CARDIOLOGY/REVIEW ARTICLE

Pulmonary Hypertension and Right Ventricular Failure in Emergency Medicine

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Pulmonary hypertension is a hemodynamic condition, defined as a mean pulmonary artery pressure by right-sided heart catheterization of at least 25 mm Hg at rest. It is classified into 5 general groups based on the underlying cause, with left ventricular failure and chronic obstructive pulmonary disease being 2 of the most common causes in the United States. Although the specifics of the pathophysiology will vary with the cause, appreciating the risks of pulmonary hypertension and right ventricular failure is critical to appropriately evaluating and resuscitating pulmonary hypertension patients in the emergency department (ED). Patients may present to the ED with complaints related to pulmonary hypertension or unrelated ones, but this condition will affect all aspects of care. Exertional dyspnea is the most common symptom attributable to pulmonary hypertension, but the latter should be considered in any ED patient with unexplained dyspnea on exertion, syncope, or signs of right ventricular dysfunction. Patients with right ventricular failure are often volume overloaded, and careful volume management is imperative, especially in the setting of hypotension. Vasopressors and inotropes, rather than fluid boluses, are often required in shock to augment cardiac output and reduce the risk of exacerbating right ventricular ischemia. Intubation should be avoided if possible, although hypoxemia and hypercapnia may also worsen right-sided heart function. Emergency physicians should appreciate the role of pulmonary vasodilators in the treatment of pulmonary arterial hypertension and recognize that patients receiving these medications may rapidly develop right ventricular failure and even death without these therapies. Patients may require interventions not readily available in the ED, such as a pulmonary artery catheter, inhaled pulmonary vasodilators, and mechanical support with a right ventricular assist device or extracorporeal membrane oxygenation. Therefore, early consultation with a pulmonary hypertension specialist and transfer to a tertiary care center with invasive monitoring and mechanical support capabilities is advised. [Ann Emerg Med. 2015;■:1-10.]

INTRODUCTION

During the last 30 years, physicians have been increasingly recognizing the risks of pulmonary hypertension and right ventricular failure, with an increasing focus on pulmonary hypertension research and clinical considerations.[1] Quantifying the burden of pulmonary hypertension is difficult because it is a heterogeneous condition, with demographics varying according to the underlying cause. The most common cause of pulmonary hypertension in the United States is left-sided heart failure, but many cases of pulmonary hypertension remain undocumented.[2] Pulmonary arterial hypertension, a distinct category of pulmonary hypertension described below, is a relatively rare disease, with estimates of 5 to 15 cases per 1 million adults,[3] although a recent study estimates more than 64,400 ED visits for it in the United States in a 5-year period.[4] There are few studies of assessment or treatment of pulmonary hypertension or right ventricular failure in the emergency department (ED), with only a few case reports[5,6] and observational studies,[7-9] but no randomized controlled trials, to our knowledge.

Although dyspnea is one of the most common chief complaints in the ED,[10] pulmonary hypertension has not traditionally been considered on the differential diagnosis.[8] Numerous high-quality studies,[11-13] reviews,[14-16] and clinical policies[17,18] have been developed for assessment and management of the patient with acute decompensated heart failure in the ED, but these primarily focus on the left side of the heart. This article will emphasize the importance of the right ventricle and describe the unique pathophysiology and treatment of pulmonary hypertension and right ventricular failure in patients presenting to the ED.

The pulmonary circulation is a low-pressure, low-resistance system, with thin-walled vessels and a large reserve of unperfused vessels. The right ventricle is typically a thin-walled structure[19] and can accommodate large changes in volume, or preload, but acutely has a limited contractile reserve to tackle increased impedance to ejection, or afterload.[20] The time course and degree of pulmonary vascular resistance affect the clinical severity of pulmonary hypertension.[21] Increased pressure in the pulmonary system will decrease right ventricular stroke volume and right ventricular output and will increase right ventricular volume (Figure 1). When the right ventricle is overloaded, the interventricular septum may bulge into the left ventricle (LV),
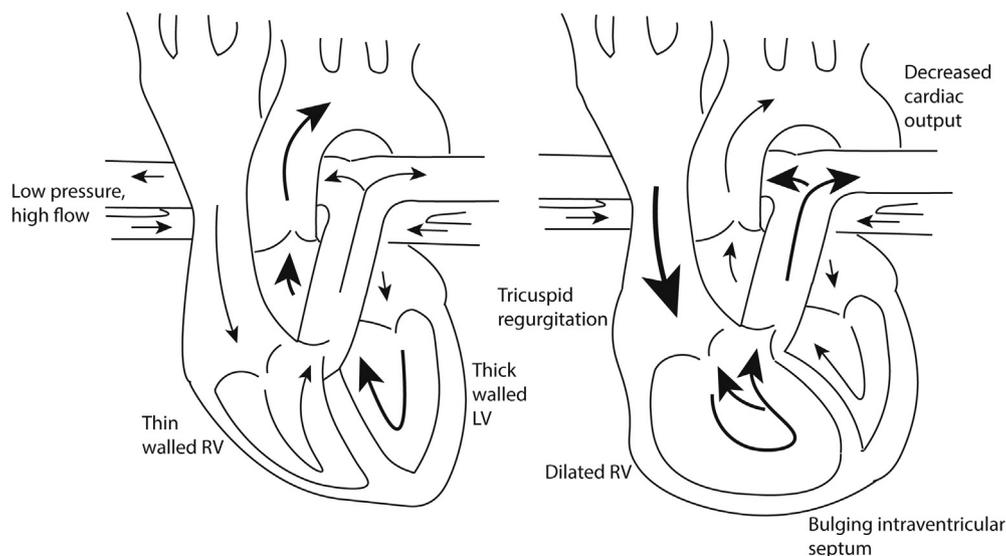
Figure 1. Normal circulation (left) and changes in pulmonary hypertension (right). *RV*, Right ventricular.

