Advanced Emergency Nursing Journal
Vol. 40, No. 4, pp. 246–259

CASES OF NOTE

OPEN

Column Editor: Kathleen S. Jordan, DNP, MS, ENP-C, FNP-BC, ENP-BC, SANE-P, FAEN

Pulmonary Arterial Hypertension Emergency Complications and Evaluation

Practical Guide for the Advanced Practice Registered Nurses in the Emergency Department

Robin Hohsfield, BSN, RN
Christine Archer-Chicko, MSN, CRNP
Traci Housten, MS, RN
Stephanie Harris Nolley, BSN, RN

Abstract
Pulmonary hypertension (PH) complicates common diseases and can lead to worsening symptoms and increased mortality. A specific group of PH, pulmonary arterial hypertension (PAH), World Health Organization Group 1, may present to the emergency department (ED). We review common ED

Author Affiliations: *Pulmonary Hypertension Program, University of Colorado Health, Aurora, Colorado (Ms Hohsfield); Pulmonary Vascular Disease Program, University of Pennsylvania Health System, Philadelphia, Pennsylvania (Ms Archer-Chicko); Johns Hopkins Pulmonary Hypertension Program, Johns Hopkins University, Baltimore, Maryland (Ms Housten); and University of Washington, Seattle, Washington (Ms Harris Nolley).*

Actelion Pharmaceuticals US, Inc., provided funding for this article produced by Katie Estes, PhD, of Estes Medical Communications LLC, on behalf of Simcoe Consultants, Inc., and did not contribute to the content nor provide any review or editorial support. The article was written independently by the authors with writing support provided by Katie Estes, PhD, and managed by Donna Simcoe, MS, MS, MBA, CMPP, of Simcoe Consultants, Inc. All statements and opinions expressed in the article are those of the authors and do not reflect those of Actelion Pharmaceuticals US, Inc., or its representatives. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Robin Hohsfield is a member of the speaker bureau and/or advisory board for Actelion Pharmaceuticals Inc., Gilead Sciences Inc., GlaxoSmithKline plc., and United Therapeutics Corporation. Christine Archer-Chicko is a member of advisory boards for Actelion Pharmaceuticals Inc., Bayer Corporation, Gilead Sciences Inc., and United Therapeutics Corporation. Traci Housten is a member of the advisory board for Actelion Pharmaceuticals Inc. and Gilead Sciences Inc. Stephanie Harris Nolley is an advisory board member for Actelion Pharmaceuticals Inc., Bayer Corporation, Gilead Sciences Inc., and United Therapeutics Corporation.

Disclosure: *The authors report no conflicts of interest.*

Corresponding Author: *Robin Hohsfield, BSN, RN, University of Colorado Health, Aurora, CO 80045 (robin.hohsfield@uchealth.org).*

DOI: 10.1097/TME.0000000000000210

presentations of patients with PAH such as cardiac arrest/sudden death, right ventricular failure, syncope, hypoxemic respiratory failure, arrhythmias, hemoptysis, pulmonary embolism, chest pain/left main compression syndrome, infection, and considerations for PAH medication administration. We include a case study to illustrate a real example with a positive outcome, and an algorithm for evaluating and triaging patients with PAH in the ED. The ability to recognize, triage, and communicate changes in PAH disease status in a multidisciplinary team approach between the patient, family, specialty pharmacy, and specialized health care providers such as the PH team, is essential for ED providers who are evaluating and treating patients with PAH. **Key words:** emergency department, pulmonary arterial hypertension, pulmonary hypertension

PULMONARY HYPERTENSION (PH), which is defined by a mean pulmonary artery pressure of 25 mmHg or more at rest as measured by right heart catheterization (Hoeper et al., 2013), often complicates common diseases, and leads to a worsening of symptoms and increased mortality (Hoeper et al., 2016). PH is categorized into five World Health Organization (WHO) groups based on differences in clinical, pathophysiological, and therapeutic characteristics (Galiè et al., 2015; Simonneau et al., 2013). Pulmonary arterial hypertension (PAH), WHO Group 1, is characterized by progressive pathological changes from abnormal proliferation of pulmonary vascular smooth muscle and endothelial cells, perivascular inflammation, and vasoconstriction (Simonneau et al., 2013). These changes occur in the precapillary pulmonary arteries and cause the vessel lumens to narrow, raising the pulmonary vascular resistance (PVR) and the pulmonary artery pressures, which increases workload on the heart (Greyson, 2010). Currently, there are 14 medications with a Food and Drug Administration (FDA)-approved indication for Group 1 PAH that involve the endothelin, nitric oxide, and prostacyclin pathways (see Table 1) (Humbert & Ghofrani, 2016). Treatment options remain expensive, complex, and most are in restricted distribution systems. Although these medical therapies can improve PAH symptoms and improve quality of life, they also have complex dose titrations and side effect profiles that can be challenging to manage or mistaken for other conditions. Current PAH medical treatments may be therapeutic and increase patient survival but are not considered curative. Lung transplantation is the only option for patients who do not respond to medical therapy (McLaughlin et al., 2009).

Right ventricular failure is one of the most common causes of morbidity and mortality in PAH (Delcroix & Naeije, 2010). Chronic elevations in PVR result in right ventricular enlargement, causing the right ventricle (RV) to become overloaded and inefficient, with a decreased right stroke volume and output. Changes in the structure of the RV eventually result in systolic and diastolic dysfunction of both ventricles and an increased risk of dysrhythmias (Greyson, 2010). These changes can lead to right heart failure (RHF), which is discussed in more detail later in this article.

In the United States, the average proportion of PAH patient emergency department (ED) visits was 12.8/100,000 adult visits ($\geq$18 years of age) (Stein, Matta, & Hughes, 2015). Specific guidelines or policies regarding how to triage and treat patients with PAH in the ED are uncommon, and guidelines for the treatment and diagnosis of PAH do not address ED triage (Badesch et al., 2009; Galiè et al., 2015; McLaughlin et al., 2009). Policies for how to treat patients with acute decompensated heart failure in the ED exist, but these focus on left heart failure (Collins et al., 2015; Silvers, Howell, Kosowsky, Rokos, & Jagoda, 2007). A recent review addressed some issues faced by ED physicians when treating patients with PAH in the United Kingdom and Ireland, but some of the treatment guidelines are specific to those health care systems (Price et al., 2017).

