CONTINUING EDUCATION

Perioperative Considerations for Patients Diagnosed With Pulmonary Hypertension Undergoing Noncardiac Surgery

Todd Tartavoulle, DNS, Laura S. Bonanno, DNP, CRNA, Stanley Hall, MD, PhD

The prevalence of pulmonary hypertension (PH) has risen in adults of all races, genders, and ethnicities. PH is a fatal disease that presents many challenges to the perioperative health care team. Through increased knowledge of PH pathophysiological changes and anesthesia medications' effect on PH, perioperative health care teams can conduct a detailed preoperative evaluation to determine appropriate therapies to administer. This will assist the perioperative health care team in reducing the pulmonary vascular resistance, optimizing the matching of right ventricle and pulmonary circulations, and reduce the incidence of intraoperative and postoperative complications.

Keywords: *pulmonary hypertension, perioperative, noncardiac surgery, anesthesia, pulmonary vasodilators.*

LEARNING OBJECTIVES—1. DESCRIBE the pathophysiology of pulmonary hypertension (PH); 2. Discuss the perioperative management of patients with PH; and 3. Describe pharmacologic and nonpharmacologic interventions that can be used in the perioperative management of patients with PH.

Pulmonary hypertension (PH) is a progressive and ultimately fatal disease that presents as an elevated blood pressure in the pulmonary arteries. PH evolves as a comorbidity of other diseases or conditions such as connective tissue diseases, lung diseases, liver disease, human immunodeficiency virus infection, and left heart failure as well as pregnancy. The disease has been associated with the usage of the diet medication Fen Phen that is a combination of two drugs, fenfluramine (Pondimin) and phentermine (Lonamin). PH and the comorbidity conditions affect a diverse segment of the population.[1]

The demographic profile of the adult PH population includes men and women of all ages, racial, and ethnic groups. The overall prevalence of PH in the general population is unknown because of the many attributable causes of the disease. Past studies have estimated the prevalence of PH in specific subgroups of PH clients. In an observational study of 277 clients with human immunodeficiency virus, approximately 46% of clients had PH.[2] A systematic review of several studies of clients with obstructive sleep apnea estimated the prevalence of PH to be 15% to 20%.[3] Several studies among clients with chronic obstructive pulmonary disease estimated the prevalence of PH to be 10% to 30%.[4] PH occurs in 10% to 45% of clients with mixed connective tissue disease.[5] In scleroderma clients, the prevalence has been estimated to be 6% to 60% of all clients, with the

Todd Tartavoulle, DNS, School of Nursing, Louisiana State University Health, New Orleans, LA; Laura S. Bonanno, DNP, CRNA, School of Nursing, Louisiana State University Health, New Orleans, LA; and Stanley Hall, MD, PhD, School of Nursing, Louisiana State University Health Sciences Center, New Orleans, LA, and Children's Hospital, New Orleans, LA.

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Address correspondence to Laura S. Bonanno, LSU Health School of Nursing, 1900 Gravier Street, New Orleans, LA 70112; e-mail address: LBONAN@lsuhsc.edu.

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variance based on the extent of disease.[5] One to four percent of systemic lupus erythematosus cases develop PH.[5]

Idiopathic pulmonary arterial hypertension (IPAH) occurs in the absence of known causes. An estimated incidence of IPAH and familial PAH ranges from one to two cases per million people in the general population. Of these cases, at least 6% of the clients have IPAH.[5] Two to four percent of clients with portal hypertension develop PH.[5]

Before the development of pharmacologic agents targeted to PH, the median survival for clients diagnosed with PH was 2.8 years.[5] Prognosis is dependent on underlying PH etiology. Connective tissue disease, specifically scleroderma, results in an approximate 2-year survival at 40% compared with 48% for 3-year survival in clients with IPAH.[5]

Between 2000 and 2002, the Centers for Disease Control and Prevention reported 807,000 adults were hospitalized with PH.[1] Of these hospitalized adult PH clients, 61% were women and 66% were aged 65 years or older.[1] During the time period 1980 to 2002, the number of PH deaths increased from 10,922 to 15,668 respectively.[1] The largest increase in mortality rates was among women.[1] Among all racial populations, the number of adult PH deaths has increased mostly among the African American population.[6] Mortality rates associated with PH are higher among the elderly, specifically men of all races aged greater than 85 years, women aged greater than 65 years, Whites aged greater than 75 years, and African Americans aged greater than 65 years.[6] PH is a progressive disease and survival of patients with untreated PH is 2 to 3 years.[6]

In 2008, the fourth World Symposium on PH sponsored by World Health Organization (WHO) met to update the clinical classification system for PH into five different categories. During the Fifth World Symposium held in 2013, the previous clinical classifications were maintained. Classification is based on the mechanisms responsible for disease causation.[7]

1. Pulmonary arterial hypertension (PAH).
2. PH owing to left heart disease.
3. PH owing to lung diseases or hypoxia.
4. Chronic thromboembolic PH.
5. PH related to disorders (such as metabolic or autoimmune) affecting the pulmonary vasculature with unclear multifactorial mechanisms.[7]

The five categories of PH encompass many etiologies, including heritable factors, connective tissue disorders, valvular heart disease, and hypoxia. Although the WHO classification is important, it does not dictate the type of anesthetic technique used.