leading to decreased LV filling and decreased cardiac output,[1,19,22] a relationship known as "interventricular dependence."[23] Moreover, elevated pressure and volume leading to right ventricular dilatation may increase tricuspid regurgitation,[24] further reducing cardiac output and decreasing end-organ perfusion.[25]

Normal mean pulmonary artery pressure is approximately 15 mm Hg,[1,26] and pulmonary hypertension is defined as a mean pulmonary artery pressure, measured by right-sided heart catheterization, of at least 25 mm Hg at rest.[22,27] By echocardiography, a right ventricular systolic pressure of more than 35 mm Hg suggests pulmonary hypertension, although confirmation requires invasive measurement.

The right ventricle can fail in both acute and chronic pulmonary hypertension. In patients with chronic pulmonary hypertension, pulmonary vascular resistance increases gradually, allowing the right ventricle to progressively compensate.[1,28] Normally, right ventricular ejection fraction depends on right ventricular preload and wall tension increases by the Frank-Starling mechanism. However, beyond a certain point of myocardial distention, ventricular function will fail, with a reduced cardiac output and an elevation in right ventricular filling pressure.[29,30]

Appreciating coronary blood flow is also crucial to understanding the risk of pulmonary hypertension. Unlike the LV, which is fed by the coronaries during diastole, the right ventricle is perfused during both diastole and systole because of low right ventricular wall tension. In pulmonary hypertension, right ventricular perfusion by the coronary arteries decreases in proportion to increases in right ventricular pressure. If the pulmonary artery pressure surpasses the systemic pressures, the right ventricle cannot

be well perfused and will become ischemic,[21,24] further diminishing right ventricular contractility and worsening right ventricular overload, beginning a catastrophic spiral (Figure 2). Because these patients have little physiologic reserve, any superimposed illness, hypo- or hypervolemia, tachyarrhythmias, or changes in oxygenation or ventilation may upset their homeostatic balance, precipitating acute on chronic right ventricular failure.[31,32]

Pulmonary hypertension is divided into 5 classifications, World Health Organization (WHO) groups 1 to 5, based on underlying cause.[33] Recognizing the various origins of pulmonary hypertension is important in the ED because not all patients with pulmonary hypertension are treated in the same manner (Table 1). However, an individual may have multiple factors contributing to development of pulmonary hypertension.

Pulmonary arterial hypertension is a group of diseases characterized by vascular remodeling of the small pulmonary arteries, with abnormal proliferation of the vascular smooth muscle and endothelial cells, inflammation, and fibrosis,[34] and is a progressive and fatal disease if untreated. It is idiopathic, formerly known as "primary pulmonary hypertension" or associated with other disease states, including connective tissue diseases, drug or toxin exposures,[3] and others.[13,34] Specific medical therapies for pulmonary hypertension are approved only for patients with group 1 disease, although pulmonary hypertension specialists may prescribe these medications for other patients as well.

