressure overload of massive clot burden is primarily via a mechanism called *homeometric autoregulation* or *the Anrep effect.* This refers to the rapid increase in contractile ventricular function after abrupt increase in afterload and is mediated by cytosolic ionized calcium [8, 10]. The coronary perfusion pattern of the normal RV free wall differs from that of the LV. Intramural RV free wall pressure does not normally rise above systemic arterial pressure, therefore, RV free wall coronary perfusion happens in both systole and diastole. In acute PE, a sudden decrease in LV preload due to obstruction of the principal pulmonary arteries, causes dramatic decline in systolic aortic root pressure. With sudden increase in RV wall tension due to acute RV dilation, RV free wall coronary perfusion declines precipitously resulting in myocardial ischemia [11]. RV dilatation also causes tricuspid valve insufficiency that result in further

decrease in RV ejection flow. When all the contractile reserve mechanisms are exhausted, a catastrophic spiral of events—including acute myocardial inflammation, hypoxic injury and focal RV myocyte necrosis—will cause irreversible RV damage. The clinical outcome is hemodynamic collapse. This pattern is collectively called obstructive shock and carries a high risk of mortality. Patients with prior RV damage including RV infarct or hypoxic pulmonary vascular vasoconstriction are more prone to acute RHF with lower clot burden.

In acute RV failure due to massive PE, pharmacologic or mechanical debulking of the pulmonary clot burden is the only known intervention that may increase the chance of survival [12].

6.3 What Is the Initial Approach?

Initial assessment should identify hemodynamically unstable patients from hemodynamically stable ones. Massive PE is a hemodynamically unstable condition defined as acute PE with sustained hypotension (systolic blood pressure <90 mmHg for at least 15 min) despite adequate volume resuscitation or requiring inotropic support. Alternative causes of hypotension such as hemorrhage, arrhythmia, left ventricular [LV] dysfunction, pulseless electrical activity, bradycardia ≤40 bpm or sepsis need to be ruled out. Sub-massive PE is less clearly defined. It is a hemodynamically stable condition defined by the absence of systemic hypotension but with either RV dysfunction or biochemical evidence of myocardial necrosis. Low risk PE is a hemodynamically stable PE with the absence of the clinical markers of adverse prognosis that define massive or submassive PE [3].

All three case presentations (Cases 1–3), had a varying degree of hemodynamic instability. Resuscitative therapy should be the initial focus of therapy for hemodynamically unstable PE. The first steps should involve oxygenating or ventilating the patient and hemodynamic stabilization with IV fluids and/or pressor support.

The patient in Case 1 required 2 L of O_2 to maintain a goal saturation above 92% and fluid resuscitation with normal saline for hemodynamic stability. The patients in Cases 2 and 3 required extreme measures of hemodynamic support with intubation and pressors. Extra corporeal membrane oxygenation (ECMO) was utilized in Case 3.

Whenever PE is suspected, the pretest probability for PE should be estimated by a scoring method such as the Modified Wells score [13]. The modified Wells score (See Table 6.1) is a clinical scoring system based on physical examination findings and risk factors for PE. A low score is considered to be <2, an intermediate score is between 2 and 6, and a high score is usually >6. The modified Wells criteria have been best validated in the outpatient setting; however, prior meta-analysis has demonstrated sensitivity for acute PE amongst inpatients with the addition of the D-dimer test [14]. Case 1 had a calculated modified Wells score of 4.5. Both cases 2 and 3 had a score of 7.5. The D dimer level in Case 1 was elevated at 800 ng/mL (reference <500 ng/mL), suggesting the need for further testing. Cases 2 and 3 did not need to be tested for D dimer given the high probability of acute PE.