Table 1. PAH-specific medications

Target pathway	Drug	Route	Typical dose	Half-life	Available at local vs. specialty pharmacy	Risks of interruption, special considerations	Resources	Pump name	Photo of pump
Nitric oxide	Sildenafil[a] (Revatio, 2014)	Oral	20 mg TID	4 hr	Insurance dependent	All: Do not administer nitrates	Pfizer: 1-800-879-3477		
	Tadalafil (Adcirca, 2009)	Oral	20 or 40 mg daily	35 hr	Insurance dependent	Do not hold doses unless speaking with PH treatment team	Adcirca: 1-800-545-5979		
	Riociguat (Adempas, 2013)[b]	Oral	0.5–2.5 mg TID	12 hr	Specialty	Missed doses of riociguat may require retitration to lower dose. Riociguat requires monthly pregnancy test for females of CBP	Bayer: 1-888-842-2937		
Endothelin	Bosentan (Tracleer, 2003)	Oral	62.5 or 125 mg BID	5 hr	Female: Specialty Male: Insurance dependent	All require monthly pregnancy test for females of CBP. Monitor for signs and symptoms of edema and anemia. Tracleer requires monthly LFTs	Actelion PH Pathways: 1-866-228-3546		
	Ambrisentan (Letairis, 2015)	Oral	5 or 10 mg daily	9 hr	Specialty		Gilead LEAP Program: 1-866-664-5327		
	Macitentan (Opsumit, 2017)	Oral	10 mg daily	16 hr	Specialty		Actelion PH Pathways: 866-228-3546		
Prostacyclin	Selexipag (Uptravi, 2017)	Oral	200-1600 mcg BID	6.2–13.5 hr of the active metabolite	Specialty	Initiation by dose titration	Actelion PH Pathways: 1-866-228-3546		
	Treprostinil (Orenitram, 2014)	Oral	Variable, tablets supplied in 0.125, 0.25, 1, 2.5, and 5 mg per label	4 hr	Specialty		United Therapeutics: 1-877-864-8437		
	Iloprost (Ventavis, 2012)	Inhaled six to nine times daily	2.5 or 5 mcg	20–30 min	Specialty	Must be administered via pump I-neb AAD device	Actelion 1-866-228-3546	I-neb AAD	

(*continues*)

Table 1. PAH-specific medications (*Continued*)

Target pathway	Drug	Route	Typical dose	Half-life	Available at local vs. specialty pharmacy	Risks of interruption, special considerations	Resources	Pump name	Photo of pump
	Treprostinil (Tyvaso, 2009)	Inhaled four times daily	One to nine breaths (6 mcg per breath) in four separate treatments daily, 4 hr apart	4 hr	Specialty	Must be administered via pump Tyvaso Inhalation System device	United Therapeutics: 1-877-864-8437	TD-100®-ir Tyvaso Inhalation System	
	Treprostinil (Remodulin, 2011)	Continuous IV or SQ infusion	Dose is ng\kg\min. Highly variable and patient specific	4 hr	Specialty	For IV prostacyclins: Do not abruptly stop infusions and maintain as dedicated line. Do not push or mix anything without proper protocol (see section *PAH Infusion Medication Compromise*)		CADD-Legacy 1 CRONO *five* CADD MS 3	
	Epoprostenol (Flolan, 2016)	Continuous IV infusion	Dose is ng\kg\min. Highly variable and patient specific	6 min	Specialty		GlaxoSmithKline: 1-888-825-5249	CADD-Legacy 1	
	Epoprostenol (Veletri, 2016)	Continuous IV infusion	Dose is ng\kg\min. Highly variable and patient specific	6 min	Specialty		Actelion: 1-866-228-3546	CADD-Legacy 1	

Note. BID = twice daily; CBP = child bearing potential; CTEPH = chronic thromboembolic pulmonary hypertension; IV = intravenous; PAH = pulmonary arterial hypertension; PH = pulmonary hypertension; LFT = liver function test; SQ = subcutaneous; TID = three times a day.

[a] IV formulation of sildenafil for use when tablets cannot be given. Dose conversion is half the normal oral dose.

[b] FDA approval for both Group 1 PAH and Group 4 CTEPH.

Patients with PAH may present to the ED for a variety of reasons, which may or may not be directly related to their existing PAH diagnosis (Wilcox, Kabrhel, & Channick, 2015). It is critical for ED staff to be aware of the risks associated with the treatment of patients with PAH (Wilcox et al., 2015) and work closely with the PH comprehensive care center to help manage this complex patient population. We have reviewed common ED presentations of patients with PAH in order of severity and highlighted special needs that can impact existing triage practices, including a case study to illustrate the potential complexities of this patient population.

EVALUATING THE CHIEF COMPLAINT

Cardiac Arrest/Sudden Death

The most critically ill patients with PAH are those with advanced hemodynamic compromise, also known as decompensated RHF. Patients may exhibit clinical signs of hypoxemia, dyspnea with minimal activity, fluid overload, and unstable vital signs (Galiè et al., 2015). Patients with PAH are thought to have little cardiac compensatory reserves and may not overcome acute decompensation. Those who develop cardiac arrest or experience sudden death and require cardiopulmonary resuscitation have a poor outcome (Hoeper et al., 2002). Hoeper and colleagues (2002) found that resuscitation was not successful in 79% of cases and only eight patients (6%) lived for 90 days. The most important factors in survival were the ability to identify the cause of the cardiopulmonary arrest and rapidly intervening to correct that problem (Hoeper et al., 2002). Approximately 50% of patients with PAH in this study had cardiopulmonary arrest occur as a result of the underlying PAH disease.