Group 2 pulmonary hypertension is based on left-sided heart disease, including heart failure with preserved or reduced ejection fraction and valvular heart disease. Elevated pulmonary venous pressures will lead to concomitant
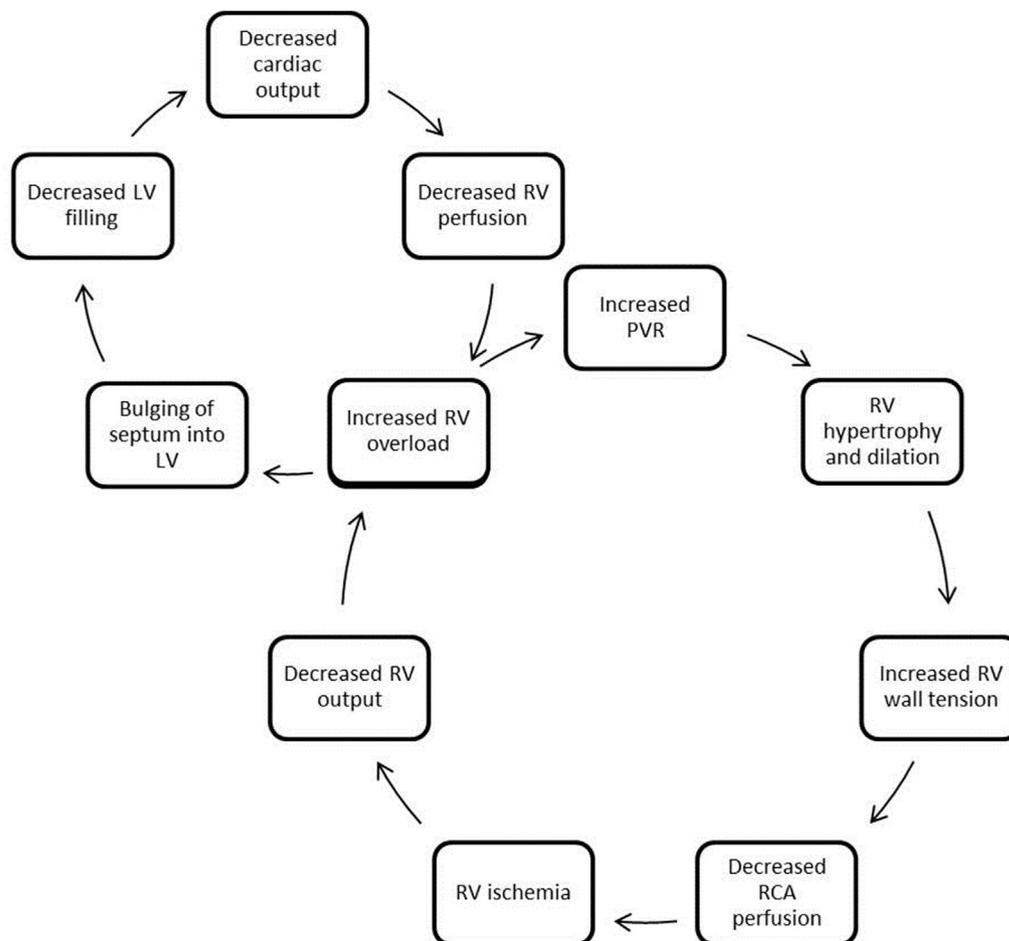
Figure 2. Pathophysiologic mechanisms in right-sided heart failure. *PVR*, Pulmonary vascular resistance; *RCA*, right coronary artery.

Table 1. Revised WHO groups for pulmonary hypertension.

Group	Examples
Group 1: pulmonary arterial hypertension	Familial, idiopathic PAH, HIV, drug induced, congenital heart disease
	Must exclude other secondary causes of PH to diagnose PAH
Group 2: pulmonary hypertension caused by left-sided heart disease	Chronic LV failure, severe mitral valve disease, severe aortic valve disease
Group 3: pulmonary hypertension caused by lung disease or hypoxemia	COPD, OSA, obesity hypoventilation syndrome
Group 4: pulmonary hypertension from chronic thromboembolic or embolic disease	Previous PE, especially recurrent PEs, large PEs, extremes of age, or PH at diagnosis of PE
	Up to 30% of patients may not have had a previous PE
Group 5: miscellaneous	Mediastinal tumors or adenopathy, sarcoidosis, hemodialysis, thyroid disorders, vasculitis

PAH, Pulmonary arterial hypertension; *PH*, pulmonary hypertension; *LV*, left ventricular; *COPD*, chronic obstructive pulmonary disease; *OSA*, obstructive sleep apnea; *PE*, pulmonary embolus.

elevations in pulmonary arterial pressure. There is no specific treatment for group 2 disease because the focus of care is to treat the underlying left-sided heart failure. Treatment often relies heavily on diuretics to manage volume overload, systemic afterload reduction, and treating reversible causes of left-sided heart disease.[35]