Table 6.1 Modified Wells Criteria (A low score is considered to be <2, an intermediate score is between 2 and 6 and a high score is usually >6)

Criteria	Points
Clinical symptoms of DVT	3
Immobilization of 3 days or more	1.5
Surgery in previous 4 weeks	1.5
History of hemoptysis	1
Malignancy	1
History of previous DVT/PE	1.5
Heart rate > 100 beats/min	1.5
Other diagnosis less likely than PE	3

An initial assessment of a patient with a suspected PE should include ABG as well as basic chemistries. Common abnormalities seen on ABGs include hypoxemia (Pa O2 < 80 mmHg), a widened Arterial-alveolar gradient for oxygen (>20 mmHg), respiratory alkalosis and hypocapnia (<40 mmHg) [15–17]. All of our cases had findings of hypoxemia and respiratory alkalosis on ABG's, making the diagnosis of acute PE very likely.

ECG abnormalities are non-specific in patients with suspected PE. The most common findings are sinus tachycardia and nonspecific ST-segment and T-wave changes (70% of patients). Other abnormalities include an S1Q3T3 pattern, a RV strain pattern and a new incomplete right bundle branch block. These findings are very uncommon (<10%), but are associated with poor prognosis [18, 19]. All three patients presented with sinus tachycardia.

In patients with a low and intermediate risk of PE, a D-dimer test is very sensitive. Therefore, a normal D-dimer (<500 ng/mL) effectively excludes PE. No further testing is required in low risk patients. A D-dimer test is best used in conjunction with the clinical probability assessment [20]. When the D-dimer level is elevated, a diagnostic imaging study should be performed, preferably with a CTPA. As Case 1 had an elevated D Dimer with an intermediate pre-test probability, CTPA was urgently ordered, which confirmed the diagnosis of PE. The other cases had a high probability of PE, therefore, the initial test was CTPA from the start.

Right heart catheterization (RHC) can monitor pressures in the PAs after catheter based lysis or thrombectomy [21]. All our patients underwent RHC which demonstrated a PA systolic pressure between 40 and 50 mmHg and an elevated PA diastolic occlusion pressure gradient (>10 mmHg). The Pulmonary Artery Pulsatility index (PAPi), defined as the ratio of pulmonary artery pulse pressure to right atrial pressure, has emerged as a powerful predictor of right ventricular failure in patients with acute inferior myocardial infarction and those undergoing left ventricular assist device placement. PAPi can serve as a

useful marker of RV dysfunction in patients with PE as well [22]. PAPi is discussed in more detail in Chap. 9.

6.4 Which Imaging Modalities Should Be Pursued for Definitive Diagnosis?

The Prospective Investigation Of Pulmonary Embolism Diagnosis (PIOPED) study conducted between 1985 and 1986 confirmed the value of high and low probability scintigraphy lung ventilation perfusion (V/Q) scan. Corresponding V/Q scan results, when combined with high and low clinical suspicion (Modified Wells scores) for acute PE, have a 96% positive predictive value and 96–98% negative predictive value [23].

PIOPED II conducted between 2001 and 2003 demonstrated 83% sensitivity and 96% specificity of CTPA in detecting PE [24].

Selective pulmonary angiography has been considered the gold standard imaging test for diagnosing PE in the past. However, this test is invasive, involves use of large doses of potentially nephrotoxic iodinated radio contrast and is not readily available in all hospitals. Hence, CTPA is currently considered the imaging modality of choice for detecting PE if not otherwise contraindicated. CTPA should be performed in all patients with an intermediate probability of PE and in those with a D-dimer level ≥500 ng/mL where the diagnostic pretest probability is moderate to high. A prospective, multicenter cohort study of 3306 patients with clinically suspected PE from both an inpatient and outpatient setting, categorized patients according to the modified Wells score—as PE "likely" (score > 4) or PE "unlikely" (score ≤ 4). Patients underwent D-dimer testing and PE was considered excluded when the D-dimer level was <500 ng/mL. Both PE "unlikely" patients who had a D-dimer level ≥500 ng/mL, and PE "likely" patients, underwent CTPA (a total of 1939 patients). CTPA excluded PE in 1505 patients who were 45.5% of the study population. In these patients, the 3-month incidence of

VTE was 1.3%, and PE was considered a possible cause of death in seven patients (0.5%) after a negative CTPA [20]. CTPA is considered most accurate for the detection of large, main, lobar, and segmental PE, and less accurate for the detection of smaller, peripheral, subsegmental PE Newer generation CTPA scanners have increased detection rates of smaller emboli.