Right Ventricular Failure

Patients with PAH may experience clinical worsening because of an acute harmful event, or simply disease progression, that worsens RV function causing RV distension, impaired RV adaptation, and myocardial oxygen consumption/delivery imbalance (Price et al., 2017). Renal dysfunction (i.e., cardiorenal failure) commonly occurs in patients with PAH because of chronic diuretic therapy used to treat RHF. Patients with PAH and RHF present to the ED with nonspecific symptoms of shortness of breath, lower extremity swelling, and fatigue, which could be signs of clinical decompensation (Allen & O'Connor, 2007).

Syncope

Syncope is the temporary loss of consciousness that has a rapid onset, short duration, and spontaneous recovery, occurring as a result of low cerebral perfusion (Demerouti, Manginas, Athanassopoulos, & Karatasakis, 2013; Wahlrab, 2012). During syncope, patients can fall and injure themselves. In patients with PAH, syncope is a serious event because it indicates low cardiac output, worsening PAH, and is a prognostic marker for increased risk of death (Galiè et al., 2015). Patients with PAH experiencing syncope should be evaluated for disease progression by their PH center emergently and may need right heart catheterization to assess current hemodynamic status.

Hypoxemic Respiratory Failure

Hypoxemia occurs in patients with PAH because of low mixed venous oxygenation in the presence of mildly altered ventilation-perfusion matching and a reduced arterial carbon dioxide level from hyperventilation (Delcroix & Naeije, 2010). Respiratory failure because of hypoxemia is rare and isolated in PAH. It occurs primarily in the presence of congenital heart disease or a right to left cardiac shunt or concomitant interstitial lung disease. Signs of acute hypoxia/hypoxic respiratory failure will prompt evaluation for causes of hypoxia (i.e., shunting from atelectasis, pneumonia, bed rest or pain following a surgical procedure, or compression of lung tissue from a dilated heart) (Delcroix & Naeije, 2010).

When patients with PAH are hypoxemic, increasing the fraction of inspired oxygen to

improve oxygenation should be used as a first line of treatment. Mechanical ventilation with intrinsic positive pressure ventilation reduces cardiac output and places strain on the RV; it is therefore not recommended unless other options are unsuccessful. Initiating heated high-flow oxygen for patients who are hypoxic, with progression to continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) as needed, is preferred over intubation and mechanical ventilation. When mechanical ventilation cannot be avoided, it is recommended to minimize hyperinflation and hypercapnia, which can worsen the PVR (Delcroix & Naeije, 2010).

Arrhythmias

Arrhythmias in patients with PAH require immediate attention, as it can lead to acute decompensation requiring admission or result in sudden death. The underlying mechanisms of arrhythmias in patients with PAH are not well understood (Demerouti et al., 2013). The most common types of arrhythmias are supraventricular tachycardias (SVTs), such as atrial fibrillation or atrial flutter. Ventricular arrhythmias typically occur in patients with PAH who have congenital heart disease. In a study of 231 patients with PAH who were followed up for 6 years, there was an annual risk of 2.8% for both atrial fibrillation and atrial flutter (Tongers et al., 2007). In advanced PAH, increased atrial stretch and myocardial fibrosis may contribute to the development of SVTs (Price et al., 2017). In patients with PAH and congenital heart disease, SVTs are common and often related to previous surgical scars or right atrial dilatation. Atrial arrhythmia is often not well tolerated in advanced disease because of loss of atrial contribution to cardiac output (Demerouti et al., 2013; Goldstein, Harada, Yagi, Barzilai, & Cox, 1990).

For patients with PAH and hemodynamically unstable arrhythmia, prompt attention to reestablish sinus rhythm is essential. Use of direct current cardioversion (DCCV) and postintervention monitoring is important. Adenosine may be used for SVTs involving the AV node before DCCV (Price et al., 2017; Tongers et al., 2007). Sedation or general anesthesia (which also carries risk for patients with PAH) may be required for DCCV and would be performed by experienced cardiac anesthesia specialists (Price et al., 2017). Beta blockers should be avoided in patients with PAH because they have negative inotropic effects that may not be tolerated in patients with heart failure. Calcium channel blockers should be avoided because they can worsen heart failure and cause systemic vasodilation, which may be life-threatening (Price et al., 2017). Amiodarone and digoxin are the agents of choice to control tachyarrhythmia. Amiodarone may be useful to cardiovert SVTs but has a slow onset of action. Digoxin may be used to control heart rate in atrial fibrillation and atrial flutter. However, these drugs and may not be the best option in unstable patients with PAH. Amiodarone is effective to maintain sinus rhythm after DCCV for atrial fibrillation (Price et al., 2017). In these cases, anticoagulation can be considered for stroke prevention.

Hemoptysis

Severe hemoptysis with uncontrolled bleeding leading to sudden death does not occur frequently, but there is a more than 50% mortality rate if patients with PAH do not receive appropriate treatment immediately (Demerouti et al., 2013). The source of bleeding is usually the bronchial circulation (90%) rather than the pulmonary circulation, and in a minority of cases, the bleeding source may occur from the aorta or systemic arterial supply to the lungs (Demerouti et al., 2013). PAH pathological changes (hypoxic vasoconstriction and intravascular thrombosis) reduce pulmonary circulation, and these patients have bronchial artery enlargement and prominent bronchial artery collateral vessels. Patients with advanced PAH disease may have more pronounced vascular changes and may develop extravasation in the respiratory tract causing significant hemoptysis (Demerouti et al., 2013).

Anticoagulation is considered useful in treating idiopathic PAH, heritable PAH, and PAH because of anorexigen use (Galiè et al., 2013); however, the presence of hemoptysis would prompt immediate discontinuation. Patients with unstable vital signs and significant bleeding should receive urgent attention to identify the cause and the source of bleeding. All presentations of hemoptysis are considered an emergency until proven otherwise and an ABC (airway, breathing, circulation) protocol must be immediately initiated (Price et al., 2017). Treatment for hemoptysis includes reversal of oral anticoagulation, reversal of heparin, administration of blood products to correct anemia, administration of oxygen, bronchoscopy, airway protection with balloon tamponade, or double-lumen endotracheal tube and selective embolization (Delcroix & Naeije, 2010; Demerouti et al., 2013; Price et al., 2017).