Group 3 pulmonary hypertension is that caused by lung disease or hypoxemia. Hypoxemia is one of the major determinants of pulmonary hypertension.[28,36] When faced with inadequate oxygenation, pulmonary arterioles constrict in a process known as hypoxic pulmonary vasoconstriction, which, along with destruction of lung parenchyma with loss of pulmonary vascular beds (as in chronic obstructive pulmonary disease), can lead to pulmonary hypertension.[37] Although chronic obstructive pulmonary disease is the most common cause of chronic pulmonary hypertension in North America,[37] obstructive sleep apnea is also increasingly common.[38-40]

Group 4 is chronic thromboembolism pulmonary hypertension. In most patients, pulmonary emboli resolve in 6 to 12 months; however, between 0.6% and 7.0% of

patients with acute pulmonary emboli develop chronic thromboembolism pulmonary hypertension.[41] The mainstay treatment for it is surgical pulmonary endarterectomy, and the most critical step in treatment is assessment for operable disease by a team specializing in chronic thromboembolism pulmonary hypertension.[42] Pulmonary arterial hypertension–targeted medical therapy may have a role in the treatment of select patients with chronic thromboembolism pulmonary hypertension but is not a replacement for pulmonary endarterectomy.

Group 5 pulmonary hypertension is that with unclear multifactorial mechanisms and includes patients with hematologic disorders, pulmonary Langerhans cell histiocytosis, neurofibromatosis, glycogen storage diseases, thyroid disorders, obstruction from masses in the mediastinum, and many other causes. These patients will have varied presentations, according to the underlying cause of disease.

Patients may present to the ED with complaints directly attributable to pulmonary hypertension, complaints related to the condition underlying their pulmonary hypertension, such as an acute exacerbation of chronic obstructive pulmonary disease, or unrelated complaints from a concurrent illness or injury. Exertional dyspnea is the most common symptom attributable to pulmonary hypertension.[3,5] Patients may also complain of chest pain from demand ischemia because of impaired coronary perfusion to the right ventricle. As right ventricular failure progresses, cardiac output becomes fixed and eventually decreases, and patients may present with exertional syncope or presyncope.[3]

Although the physical examination result may be normal or near normal in the early stages of disease,[5] progression will lead to classic signs of right ventricular failure. Depending on the cause of pulmonary hypertension, patients may initially have normal pulse oximetry values, but may desaturate with ambulation later in the course of the disease.[3]

Pulmonary hypertension should be considered in any ED patient with unexplained dyspnea on exertion, syncope, or signs of right ventricular dysfunction.[27] Patients with a history of pulmonary emboli who present with dyspnea and no explanation on ED testing should be considered at risk for chronic thromboembolism pulmonary hypertension. Despite increasing awareness, there is often considerable delay between onset of symptoms and diagnosis. In 2011, an analysis of a pulmonary arterial hypertension database found that 21% of patients had symptoms for greater than 2 years before diagnosis,[43] and the majority of patients received a diagnosis in late stages of the disease. Delayed diagnosis is correlated with poorer survival,[44] and identifying patients with pulmonary arterial hypertension earlier allows targeted therapies to be initiated before the development of significant

right-sided heart failure.[27] Therefore, the emergency physician may improve a patient's prognosis by considering pulmonary hypertension and referring the patient for timely follow-up.

Pulmonary hypertension is not usually diagnosed in the ED because right-sided heart catheterization is needed for definitive diagnosis. However, pulmonary hypertension should be suspected in patients with predisposing conditions, such as chronic obstructive pulmonary disease, left-sided heart failure, or connective tissue diseases such as scleroderma.[45] In these patients, records should be reviewed for previous echocardiographic or right-sided heart catheterization data to confirm and quantify the magnitude of pulmonary hypertension.

Most laboratory values, ECG findings, and chest radiograph findings are nonspecific in pulmonary hypertension. However, one of the few studies of right ventricular failure in the ED demonstrated that in patients presenting to the ED with dyspnea, elevated N-terminal pro brain natriuretic peptide (BNP) levels correlate with echocardiography and provide prognostic information.[9] Specifically, right ventricular failure with an N-terminal proBNP level greater than 1,500 pg/mL is associated with decreased survival. In contrast, N-terminal proBNP levels of less than 300 pg/mL are associated with a very low risk for mortality or clinically significant echocardiographic abnormalities.[9] Emergency physicians should recall that isolated right ventricular failure, even when severe, will not demonstrate pulmonary edema by chest radiograph.