Estimates of the incidence of PE in the general population have increased following the introduction of higher resolution CTPA; however, PE related mortality remains unchanged despite the use of CTPA [25]. In patients who cannot undergo CTPA (such as renal failure or contrast allergy), a V/Q scan is a viable option. The results of the V/Q scan should be considered along with the clinical probability of having PE. Amongst patients with a normal V/Q scan and any clinical probability, no further testing is needed. In patients with a low-probability V/Q scan and low clinical probability (Wells score < 2) no further testing is required. In patients with a high-probability V/Q scan and high clinical probability (e.g, Wells score > 6), immediate treatment with anticoagulation is indicated. All other combinations of V/Q scan results and clinical pretest probabilities are indeterminate and further testing is often recommended [26].

Magnetic Resonance Pulmonary Angiography (MRPA) can substitute for CTPA to avoid radiation exposure for young or pregnant patients. However, MRPA is less sensitive and more dependent on the experience of the technologist performing the scan, compared with CTPA. MRPA requires no ionizing radiation, and the examination can be combined with MR venography in the same setting. MRPA was studied prospectively in 371 adults with suspected PE. Among the 75% of patients who had technically adequate images, MRPA alone showed a sensitivity and specificity of 78% and 99%, respectively [27].

Catheter-based pulmonary angiography is more invasive and slightly less sensitive than CTPA, and is usually reserved for patients undergoing concurrent therapeutic interventions. In emergent circumstances, TTE can also be used when a

rapid or presumptive diagnosis for PE is considered. TTE findings of PE include a dilated RV, reduced right ventricular systolic function, and elevated PA systolic pressure. McConnell's sign is an echocardiographic finding of PE whereby the RV free wall is akinetic, while the RV apex is spared [28]. In most cases however, particularly those who are hemodynamically stable, echocardiography is generally considered insensitive, since abnormalities are frequently absent in patients with PE [29].

6.5 What Is the Contemporary Management of Acute Pulmonary Artery Embolism?

For most patients who become hemodynamically stable following resuscitation, and in whom the clinical suspicion for PE is high, immediate anticoagulation (AC) is recommended [3, 30]. While results are pending, AC must be individualized according to the clinical suspicion for PE, hemodynamic status, and contraindications to anticoagulation. A prior study has demonstrated a clear improvement in in-hospital mortality and a long term reduction in pulmonary hypertension from AC amongst such group of patients [31]. The choice of AC depends on multiple factors including hemodynamic stability, renal function, and whether an invasive procedure is anticipated. The option include low molecular weight heparin, IV unfractionated heparin or long acting oral anticoagulants (Direct Oral Anticoagulant: DOAC or Vitamin K Antagonists: VKA) [32, 33].

For patients with a high clinical suspicion for PE, empiric administration of systemic thrombolytic therapy can be lifesaving as an adjunct to any AC. A recent meta-analysis showed that amongst massive (high-risk) PE patients, systemic thrombolytic therapy versus no therapy decreased the composite endpoint of death and recurrent thromboembolism (9.4% versus 19%) [34]. Another large trial compared placebo plus heparin with thrombolytic therapy plus heparin in 1005 patients with acute PE who were normotensive and had evi-

dence of RV dysfunction [35]. Compared with heparin alone, thrombolysis resulted in a reduction in the primary endpoint of death and hemodynamic decompensation at 7 days following randomization. The thrombolysis arm was associated with increased extracranial bleeding, major bleeding and hemorrhagic stroke (2% versus 0.2%). The use of thrombolytic therapy as a life-saving measure should be individualized and based on the clinical setting and results of available investigational test results. The initiation of AC should never be delayed while considering other, more aggressive interventional therapies [36]. It is important to keep in mind that sometimes a clear diagnosis could be difficult to make and may require a multidisciplinary team approach. Some highly specialized centers have incorporated a "Pulmonary Embolism Response Team" (PERT) to facilitate this process rapidly [32, 33] with a high success rate. PERT consists of emergency room physicians as well as a radiologist, pulmonologist, intensivist, pharmacist, vascular and interventional cardiologist.