Pulmonary Embolism

Acute pulmonary embolism (PE) causes obstruction of the pulmonary vascular bed and release of vasoconstrictors (thromboxane A2 and serotonin), which contribute to an increase in PVR (DiLucente, 2001; Smulders, 2000). Rapid increase in PVR results in worsening right ventricular dilation, increase in RV pressure, and volume overload. An acute intermediate- or high-risk PE may cause acute elevation in PVR, acute PH, and acute RV dysfunction. Hemodynamic instability may occur if there is significant thrombosis load and neurohormonal reaction (Smulders, 2000). Patients with PAH may already have a baseline ventilation perfusion scan and chest computed tomography (CT) angiogram as part of their PH diagnosis that can be used for comparison.

Chest Pain/Left Main Compression Syndrome

Patients with PAH frequently report symptoms of chest pain or angina. Angina in PAH most commonly results from a complex interplay of RV dilation and hypertrophy that can lead to decreased perfusion, while at the same time, the increased PVR leads to higher oxygen demand by the RV. However, patients with PAH may develop chest pain from progressive pulmonary artery dilatation, which may cause extrinsic compression of the left main coronary artery. Although this complication occurs independent of pathologic hemodynamic changes, it may lead to angina, left ventricular (LV) dysfunction, and sudden cardiac death (Demerouti et al., 2013). Incidence of left main compression syndrome (LMCS) is not known, but has been estimated to occur in 5%–44% of patients with PH (Demerouti et al., 2013). It is thought that severe and long-standing PH is a well-known risk factor for the development of LMCS (Demerouti et al., 2013). Diagnostic studies such as cardiac CT or magnetic resonance angiography can be useful, but coronary angiography is the standard test to confirm diagnosis of LMCS (Demerouti et al., 2013). Once LMCS is confirmed, it is critical to restore unobstructed coronary blood flow. In addition to standard treatment options, optimization of PH therapy should be implemented to relieve the RHF.

Infection

Infection is not well tolerated in patients with PAH and can cause significant morbidity and mortality (Kurzyna et al., 2008). Even small infections can cause hypoxemia and worsen RHF, which may lead to death. One common cause of infection in patients with PAH who are being treated with intravenous (IV) prostacyclins is via a central line (Centers for Disease Control and Prevention, 2007; Oudiz et al., 2004). The dedicated line for IV prostacyclin must not be flushed or used for blood draws, even for blood cultures. Blood cultures are drawn from a peripheral site to prevent interruption of IV prostacyclin therapy. It is important that patients are evaluated for bacteremia, even in the absence of clinical signs of infection. If it is determined that the catheter is the source of infection, the patient will need to be admitted for IV antibiotics, a peripherally inserted central catheter (PICC)

line will need to be placed for infusion of prostacyclin, and then the catheter that is the source of infection can be removed.

PAH Medication Considerations

Depending on the medication or device, verify the dose, schedule, how many doses have been completed, and when the next dose is due (see Table 1).

PAH Infusion Medication Considerations

Patients with PAH who are being treated with IV prostacyclins have long-term central venous access catheters for their continuous infusions. Infusion pumps cannot go into the MRI room and the PH center should be contacted to ensure proper pump use. Infusions must never be interrupted, even if the patient is hypotensive, without consultation with the PH center. Infused prostacyclin medications have a very short half-life (see Table 1), and interruption has been associated with acute RHF and death (Cuiper, Price, & Christman, 1996). Patients with PAH presenting with the chief complaint of abrupt compromised infusion line and therefore have interruption of continuous IV or subcutaneous prostacyclins require immediate attention to reestablish the infusion via alternative access (see Table 1). Abrupt interruptions may be caused by displaced or dysfunctional central lines, malfunctioning infusion pumps, or error in dosing. Signs and symptoms of acute loss of infusion can include dyspnea, chest pain, fatigue, edema, cyanosis, pallor, and hypertension.

Patients may report that the infusion line has been pulled and has fallen out. It is imperative that a new line is established as soon as possible and to establish how long the infusion has been interrupted. Two peripheral IV catheters (one for infusion, one as back-up for urgent access) should be inserted and the infusion restarted.

Patients may report that the central line has a hole and the line may be leaking IV prostacyclin. In this case, the line will need to be repaired or replaced depending on where the hole is found. Two peripheral lines should be inserted and infusion reestablished while determining whether the catheter can be replaced or repaired. Do not flush the line until prostacyclin medication has been removed. Before any manipulation of the catheter, remove all IV prostacyclin by withdrawing 10 cc of blood, which will include the prostacyclin medication, and then flush slowly with 10-cc normal saline solution before performing any manipulation of the catheter.

Patients may present to the ED with an infusion pump alarm and the medication may not be infusing. First, determine whether the issue is a pump malfunction or whether it is a catheter malfunction. Establish a peripheral IV and start the infusion via the patient's pump. If the infusion is not working via the peripheral IV, consider a pump malfunction. Patients who have two pumps are taught to change to the new pump if the current pump has an alarm (see Table 1). Specialty pharmacy is available 24 hr a day and can be contacted for any pump malfunction (see Table 1). If both pumps are not infusing, the central line, cassette, tubing, and central line cap should be inspected for problems and exchanged. If no problem is identified, it is likely that the patient's long-term venous access catheter is clotted. This can be assessed by trying to aspirate 10 cc of blood. Do not clear the line by flushing or using tissue plasminogen activator, as this can bolus the drug and cause death. If the catheter is clotted, it will need to be replaced with a new central line catheter after discussion with the PH center.

Dosing of IV prostacyclins in patients with PAH is complex, highly individualized, and has many components for consideration. Although patients have dosing sheets and have received extensive education from the PH center about their self-administered treatment, they may be confused about dose amount and pump rate. Dose calculation is determined by drug concentrations, pump rate, and dosing weight (see Table 1). It is very important for ED staff to call the patient's specialty pharmacy and/or PH center to verify the dose required for treating the patient.