Chest computed tomography (CT) may demonstrate evidence of pulmonary hypertension.[5] Pulmonary artery dilatation on CT correlates well with pulmonary artery pressure,[46,47] and CT scans can evaluate right ventricular size and detect interventricular septal bowing.[47,48] Enlargement of the right ventricle to greater than nine tenths of the size of the LV by CT scan correlates with an increased risk of adverse events[49] and death in patients with acute pulmonary emboli.[50] CT imaging can also assess for an underlying cause or precipitant of right ventricular failure with findings such as a pulmonary emboli, pneumonia, or ground-glass opacities consistent with chronic pulmonary edema.[3]

Although right-sided heart catheterization is required to establish a definitive diagnosis, transthoracic echocardiography is an important noninvasive screening tool to assess for the possibility of pulmonary hypertension.[5,6] In the ED, bedside cardiac ultrasonography may be used to evaluate for right ventricular enlargement, defined as the right ventricle's being greater than two thirds the size of the LV on the apical 4-chamber view.[51] The parasternal short axis view may visualize flattening of the interventricular septum, which is identified by a D-shaped LV.[51]

In addition to bedside ultrasonography, conducting a formal echocardiogram is important. It can detect elevated pulmonary artery pressures from Doppler flow across the tricuspid valve and detail abnormalities of the interventricular septum, including septal bowing into the LV and paradoxic movement of the septum into the LV during systole. Later stages of pulmonary hypertension may lead to findings of severe tricuspid regurgitation, right ventricular hypertrophy, and right ventricular hypokinesis.

Several studies have shown that echocardiograms for patients with unexplained dyspnea uncover a high rate of pulmonary hypertension and right ventricular dysfunction.[8] In a secondary analysis of the Pulmonary Embolism Rule Out Criteria database, Russell et al[8] found that 19% of patients with a CT scan negative for any acute process but with persistent dyspnea in the ED had an echocardiogram result with right ventricular dysfunction or overload. In the proBNP in the Investigation of Dyspnoea in the Emergency Department (PRIDE) study, ED patients with unexplained dyspnea had a 30% prevalence of right ventricular dysfunction by echocardiogram.[9] These studies support prompt referral for echocardiogram as an appropriate step for patients with unexplained dyspnea in the ED.[8]

Patients with pulmonary hypertension who present to the ED with acute cardiopulmonary decompensation or any severe systemic illness (eg, sepsis) have complicated physiology and are challenging to resuscitate. Understanding the cause of pulmonary hypertension is important for planning resuscitation because treating the underlying cause is often the priority. Although patients may have pain or anxiety, use of narcotics and sedatives must be judicious to avoid respiratory depression and hypoventilation. Patients being treated with pulmonary vasodilators for pulmonary arterial hypertension must continue to receive these medications because withdrawal can precipitate a pulmonary hypertension crisis and death[32] (Table 2).

Appreciating the volume status of any critically ill patient can be challenging, but that of patients with pulmonary hypertension can be especially difficult to assess and manage. The goal is to optimize preload of the right ventricle to maximize perfusion while taking care to not overload it and decrease output.[24] In the majority of cases, right ventricular failure is associated with excessive preload.[31] Therefore, further volume resuscitation may paradoxically lead to both increased right ventricular wall stress and reduction in left ventricular filling because of interventricular dependence, whereas reduction in right ventricular volume with diuresis may improve cardiac output.[52] However, if the patient is not fluid overloaded, or is diuresed too extensively, diuresis may decrease an already low cardiac output.[30] The physical examination in patients with pulmonary hypertension is

Table 2. Right ventricular failure management considerations.

PH Group	ED Management
RV failure in PAH (group 1)	Continue/resume pulmonary vasodilator regimen, especially in cases of pump malfunction
	Early consultation with PH specialist
	If PH specialist not available, consider emergency cardiology or pulmonary consultation
	Consider risks of volume overload (no large-volume boluses)
	Provide hemodynamic support with inotropes, vasopressors, pulmonary vasodilators as indicated
	Consider early referral for mechanical support, including RVAD or ECMO
RV failure in other types of PH (groups 2–5)	Aggressively treat underlying condition, such as diuresis for PH from left-sided heart failure or bronchodilators for PH from COPD
	Correct hypoxemia and respiratory acidosis
	Consider ionotropic support as indicated, with norepinephrine as a first-line agent
	Early consultation with cardiologist, pulmonologist, or PH specialist
	For patients with CTEPH, provide emergency referral to a center with expertise in pulmonary endarterectomy
	Consider early referral for mechanical support with RVAD or ECMO

PAH, Pulmonary arterial hypertension; *RVAD*, right ventricular assist device; *ECMO*, extracorporeal membrane oxygenation; *CTEPH*, chronic thromboembolism pulmonary hypertension.

often unreliable for determining volume status. Because of tricuspid regurgitation and chronically elevated right-sided pressures, central venous pressure is not an accurate indicator of LV preload in patients with pulmonary hypertension.[32] However, following trends in central venous pressure is useful,[31] and therefore early placement of a central venous line should be considered.