For patients who have contraindications to AC or have an unacceptably high bleeding risk, placement of an IVC filter may be considered. An IVC filter can be considered in patients with significant DVT clot burden who are at risk of pulmonary artery embolism but with no active PE or those patients with a clot in transit after successful clot retrieval [37]. Retrievable filters are generally preferred. They should be removed after the patient can be safely anticoagulated, and the burden of clot has resolved. IVC filters are associated with multiple complications including thrombosis, migration, injury to the IVC and fractures; therefore the retrieval should be within 2–3 months after deployment [38].

6.6 What Are the Endovascular Strategies for Pulmonary Artery Embolism?

Systemic thrombolytic therapy is a widely accepted treatment for patients with PE who subsequently develop hemodynamic instability [39]. Multiple catheter-based techniques

have been developed for the management of PE. These techniques offer the benefits of less risk of bleeding and localized treatment of a formed clot along with reduced pulmonary arterial hypertension in the long term, when compared with systemic thrombolysis [40]. The techniques include manual thrombus breakdown and aspiration (embolectomy), localized treatment with a thrombolytic agent such as tPA (tissue plasminogen agent) or a combination of these therapies. Techniques utilized are ultrasound guided thrombolysis, rheolytic embolectomy, rotational embolectomy and suction embolectomy. The data behind these techniques are based on small observational studies, and the superiority of one over the other has not been validated [41, 42]. Typically, rotational devices do not require venotomy, thus avoiding the additional risk of vascular complications. More advanced catheter techniques have been used for the removal of large fresh thromboemboli in the IVC or right heart chambers (clot in transit) or for use during extracorporeal bypass. Such devices cannot easily access the distal PAs due to the small sized caliber of these vessels.

The use of catheter-directed thrombus removal or thrombolysis, should be limited to patients with high risk of bleeding, in shock, or who have failed systemic thrombolysis.

Lower doses of systemic thrombolytic therapy could help expedite the resolution of pulmonary hypertension amongst patients with PE. In the Moderate Pulmonary Embolism Treated with Thrombolysis (MOPETT) trial [40], 121 patients were randomly assigned to receive either heparin alone—unfractionated or low molecular weight—or the combination of half of the standard dose of tPA plus heparin. Compared with conventional therapy, this lower-dose regimen of tPA resulted in lower rates of pulmonary hypertension and similar rates of bleeding, recurrent PE, and mortality (5% versus 1.6%).

The Ultrasound Accelerated Thrombolysis of Pulmonary Embolism (ULTIMA) study randomized 59 patients with acute intermediate risk PE to IV heparin alone or ultrasound-assisted catheter-directed thrombolysis (USAT) followed by

IV heparin [43]. The USAT regimen consisted of high frequency ultrasound combined with 10–20 mg of tPA infused over 15 h. At 24 h, compared to conventional anticoagulation, USAT resulted in an improved RV:LV ratio (mean difference 0.3 versus 0.03), suggesting a hemodynamic benefit. At 90 days, there was no difference in mortality or major bleeding between the groups. Another single-arm prospective trial in a similar population, the Submassive and Massive Pulmonary Embolism Treatment with Ultrasound Accelerated Thrombolysis Therapy (SEATTLE II) trial described similar results [44].

6.7 What Are the Surgical Options for Pulmonary Embolism?

Surgical embolectomy, usually the last resort, is reserved as an option in specialized centers with available expertise. Considerations for surgical embolectomy are hemodynamic instability due to acute PE for patients in whom thrombolysis (systemic or catheter-directed) is contraindicated, and/or has failed [45, 46]. Additional indications may include echocardiographic evidence of an embolus trapped within a patent foramen ovale or present in the right atrium or RV [47]. The surgical approach is commonly associated with high mortality, particularly in the elderly (up to 46%) [45, 46]. Proximal emboli are usually amenable to surgical removal whereas distal thrombus is generally not amenable to surgery. Prior data has not demonstrated any difference in 30-day mortality amongst patients who underwent surgical embolectomy compared with patients who underwent thrombolysis (15% versus 13%) [48]. Some retrospective series have supported the role of surgical embolectomy amongst only unstable PE patients [49].