Patients' nonadherence to their medication regimen can include losing their pump, running out of medication, incorrectly setting the pump, and/or battery failure. Issues such as patient nonadherence (which may cause clinical worsening) are important to the PH center team, and it is recommended to notify them after the urgent issue is addressed.

PAH Inhalation Medication Considerations

Patients with PAH can be on inhaled therapies given via specialized nebulizers (see Table 1). Patients are taught to always bring their devices with them to ensure they can receive their inhalations. ED staff would need to ensure that patients have access to their inhaled medication while they are in the ED. If there are any issues with gaining access to the inhaled medication, contact the PH specialist and the specialty pharmacy.

PAH Oral Medication Considerations

Patients with PAH may be on oral medications, and if one or more doses is missed, special considerations need to be taken. In particular, two missed doses of oral treprostinil require restarting at a lower dose and retitrating the medication (Orenitram, 2014). For a short-term interruption of treatment where patients are unable to take the oral medication, temporary infusion or injection can be considered (Orenitram., 2014). In all cases, contact the PH specialist and specialty pharmacy for specific instructions.

TRIAGE OF PATIENTS WITH PAH WHO PRESENT TO THE ED

With an understanding of the limited cardiac reserve of patients with PAH, ED providers need to promptly recognize the signs and symptoms of RHF, identify the cause of the clinical deterioration, provide early interventions to improve RV function, and assess for end organ involvement (renal dysfunction, liver dysfunction) (see Figure 1) (Skhiri, Hunt, Denault, & Haddad, 2010). It is not expected that ED providers will perform critical care-level interventions, but that they anticipate that patients with PAH and decompensated heart failure will need to transfer to a critical

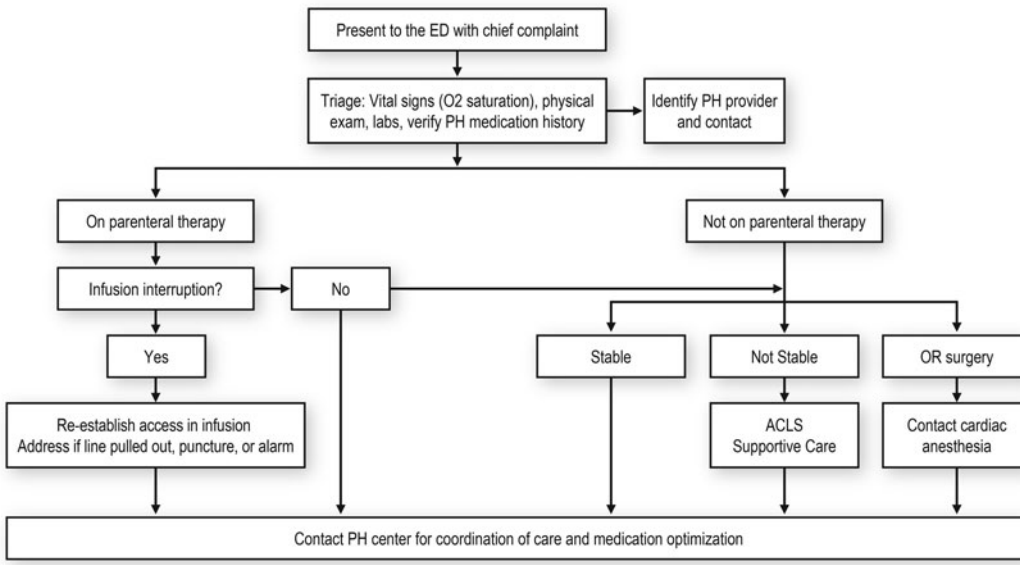

Figure 1. Algorithm for evaluating and triaging the patient with pulmonary arterial hypertension in the emergency department.

care setting or to an experienced PH center for advanced care. If a patient with PAH appears in distress at rest, he or she must be attended to urgently.

Vital Sign Assessment and Symptoms

During triage when assessing vital signs (temperature, heart rate and rhythm, respiratory rate, systemic blood pressure (BP), resting pulse oximetry, and weight) in patients with PAH, it is helpful to compare the presenting values to the patient's baseline values (see Figure 1). If possible, ambulatory oxygen saturation can be measured as a possible indicator of clinical worsening even as resting vital signs remain unchanged (Rich & Rich, 2014). Low Spo_2 is not typical of acute decompensation in PAH and should prompt evaluation for other etiology of hypoxia. If the patient with PAH appears comfortable, stable, and lucid, then providers may take time to thoroughly interview the patient. It is important to assess the rate of symptom progression (increasing edema, worsening lightheadedness/dizziness, change in activity tolerance, occurrence(s) of syncope, episodes of chest discomfort, etc.).

Physical Examination

Routine physical examination of patients with PAH will focus on assessing increased jugular venous pressure, systolic murmur, lung sounds, edema of lower legs, abdominal distension with ascites, enlarged liver and spleen, and integrity of central line access and catheter exit site.

Screening Laboratory Tests

Routine laboratory testing performed includes basic metabolic panel, liver function studies, complete blood count, coagulation studies, albumin level, thyroid function studies, and N-terminal pro b-type natriuretic peptide (NT-proBNP)/BNP (see Figure 1). Laboratory results should be compared with the patient's baseline values, which may differ from results seen in other patient groups. Multiple laboratory abnormalities can indicate worsening of PAH symptoms. As clinically indicated, drug toxicity screening or a pregnancy test (if the patient is female and of childbearing potential) should be considered.

Renal function and electrolytes ought to be considered in the context of the patient's baseline values. Diuretics, often in high doses, can be standard therapy for patients with PAH. Laboratory values of NT-proBNP/BNP can be informative in evaluating cardiac causes of worsening dyspnea and particularly helpful when compared to prior values for the patient. Screening for thyroid abnormalities can also be useful as thyroid disease is common in patients with PAH (Galiè et al., 2015; Kingman et al., 2017). In addition, patients with PAH are predisposed to anemia, or obscure or overt hemorrhage, which may be caused by medication side effects (such as endothelin receptor antagonists) or underlying concomitant condition (Kingman et al., 2017; Sitbon et al., 2015). PH providers/centers will be able to provide critical insight to the patient's history, course of treatment, and offer recommendations on managing the current emergency.