In the setting of clear evidence of volume loss, clinicians should use low-volume boluses, such as 250 mL of normal saline solution, with repeated reassessment of the effects on blood pressure, urine output, and lactate to reduce the risk of precipitating or worsening volume overload.[31] Expedited transfer of the patient to an ICU or cardiac catheterization laboratory for placement of a pulmonary artery catheter may be beneficial.[29,30,32] Although the use of pulmonary artery catheters in heterogeneous populations of critically ill patients has not improved outcomes,[53,54] pulmonary artery catheters are the most reliable method to diagnose right ventricular failure and manage fluid balance in the ICU.[30,55]

Systemic hypotension should be avoided. The cardiac output in most patients with advanced pulmonary hypertension cannot be augmented because of "fixed" pulmonary vascular resistance. Therefore, any reduction in systemic vascular resistance (SVR) will not be followed by a

compensatory increase in cardiac output, thus magnifying the degree of hypotension. In addition, as described above, as right ventricular pressures approach systemic arterial pressures, right coronary perfusion will decrease. Augmenting aortic root pressure with vasopressors can thus prevent right ventricular ischemia. The ideal hemodynamic medication would augment cardiac output, maintain SVR, decrease pulmonary vascular resistance, and not increase tachycardia or dysrhythmias.[31] Unfortunately, no sole agent exists to achieve these goals. All vasopressors and inotropes have multiple effects on the hemodynamic status, and agents should be selected with an appreciation for their effects.[29] Following the trends of the systemic blood pressure, central venous pressure, urine output, lactate level, and oxygen saturation are crucial in evaluating a patient's response to each intervention.[31]

Norepinephrine offers several advantages in the emergency care of these patients. It is of proven benefit in several types of shock, especially septic shock.[56-58] It helps maintain coronary perfusion pressure and slightly augment inotropy. On balance, especially if a component of distributive shock is suspected, norepinephrine is an appropriate first-line vasopressor despite potential increases in pulmonary vascular resistance from α-stimulation.[29,59] Phenylephrine should be avoided in patients with pulmonary hypertension[60] because of increases of the pulmonary vascular resistance,[29,59,60] whereas vasopressin may actually decrease pulmonary vascular resistance through a nitric oxide–based mechanism.[61] Although dobutamine increases cardiac output, it has 2 major disadvantages of increased tachycardia[30] and decreased SVR, limiting its use as a single agent because of the risk of systemic hypotension.[29]

Patients with pulmonary hypertension or right ventricular dysfunction generally do not tolerate arrhythmias well because they depend on atrial contractions and adequate filling time to maintain cardiac output.[62,63] In general, β-blockers and calcium channel blockers should be avoided in patients with pulmonary arterial hypertension or those with other groups of pulmonary hypertension with frank right ventricular failure because they may further impair right ventricular function. Electrocardioversion of new-onset atrial fibrillation should be strongly considered.[30]

Recalling that the pathophysiologic mechanism in pulmonary arterial hypertension is abnormal proliferation of the pulmonary vascular smooth muscle and endothelial cells, inflammation, and fibrosis, pulmonary vasodilators are approved for treatment of this condition. Vasodilators are not beneficial in all pulmonary hypertension because patients with pulmonary hypertension from LV dysfunction may have worsening pulmonary edema if pulmonary arteries are dilatated, and patients with pulmonary hypertension from lung disease or hypoxemia may have worsening ventilation-perfusion matching with systemic vasodilators. Therefore, pulmonary hypertension specialists typically use these medications for patients in group 1, and possibly groups 4 and 5. There are 2 types of pulmonary vasodilators, with one being oral and intravenous medications with selective effects on the pulmonary vasculature, and the other being inhaled agents that are delivered directly to the lungs. As opposed to intravenous delivery, which causes nonspecific dilatation of pulmonary beds with variable ventilation-perfusion matching, inhalation of vasodilators may improve ventilation-perfusion mismatch by directing blood flow to ventilated areas of the lung.[24] Emergency physicians should be aware of the pharmacology of medications used in their patients with pulmonary hypertension and understand options for emergency use in severe right ventricular failure (Table 3). Inhaled nitric oxide promotes vascular smooth muscle relaxation. Effects are limited to ventilated areas of the lung, thereby improving ventilation-perfusion matching while decreasing pulmonary artery pressure and pulmonary vascular resistance.[55,64,65] Prostacyclins result in pulmonary vasodilation, with subsequent decreases in pulmonary artery pressure and pulmonary vascular resistance. Epoprostenol is one of the most commonly used prostacyclins and is administered intravenously or by inhalation, although to our knowledge there are no prospective studies on critically ill patients with acute right ventricular failure.[55] Endothelin receptor antagonists block endothelin's vasoconstrictive, proliferative, and proinflammatory effects, thereby increasing cardiac output and decreasing pulmonary artery pressure.[55] Phosphodiesterase-5 inhibitors, such as sildenafil and tadalafil, block degradation of cyclic guanosine monophosphate, decreasing pulmonary artery pressure and increasing cardiac output in pulmonary hypertension. These medications are commonly used in outpatient treatment of pulmonary arterial hypertension.