Complications include those associated with cardiac surgery and anesthesia as well as embolectomy-specific complications, such as perforation of the pulmonary artery and cardiac arrest.

6.8 What Is the Prognosis of Acute Pulmonary Embolism?

Massive PE has a mortality rate of approximately 8%. Amongst patients presenting with shock or hemodynamic collapse, the mortality has been reported to be as high as 40% [50]. RV dysfunction, RV dilatation and elevated PA pressures can be used to assess the prognosis for patients [51]. Factors that may contribute to early morbidity include alveolitis from an evolving pulmonary infarction, superimposed pneumonia, and medical comorbidities [52]. For subsegmental PE, the prognosis is better and is largely determined by comorbidities including malignancy, older age, male gender, chronic obstructive pulmonary disease, and heart failure [53].

Case Conclusion

- *Case 1*:

  The patient was assessed in the emergency room and was diagnosed with a massive PE requiring anticoagulation with IV unfractionated heparin. Due to persistent hypotension and tachycardia, she was considered a candidate for systemic thrombolysis. She was considered low risk for major bleeding, including intra cranial bleeding. The PERT favored catheter directed thrombolysis using low dose tPA for the next 12 h. She stabilized with significant improvement in RV size and function within 24 h of tPA infusion. She was maintained on a DOAC for the next 3 months.

- *Case 2*:

  The patient underwent suction embolectomy with removal of the serpentine mass from the IVC/RA and RV. An IVC filter was deployed and catheter directed thrombolysis was then performed for the following 12 h. Marked improvement in the RV size and function was noted 24 h, post procedure. The patient was successfully weaned off vasopressors and extubated. He was anticoagulated for a total of 6 months and the IVC filter was retrieved 3 months post procedure.

- *Case 3*:
  The patient had a worsening course and required mechanical ventilation and multiple inotropic/ vasopressor support. The decision was made to advance therapy to veno-arterial (VA) ECMO support. Catheter directed thrombolysis was performed. His RV dysfunction and hemodynamics improved. He was weaned off VA ECMO support, but developed a left facial droop later during the course of the hospitalization. Urgent CT scan showed no areas of hemorrhage, although MRI revealed a right thalamic stroke. Transesophageal echocardiogram failed to show any PFO or aortic atheroma. The likely cause of the stroke was thought to be a complication related to ECMO. He underwent extensive physical and occupational therapy and was able to return to work with minimal residual deficit.

Clinical Pearls

- Acute right heart failure is the major pathophysiologic manifestation of massive Acute Pulmonary Embolism.
- Whenever PE is suspected, the pretest probability for PE should be estimated by a well validated scoring method such as the Modified Wells Score.
- CTPA is currently considered the imaging modality of choice for detecting PE.
- For patients with acute PE who are hemodynamically stable, immediate AC is recommended, if not otherwise contraindicated.
- For patients with acute PE who are hemodynamically unstable, systemic thrombolysis should be considered. The use of catheter-directed thrombus removal or thrombolysis should be limited to select patient population and centers.
- Patients with Acute PE who develop acute right heart failure and shock usually carry a poor prognosis.