Other useful tests could include 12-lead electrocardiogram, chest x-ray, and transthoracic echocardiogram (Price et al., 2017). Diagnostic and clinical findings that may indicate a poor prognosis include: one or more episodes of syncope; volume overload such as ascites and anasarca; highly elevated NT-proBNP/BNP levels; severe hypoxemia; end organ involvement (renal and liver dysfunction); and echocardiogram results of largely dilated right atrium, largely dilated RV, severely decreased RV function, underfilled LV, and pericardial effusion (Delcroix & Naeije, 2010; Galiè et al., 2015).

PAH Medication Therapy

During triage, it is important to ensure patients' adherence to current medications and address considerations for specific medications (see Table 1 and Figure 1). The ED provider should determine whether patients have their medication delivery devices and associated supplies and medication with them,

whether the patient is receiving parenteral or nonparenteral therapy and/or other PAH medications, and can identify when the next dose is due. It is helpful for the nurse to note this in the medical record for other ED staff as the patient moves through the ED process.

Communication With PH Specialists and the Specialty Pharmacy

Contacting the PH center and specialty pharmacy soon after a patient with PAH is admitted to the ED can be beneficial and save time and effort during evaluation and triage. The PH provider(s) may be able to provide insight on the patient's history, course of treatment, and offer recommendations on managing the current emergency. The PH program will have staff on-call that can efficiently provide complete medical histories, context for test results and vital signs, and help with troubleshooting inhaled and infused delivery system malfunctions. The patient's specialty pharmacy can provide medication dose, adherence, and supply information. For patients on infused PAH medications, the phone number for the specialty pharmacy will be located on the infusion pump.

Surgery

Surgery (particularly unplanned surgery) is very high risk in patients with PAH. A PAH specialist should always be consulted when considering surgery, and a cardiac anesthesiologist with PH experience is essential to achieve the best outcome. When possible, the patient with PAH should be transferred to a comprehensive center because of their experience in caring for patients with PAH. Elective surgery is not recommended, but if necessary, would be best performed at a comprehensive center. It is recommended that the surgery involve the least invasive procedure warranted to treat the condition. Involvement of the PH specialist is critical, as PAH medications may need to be adjusted in the preoperative, perioperative, and/or postoperative period. After surgery or invasive procedures, patients may need to be transitioned to a higher level of care for closer monitoring and management.

CASE STUDY OF HEMORRHAGE IN A PATIENT WITH PAH PRESENTING TO THE ED

Patient consent was obtained before compilation of this case study.

A 35-year old woman with severe PAH presented to the ED at a hospital with an accredited PH Comprehensive Care Center. The patient had a complaint of abdominal pain/distension for 2 days and vaginal spotting for 1 month. When she walked into the ED, she experienced lightheadedness and dizziness and thought she was not getting enough of her infused prostacyclin medication. Her usual side effects were absent, and she was feeling more short of breath.

The patient had a history of PAH in association with prior exposure to methamphetamines and obstructive sleep apnea. Specific PAH therapy included a phosphodiesterase-5 (PDE-5) inhibitor, tadalafil, an endothelin antagonist, ambrisentan, and a prostacyclin, epoprostenol sodium, delivered as a chronic continuous IV infusion via a single-lumen tunneled Hickman catheter. Sleep apnea was being treated with CPAP at 9 cm H_2O and 2 L/min oxygen bled in. Other medications for PAH included diuretics for peripheral edema because of chronic RHF, and warfarin for central line prophylaxis. For contraception in PAH, an intrauterine device had been placed 2 years ago. In addition, the patient had a history of chronic pain and anxiety.

The patient's symptoms began with abdominal distention and bilateral lower quadrant pain. Initially, she had bulging flanks that progressed to diffuse distension, and then she had a small bowel movement the day before that was diarrhea, with no melena or blood, decreased appetite, nausea because of abdominal pain, no chest pain or fever, but complaint of chills, worsening headache, dizziness, palpitations, decreased urination, and vaginal spotting (patient held warfarin). The patient came to the ED because of worsening symptoms.

The PH specialist on call was notified of the patient's admission to the ED. Physical examination was positive for chills and change in appetite, shortness of breath, palpitations, nausea, abdominal pain, diarrhea, constipation, abdominal distention, and dizziness.

Abdominal x-ray per the radiologist showed cardiomegaly, right sided with PH, but no obstruction. Complete blood count with critical hemoglobin (Hgb) was 6.2 g/dl, mild hypokalemia, elevated creatinine was consistent with dehydration, negative lipase, and normal hepatic function panel. BNP was elevated at 630 ng/L compared with 381 ng/L 2 weeks prior. The PH specialist recommended and performed paracentesis, which returned frank blood. The PH specialist agreed with general surgery recommendation to transfuse with 2-U packed red blood cells.

A bedside ultrasound revealed a ruptured ovarian cyst; the gynecologist confirmed a bleeding ovarian cyst. Systolic BP was 107 mmHg. A CT scan revealed hepatomegaly and passive congestion with a small high-dense area with blush, however, no surrounding hematoma. Large amounts of fluid were found in the abdomen, likely blood, as well as blood around the ovary. General surgery recommended admission to medical intensive care unit as there was no obvious acute arterial bleeding. A repeat Hgb and international normalized ratio were performed, and intensive care unit attending recommended admission.

The patient was reassessed and found to be more uncomfortable, grunting with breathing, and had worsening abdominal distension, as the second unit of blood was infusing slowly. Repeat Hgb dropped from 6.2 to 6.0 g/dl, systolic BP was in the 100s mmHg. The patient was immediately transferred to the operating room (OR) for unplanned surgery. A cardiac anesthesiologist with experience in PH provided anesthesia during surgery. An exploratory laparotomy was performed, which revealed a hemoperitoneum from a ruptured right hemorrhagic ovarian cyst. A right oophorectomy and left tubal ligation with placement of pelvic Jackson-Pratt drain was performed. Postoperatively, the patient was transferred to the medical intensive care unit. During hospitalization, the patient was aggressively diuresed to decrease the amount of residual ascetic fluid. A follow-up CT scan of the abdomen and abdominal sonogram showed a small amount of ascites fluid. Throughout hospitalization, the patient was continued on all PAH-specific medications without dose adjustment. Warfarin was resumed prior to discharge. Increased diuretics during admission were continued at hospital discharge with furosemide 80 mg twice daily and spironolactone 25 mg daily. The patient was scheduled for follow-up laboratory tests in 1 week with return clinic visit. The duration of hospitalization was 2 weeks.