Established pulmonary arterial hypertension therapies should be continued in the ED and inpatient settings to prevent rebound pulmonary hypertension. If the patient has been prescribed an oral medication but is unable to receive it, starting an inhaled or intravenous therapy should be considered in consultation with a pulmonary hypertension specialist.[66]

Given the multiple risks of sedation, vasodilation, and increasing intrathoracic pressure, every attempt should be made to avoid intubation of patients with right ventricular failure, keeping in mind the hemodynamic risks of worsening hypoxemia, hypercarbia, and metabolic acidosis. Acute, sometimes fatal hemodynamic collapse is a well-recognized complication of intubation in these patients,

Table 3. Pulmonary vasodilators and emergency considerations.

Class of Medication	Delivery	Mechanism of Action	Emergency Considerations
iNO	Inhalation	Relaxes vascular smooth muscle Inhibits platelet aggregation	Not used as a long-term therapy in PAH May be used in severe RV failure, massive pulmonary embolism Will decrease PVR; minimal effects on SVR Will improve V/Q mismatch

Prostacyclins
  Epoprostenol
    (Flolan, Veletri)
  Treprostinil
  Iloprost
	Intravenous, inhalation
	Intravenous, inhaled, subcutaneous
	Inhaled
		Relaxes vascular smooth muscle	Intravenous formulations may be used as long-term therapy in PAH
			Sudden withdrawal can lead to rebound PH
			May be used instead of iNO for severe RV failure
			Will decrease both SVR and PVR if given intravenously
			Will decrease only PVR if inhaled
			Will worsen V/Q mismatch if given intravenously; will improve V/Q mismatch if inhaled

Endothelin
    receptor antagonists
  Bosentan
  Macitentan
  Ambrisentan
	Oral	Inhibits the vasoconstrictive properties of endothelin	Used as long-term therapy in PAH
			Minimal emergency use
			Patients should continue to receive this medication unless changes prescribed by PH specialist

PDE-5 inhibitors, sildenafil, tadalafil	Oral, intravenous (sildenafil)	Block degradation of cyclic guanosine monophosphate to allow vascular smooth muscle relaxation	Used as long-term therapy in PAH Minimal emergency use Patients should continue to receive this medication unless changes prescribed by PH specialist

iNO, Inhaled nitric oxide; *V/Q,* ventilation-perfusion; *PDE,* phosphodiesterase.

probably because of a combination of factors, including decreased venous return and sedation-induced decrease in SVR. Positive-pressure ventilation will decrease preload but will also increase right ventricular afterload, thereby worsening systemic hypotension.[30,31] If a patient in the ED has respiratory failure, noninvasive ventilation with continuous positive airway pressure or bilevel positive airway pressure may be cautiously initiated because it can be removed if the patient begins to deteriorate. Although continuous positive airway pressure is a well-established treatment for patients with obstructive sleep apnea and pulmonary hypertension,[38] and bilevel positive airway pressure has demonstrated excellent outcomes in chronic obstructive pulmonary disease and congestive heart failure, noninvasive ventilation has not been studied in pulmonary hypertension patients in distress, to our knowledge.

If intubation and mechanical ventilation are unavoidable, hypotension and loss of right ventricular contractility must be prevented. Emergency physicians should be aware of and prepared for profound hemodynamic alterations that can occur with rapid sequence intubation in a patient with right ventricular failure.[31] Therefore, guidelines for mechanical ventilation settings in patients with pulmonary hypertension generally parallel those for acute respiratory distress syndrome, with a goal of low tidal volumes and low plateau pressures, although minimal positive end expiratory pressure should be used. An additional important exception is that these patients cannot tolerate permissive hypercarbia and

hypoxia because both can contribute to pulmonary vasoconstriction.[22,31,55]

Some patients with pulmonary arterial hypertension receive continuous infusions of epoprostenol or the long-acting prostanoid, treprostinil, through continuous intravenous infusion, requiring a central venous catheter and portable infusion pump.[67] Because abrupt discontinuation of the infusion may lead to rebound pulmonary hypertension, acute right ventricular failure, and death, a delivery system malfunction should be considered a life-threatening emergency by the triage staff and emergency physicians.[34,67] If a patient presents to the ED with malfunction of an infusion system, an intravenous line should be placed immediately and the pump reinitiated while the patient's pulmonary hypertension specialist is called for further guidance. Under no circumstances should a long-term prostanoid infusion be interrupted. If the patient presents with catheter occlusion or pump malfunction, the infusion should be reinitiated acutely through a peripheral intravenous catheter.