References

1. Stein PD, et al. Clinical characteristics of patients with acute pulmonary embolism: data from PIOPED II. Am J Med. 2007;120(10):871–9.
2. Castelli R, et al. Syncope in patients with pulmonary embolism: comparison between patients with syncope as the presenting symptom of pulmonary embolism and patients with pulmonary embolism without syncope. Vasc Med. 2003;8(4):257–61.
3. Jaff MR, 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. 2011;123(16):1788–830.
4. Konstantinides SV, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014;35(43):3033–69, 3069a–3069k.
5. Belohlavek J, Dytrych V, Linhart A. Pulmonary embolism, part I: epidemiology, risk factors and risk stratification, pathophysiology, clinical presentation, diagnosis and nonthrombotic pulmonary embolism. Exp Clin Cardiol. 2013;18(2):129–38.
6. Ryu JH, et al. Saddle pulmonary embolism diagnosed by CT angiography: frequency, clinical features and outcome. Respir Med. 2007;101(7):1537–42.
7. Sardi A, et al. Saddle pulmonary embolism: is it as bad as it looks? A community hospital experience. Crit Care Med. 2011;39(11):2413–8.
8. Greyson CR. Pathophysiology of right ventricular failure. Crit Care Med. 2008;36(1 Suppl):S57–65.
9. Ventetuolo CE, Klinger JR. Management of acute right ventricular failure in the intensive care unit. Ann Am Thorac Soc. 2014;11(5):811–22.
10. von Anrep G. On the part played by the suprarenals in the normal vascular reactions of the body. J Physiol. 1912;45(5):307–17.
11. Guyton AC, Lindsey AW, Gilluly JJ. The limits of right ventricular compensation following acute increase in pulmonary circulatory resistance. Circ Res. 1954;2(4):326–32.
12. Konstantinides SV, 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. 2019;54(3):ehz405.
13. Wang RC, et al. The impact of clinical decision rules on computed tomography use and yield for pulmonary embolism: a systematic review and meta-analysis. Ann Emerg Med. 2016;67(6):693–701.e3.
14. Bass AR, et al. Clinical decision rules for pulmonary embolism in hospitalized patients: a systematic literature review and meta-analysis. Thromb Haemost. 2017;117(11):2176–85.
15. Stein PD, et al. Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute pulmonary embolism and no pre-existing cardiac or pulmonary disease. Chest. 1991;100(3):598–603.
16. Stein PD, Goldhaber SZ, Henry JW. Alveolar-arterial oxygen gradient in the assessment of acute pulmonary embolism. Chest. 1995;107(1):139–43.
17. Stein PD, et al. Arterial blood gas analysis in the assessment of suspected acute pulmonary embolism. Chest. 1996;109(1):78–81.
18. Stein PD, Saltzman HA, Weg JG. Clinical characteristics of patients with acute pulmonary embolism. Am J Cardiol. 1991;68(17):1723–4.
19. Shopp JD, et al. Findings from 12-lead electrocardiography that predict circulatory shock from pulmonary embolism: systematic review and meta-analysis. Acad Emerg Med. 2015;22(10):1127–37.
20. van Belle A, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA. 2006;295(2):172–9.
21. Cozzi PJ, Hall JB, Schmidt GA. Pulmonary artery diastolic-occlusion pressure gradient is increased in acute pulmonary embolism. Crit Care Med. 1995;23(9):1481–4.
22. Kochav SM, et al. Prognostic impact of pulmonary artery pulsatility index (PAPi) in patients with advanced heart failure: insights from the ESCAPE trial. J Card Fail. 2018;24(7):453–9.
23. PIOPED Investigators. Value of the ventilation/perfusion scan in acute pulmonary embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA. 1990;263(20):2753–9.