Discussion

This case demonstrates a classical presentation of a hemorrhagic ovarian cyst that escalates to a life-threatening emergency in a rare patient with severe PAH. However, this case demonstrates that appropriate referral and management can improve patient outcomes when a patient presents to a PH comprehensive care center, has early consultation with the PH specialist, rapid assessment and diagnosis by the emergency medical team, and admission to the OR for immediate surgical intervention with sedation by a cardiac anesthesiologist.

IMPLICATIONS FOR ADVANCED PRACTICE REGISTERED NURSES

The recent advances in treatment for PAH have afforded a longer lifespan for patients with the disease. These advances have also resulted in more frequent visits to the ED as patients who live longer can experience complications related or unrelated to their disease. Therefore, it has become critical for nurses and ED staff to become familiar with PAH and the special considerations of these patients. The overview of treatment considerations outlined in this article provides nurses and ED staff with valuable resources for when

they encounter patients with PAH and provides a reminder to always consult the PH specialists and specialty pharmacy to ensure these patients receive appropriate care.

CONCLUSION

Diagnosis and ongoing clinical management of PAH requires specialized training and expertise. In the United States, there are currently 54 formally accredited PH care centers and additional highly skilled programs that have not yet sought recognition (Pulmonary Hypertension Association, 2017). However, few patients with PH live, work, and travel in areas where the closest emergency facility would be an accredited center or in the same health system as their PH provider. The ability to recognize, triage, and communicate changes in disease status between the patient, family, specialty pharmacy, and specialized health care providers is essential for ED providers. It is crucial to reach out to the patient's specialized PH program when the patient presents to the ED. PH programs always advise patients to notify them if they are hospitalized. A multidisciplinary team approach is imperative in managing complex PAH disease in patients with comorbidities to ensure rapid diagnosis, appropriate assessment and intervention, and provide optimum outcomes.

REFERENCES

Adcirca® (tadalafil) [package insert]. (2009). Indianapolis, IN: Eli Lilly and Company.

Adempas® (riociguat) [package insert]. (2013). Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.

Allen, L. A., & O'Connor, C. M. (2007). Management of acute decompensated heart failure. *Canadian Medical Association Journal*, *176*(6), 797–805.

Badesch, D. B., Champion, H. C., Sanchez, M. A., Hoeper, M. M., Loyd, J. E., Manes, A., . . . Torbicki, A. (2009). Diagnosis and assessment of pulmonary arterial hypertension. *Journal of the American College of Cardiology*, *54*(1 Suppl.), S55–S66.

Centers for Disease Control and Prevention. (2007). Bloodstream infections among patients treated with intravenous epoprostenol or intravenous treprostinil for pulmonary arterial hypertension—seven sites, United States 2003–2006. *Morbidity and Mortality Weekly Report*, *56*, 170–172.

Collins, S. P., Storrow, A. B., Albert, N., Butler, J., Ezekowitz, J. A., Felker, G. M., . . . Lenihan, D. J. (2015). Early management of patients with acute heart failure: State of the art and future directions—a consensus document from the SAEM/HFSA acute heart failure working group. *Academic Emergency Medicine*, *22*(1), 94–112.

Cuiper, L. L., Price, P. V., & Christman, B. W. (1996). Systemic and pulmonary hypertension after abrupt cessation of prostacyclin: Role of thromboxane A2. *Journal of Applied Physiology*, *80*, 191–197.

Delcroix, M., & Naeije, R. (2010). Optimising the management of pulmonary arterial hypertension patients: Emergency treatments. *European Respiratory Review*, *19*(117), 204–211.

Demerouti, E. A., Manginas, A. N., Athanassopoulos, G. D., & Karatasakis, G. T. (2013). Complications leading to sudden cardiac death in pulmonary arterial hypertension. *Respiratory Care*, *58*(7), 1246–1254.

DiLucente, M. R. (2001). Pulmonary embolism: A nursing perspective. *Advanced Emergency Nursing Journal*, *23*(1), 53–60.

Flolan® (epoprostenol) [package insert]. (2016). Research Park Triangle, NC: GlaxoSmithKline.

Galiè, N., Corris, P. A., Frost, A., Girgis, R. E., Granton, J., Jing, Z. C., . . . Rubin, L. J. (2013). Updated treatment algorithm of pulmonary arterial hypertension. *Journal of the American College of Cardiology*, *62*(25), D60–D72.

Galiè, N., Humbert, M., Vachiery, J. L., Gibbs, S., Lang, I., Torbicki, A., . . . Ghofrani, A. (2015). 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *European Respiratory Journal*, *46*(4), 903–975.

Goldstein, J. A., Harada, A., Yagi, Y., Barzilai, B., & Cox, J. L. (1990). Hemodynamic importance of systolic ventricular interaction, augmented right atrial contractility and atrioventricular synchrony in acute right ventricular dysfunction. *Journal of the American College of Cardiology*, *16*(1), 181–189.

Greyson, C. R. (2010). The right ventricle and pulmonary circulation: Basic concepts. *Revista Española de Cariología*, *63*(1), 81–95.

Hoeper, M. M., Galié, N., Murali, S., Olschewski, H., Rubenfire, M., Robbins, I. M., . . . Barst, R. J. (2002). Outcome after cardiopulmonary resuscitation in patients with pulmonary arterial hypertension. *American Journal of Respiratory and Critical Care Medicine*, *165*(3), 341–344.

Hoeper, M. M., Bogaard, H. J., Condliffe, R., Frantz, R., Khanna, D., Kurzyna, M., . . . Badesch, D. B. (2013).