Patients may occasionally present to the ED with adverse effects from pulmonary vasodilators. Because of the associated systemic vasodilation, some patients develop flushing, headache, diarrhea, jaw discomfort with eating, and foot pain. If a patient presents to the ED with these adverse effects, the pulmonary hypertension specialist prescribing the medication should be contacted. Again, the medication must not be stopped or dose decreased by the emergency team.

In some cases, patients may be refractory to appropriate volume management, vasopressors or inotropes, and pulmonary vasodilators. In these cases, they should be referred for emergency consideration of a right ventricular assist device or extracorporeal membrane oxygenation. Inhaled nitric oxide drains blood from the vena cava or right atrium and returns it to the pulmonary artery, thus unburdening the failing right ventricle.[24] Venoarterial extracorporeal membrane oxygenation drains deoxygenated blood from the venous circulation and returns oxygenated blood to the arterial circulation. Venoarterial extracorporeal membrane oxygenation can thus provide biventricular cardiac support, as well as respiratory support. For this reason, it would seem to be the preferred mechanical support for patients with right ventricular failure in the setting of pulmonary hypertension or acute pulmonary emboli.[24] These options are offered only at select centers, so ED transfer may be necessary.

The majority of patients who present to the ED with an exacerbation of pulmonary hypertension will require inpatient admission,[4] and patients with right ventricular failure should be admitted to an ICU. Syncope in pulmonary hypertension, especially pulmonary arterial hypertension, is very concerning and requires inpatient admission and evaluation.[63]

In some circumstances, patients will present to the ED with increasing dyspnea on exertion but may have reassuring evaluation results. An important test to check before discharge is a walking oxygen saturation.[3] If patients are able to ambulate in the ED without desaturating and meet no other criteria for inpatient admission, they may be discharged to follow-up as outpatients. However, given the prevalence of undiagnosed pulmonary hypertension, the patient with no other demonstrated cause of dyspnea should be referred for prompt outpatient echocardiogram, along with timely follow-up.

Few studies have assessed the outcomes of patients who present to the ED with pulmonary hypertension. Patients with pulmonary arterial hypertension are at high risk of sudden cardiac death,[63,68] and cardiopulmonary resuscitation remains largely unsuccessful in patients with pulmonary arterial hypertension and right ventricular failure.[30] In a survey of 3,130 pulmonary arterial hypertension patients from 1997 to 2000, resuscitation after cardiac arrest was unsuccessful in 79% of patients, and only 6% survived for longer than 3 months.[62] However, there may not be sufficient time to discuss prognosis when a patient presents in extremis, and patient and family preferences should always be considered.

Pulmonary hypertension is a hemodynamic condition, classified into 5 general groups based on the underlying cause, with left ventricular failure and chronic obstructive pulmonary disease being 2 of the most common causes in the United States. Emergency physicians should consider undiagnosed pulmonary hypertension in dyspneic patients with otherwise negative evaluation results and refer them for early echocardiograms. Patients with right ventricular failure are often volume overloaded, and close volume management is imperative. Vasopressors and inotropes can augment cardiac output and reduce the risk of exacerbating right ventricular ischemia. Intubation should be avoided if possible, with care taken to also avoid hypoxemia and hypercapnia. Patients receiving pulmonary vasodilators cannot miss receiving them because this may precipitate rebound pulmonary hypertension. Patients may require interventions not readily available in the ED, such as a pulmonary artery catheter placement, inhaled pulmonary vasodilators, and mechanical support with inhaled nitric oxide or extracorporeal membrane oxygenation. Therefore, early transfer to a tertiary care center with pulmonary hypertension specialists is advised. Regardless, prompt consultation with a pulmonary hypertension specialist is always appropriate for ED patients with pulmonary hypertension.

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Editor's Capsule Summary Pulmonary hypertension is a hemodynamic condition, defined as a mean pulmonary artery pressure by right-sided heart catheterization of at least 25 mm Hg at rest. Pulmonary hypertension is classified into 5 general groups based on the underlying cause, with left ventricular failure and chronic obstructive pulmonary disease being 2 of the most common causes in the United States. Although the specifics of the pathophysiology will vary with the cause, appreciating the risks of pulmonary hypertension and right ventricular failure is critical to appropriately evaluating and resuscitating pulmonary hypertension patients in the emergency department.