24. Sostman HD, et al. Acute pulmonary embolism: sensitivity and specificity of ventilation-perfusion scintigraphy in PIOPED II study. Radiology. 2008;246(3):941–6.
25. Wiener RS, Schwartz LM, Woloshin S. Time trends in pulmonary embolism in the United States: evidence of overdiagnosis. Arch Intern Med. 2011;171(9):831–7.
26. Costello P, Gupta KB. Pulmonary embolism: imaging modalities--V/Q scan, spiral (helical) CT, and MRI. Semin Vasc Med. 2001;1(2):155–64.
27. Stein PD, et al. Gadolinium-enhanced magnetic resonance angiography for pulmonary embolism: a multicenter prospective study (PIOPED III). Ann Intern Med. 2010;152(7):434–43, w142–3.
28. Sosland RP, Gupta K. Images in cardiovascular medicine: McConnell's Sign. Circulation. 2008;118(15):e517–8.
29. Fields JM, et al. Transthoracic echocardiography for diagnosing pulmonary embolism: a systematic review and meta-analysis. J Am Soc Echocardiogr. 2017;30(7):714–723.e4.
30. Sista AK, et al. Stratification, imaging, and management of acute massive and submassive pulmonary embolism. Radiology. 2017;284(1):5–24.
31. Barritt DW, Jordan SC. Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. Lancet. 1960;1(7138):1309–12.
32. Kabrhel C, et al. A multidisciplinary pulmonary embolism response team. Chest. 2013;144(5):1738–9.
33. Kabrhel C, et al. A multidisciplinary pulmonary embolism response team: initial 30-month experience with a novel approach to delivery of care to patients with submassive and massive pulmonary embolism. Chest. 2016;150(2):384–93.
34. Wan S, et al. Thrombolysis compared with heparin for the initial treatment of pulmonary embolism: a meta-analysis of the randomized controlled trials. Circulation. 2004;110(6):744–9.
35. Meyer G, et al. Fibrinolysis for patients with intermediate-risk pulmonary embolism. N Engl J Med. 2014;370(15):1402–11.
36. Dudzinski DM, Piazza G. Multidisciplinary pulmonary embolism response teams. Circulation. 2016;133(1):98–103.
37. Haut ER, et al. The effectiveness of prophylactic inferior vena cava filters in trauma patients: a systematic review and meta-analysis. JAMA Surg. 2014;149(2):194–202.

38. PREPIC Study Group. Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. Circulation. 2005;112(3):416–22.
39. Jerjes-Sanchez C, et al. Streptokinase and heparin versus heparin alone in massive pulmonary embolism: a randomized controlled trial. J Thromb Thrombolysis. 1995;2(3):227–9.
40. Sharifi M, et al. Moderate pulmonary embolism treated with thrombolysis (from the "MOPETT" trial). Am J Cardiol. 2013;111(2):273–7.
41. Nassiri N, et al. Massive and submassive pulmonary embolism: experience with an algorithm for catheter-directed mechanical thrombectomy. Ann Vasc Surg. 2012;26(1):18–24.
42. Eid-Lidt G, et al. Combined clot fragmentation and aspiration in patients with acute pulmonary embolism. Chest. 2008;134(1):54–60.
43. Kucher N, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. Circulation. 2014;129(4):479–86.
44. Piazza G, 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(10):1382–92.
45. Keeling WB, et al. Midterm benefits of surgical pulmonary embolectomy for acute pulmonary embolus on right ventricular function. J Thorac Cardiovasc Surg. 2016;152(3):872–8.
46. Osborne ZJ, et al. Surgical pulmonary embolectomy in a community hospital. Am J Surg. 2014;207(3):337–41; discussion 340–1.
47. Bloomfield P, Boon NA, de Bono DP. Indications for pulmonary embolectomy. Lancet. 1988;2(8606):329.
48. Lee T, 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. 2018;155(3):1084–90.e12.
49. Neely RC, et al. Surgical embolectomy for acute massive and submassive pulmonary embolism in a series of 115 patients. Ann Thorac Surg. 2015;100(4):1245–51; discussion 1251–2.
50. Dalen JE, Alpert JS. Natural history of pulmonary embolism. Prog Cardiovasc Dis. 1975;17(4):259–70.

51. ten Wolde M, et al. Prognostic value of echocardiographically assessed right ventricular dysfunction in patients with pulmonary embolism. Arch Intern Med. 2004;164(15):1685–9.
52. Masotti L, et al. Prognostic stratification of acute pulmonary embolism: focus on clinical aspects, imaging, and biomarkers. Vasc Health Risk Manag. 2009;5(4):567–75.
53. den Exter PL, et al. Risk profile and clinical outcome of symptomatic subsegmental acute pulmonary embolism. Blood. 2013;122(7):1144–9; quiz 1329.