Definitions and diagnosis of pulmonary hypertension. *Journal of the American College of Cardiology*, *62*, D42–D50.

Hoeper, M. M., Humbert, M., Souza, R., Idrees, M., Kawut, S. M., Sliwa-Hahnle, K., . . . Gibbs, J. S. (2016). A global view of pulmonary hypertension. *The Lancet Respiratory Medicine*, *4*(4), 306–322.

Humbert, M., & Ghofrani, H. A. (2016). The molecular targets of approved treatments for pulmonary arterial hypertension. *Thorax*, *71*(1), 73–83.

Kingman, M., Archer-Chicko, C., Bartlett, M., Beckmann, J., Hohsfield, R., & Lombardi, S. (2017). Management of prostacyclin side effects in adult patients with pulmonary arterial hypertension. *Pulmonary Circulation*, *7*(3), 598–608.

Kurzyna, M., Zyłkowska, J., Fijałkowska, A., Florczyk, M., Wieteska, M., Kacprzak, A., . . . Torbicki, A. (2008). Characteristics and prognosis of patients with decompensated right ventricular failure during the course of pulmonary hypertension. *Kardiologia Polska*, *66*(10), 1033–1039.

Letairis® (ambrisentan) [package insert]. (2015). Foster City, CA: Gilead Sciences, Inc.

McLaughlin, V. V., Archer, S. L., Badesch, D. B., Barst, R. J., Farber, H. W., Lindner, J. R., . . . ACCF/AHA. (2009). American College of Cardiology Foundation Task Force on Expert Consensus Documents; American Heart Association; American College of Chest Physicians; American Thoracic Society, Inc; Pulmonary Hypertension Association. ACCF/AHA 2009 expert consensus document on pulmonary hypertension a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians; American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *Journal of the American College of Cardiology*, *53*(17), 1573–1619.

Opsumit® (macitentan) [package insert]. (2017). South San Francisco, CA: Actelion Pharmaceuticals, US, Inc.

Orenitram® (treprostinil) [package insert]. (2014). Research Triangle Park, NC: United Therapeutics Corp.

Oudiz, R. J., Widlitz, A., Beckmann, X. J., Camanga, D., Alfie, J., Brundage, B. H., & Barst, R. J. (2004). Micrococcus-associated central venous catheter infection in patients with pulmonary arterial hypertension. *Chest*, *126*(1), 90–94.

Price, L. C., Dimopoulos, K., Marino, P., Alonso-Gonzalez, R., McCabe, C., Kemnpy, A., . . . Wort, S. J. (2017). The CRASH report: Emergency management dilemmas facing acute physicians in patients with pulmonary arterial hypertension. *Thorax*, *72*(11), 1035–1045.

Pulmonary Hypertension Association. (2017). *PH Care Centers: Providing excellence in pulmonary hypertension care*. Retrieved from https://phassociation.org/phcarecenters/accredited-centers/

Remodulin® (treprostinil) [package insert]. (2011). Research Park Triangle, NC: United Therapeutics Corp.

Revatio® (sildenafil) [package insert]. (2014). New York, NY: Pfizer Labs.

Rich, J. D., & Rich, S. (2014). Clinical diagnosis of pulmonary hypertension. *Circulation*, *130*, 1820–1830.

Silvers, S. M., Howell, J. M., Kosowsky, J. M., Rokos, I. C., & Jagoda, A. S. (2007). American College of Emergency Physicians. Clinical policy: Critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. *Annals of Emergency Medicine*, *49*(5), 627–669.

Simonneau, G., Gatzoulis, M. A., Adatia, I., Celermajer, D., Denton, C., Ghofrani, A., . . . Souza, R. (2013). Updated clinical classification of pulmonary hypertension. *Journal of the American College of Cardiology*, *62*(25 Suppl.), D34–D41.

Sitbon, O., Channick, R., Chin, K. M., Frey, A., Gaine, S., Galiè, N., . . . GRIPHON Investigators. (2015). Selexipag for the treatment of pulmonary arterial hypertension. *New England Journal of Medicine*, *373*(26), 2522–2533.

Skhiri, M., Hunt, S. A., Denault, A. Y., & Haddad, F. (2010). Evidence-based management of right heart failure: A systematic review of an empiric field. *Revista Española de Cariología*, *63*(4), 451–471.

Smulders, Y. M. (2000). Pathophysiology and treatment of haemodynamic instability in acute pulmonary embolism: The pivotal role of pulmonary vasoconstriction. *Cardiovascular Research*, *48*(1), 23–33.

Stein, P. D., Matta, F., & Hughes, P. G. (2015). Scope of problem of pulmonary arterial hypertension. *The American Journal of Medicine*, *128*(8), 844–851.

Tongers, J., Schwerdtfeger, B., Klein, G., Kempf, T., Schaefer, A., Knapp, J. M., . . . Hoeper, M. M. (2007). Incidence and clinical relevance of supraventricular tachyarrhythmias in pulmonary hypertension. *American Heart Journal*, *153*, 127–132.

Tracleer® (bosentan) [package insert]. (2003). Mississauga, Ontario, Canada: Patheon, Inc.

Tyvaso® (treprostinil) [package insert]. (2009). Research Park Triangle, NC: United Therapeutics Corp.

Uptravi® (selexipag) [package insert]. (2017). South San Francisco, CA: Actelion Pharmaceuticals, US Inc.

Veletri® (epoprostenol) [package insert]. (2016). South San Francisco, CA: Actelion Pharmaceuticals US, Inc.

Ventavis® (iloprost) [package insert]. (2012). South San Francisco, CA: Actelion Pharmaceuticals, US Inc.

Wahlrab, L. (2012). The differential diagnosis of syncope: A guide for emergency department advanced practice nurses. *Advanced Emergency Nursing Journal*, *34*(4), 341–349.

Wilcox, S. R., Kabrhel, C., & Channick, R. N. (2015). Pulmonary hypertension and right ventricular failure in emergency medicine. *Annals of Emergency Medicine*, *66*(6), 619–628.