The severity of PH is assessed via a modified version of the New York Heart Association's system. Functional class for PH is known as WHO functional class. The severity and symptoms of PH determine the functional class. Table 1 presents the WHO functional class for PH.[8]

Pathophysiology

PH is a chronic and incurable disease that presents many challenges to the patient and the operating room (OR) health care team. In PH, increasing pulmonary artery pressure and pulmonary vascular resistance (PVR) causes pressure in the pulmonary artery to become elevated causing right ventricular dysfunction. PH can occur at any age and affects individuals of all races and ethnic backgrounds.[9]

Arteries and arterioles comprise the pulmonary vasculature and branch into the lungs to create a dense capillary bed to advance blood flow. The pulmonary capillary bed is a high volume, low resistance, highly vascularized system. Blood is delivered to and taken away by arteries and venous circulations, respectively. The compliance of the pulmonary circulation is higher than that of the systemic circulation. The pressure and resistance of the pulmonary circulation is much lower than

Table 1. World Health Organization (WHO) Functional Classification System[8]

- Class I: No symptoms with ordinary physical activity.
- Class II: Symptoms (dyspnea, chest pain, fatigue, and near fainting) with ordinary activity. Slight limitation of activity.
- Class III: Symptoms with less than ordinary activity. Marked limitation of activity.
- Class IV: Symptoms at rest.

that of the systemic circulation because of the higher level of recruitment and dispensability that occurs in the pulmonary vessels. Recruitment refers to the fact that there are many parallel vessel pathways (about 1,000 capillaries per alveolus), which are not open at lower levels of pulmonary blood flow. When cardiac output increases, these vessels open, which keeps resistance and pressure low. Compared with systemic blood vessels, pulmonary vessels are much more distensible because they are thinner walled and have much less smooth muscle. When cardiac output increases, pulmonary vessels are easily stretched, which keep resistance and pressure low. Pressures in the pulmonary artery are 18 to 30/4 to 14 mm Hg and normal mean pulmonary artery pressure (MPAP) is 14 ± 3.3 mm Hg.[6]

A right heart catheterization is used to diagnose PH. An MPAP greater than 25 mm Hg at rest is criteria to be diagnosed with PH. The most common type of PH is PAH. The most frequent cause of PAH is idiopathic (of unknown origin) and is most common in young females aged 20 to 40 years. PAH frequently presents in these patients prenatally because of the physiological stresses of pregnancy and delivery. There are several etiologies of PH including elevations in pulmonary artery pressure resulting from increased pulmonary artery resistance, increased pulmonary venous pressures, and increased blood flow or a combination of these factors. As PH progresses, the increased resistance in the pulmonary vessels causes right ventricular hypertrophy. As the right ventricle hypertrophies and impinges on the left ventricle, activity intolerance occurs and eventual death. The evolution of PH may be insidious as vague symptoms of dyspnea, and fatigue are initial complaints by the PH patient. The signs and symptoms are related to the severity of right heart failure. Selecting the appropriate diagnostic tests to identify PH can be challenging when there is no suspicion of PH.[10]

Treatment of PH depends on the etiology. Treatments may improve the symptoms of PH and slow disease progression. PH treatments can be divided into three categories including conventional therapy (oxygen, warfarin, and diuretics), targeted therapy (calcium channel blockers, endothelin receptor antagonists, phosphodiesterase 5 inhibitors, prostaglandins, and soluble guanylate cyclase stimulators), and surgery (pulmonary endarterectomy, atrial septostomy, and transplant surgery).[11]

PH patients undergoing a surgical procedure are at an increased risk for a negative outcome. PH is associated with significant morbidity and mortality regardless of the type of anesthesia administered. During a surgical procedure, several types of medications used for anesthesia are administered, fluctuations in intravascular volume may take place, and changes in the autonomic nervous system may occur causing alterations in preload and afterload. Patients with PH undergoing a surgical procedure are relatively unable to accommodate certain alterations in preload and afterload. The perioperative health care team must have an understanding of the pathophysiology, cause, and severity of PH in the perioperative patient. The perioperative health care team includes the anesthesia provider (Certified Registered Nurse Anesthetist [CRNA] or anesthesiologist), preoperative nurse, OR nurse, surgeon, pharmacist, and postanesthesia care nurse. The perioperative health care team will then be able to conduct a risk assessment, optimize cardiac function (right ventricle) before surgery, and deliver appropriate intraoperative and postoperative management.[12] The focus of this article is on the perioperative management of patients with PH undergoing noncardiac surgery.

PH and Anesthesia

PH is a disease that is difficult to manage, and anesthesia is relatively contraindicated in patients diagnosed with PH. Life expectancy in the PH population has increased with the advent of new and improved treatments, and as a result, more patients with PH are presenting for elective surgical procedures. Anesthesiologists, CRNAs, PH experts, surgeons, perioperative nurses, and pharmacists should all be involved in the perioperative medical management of the patient with PH. Health care providers in the perioperative setting should understand the cause of the PH, as well as type and classification. This allows the provider to develop a plan of care that incorporates the potential risks and benefits associated with the use of various medications perioperatively including anesthetic agents.[10] The perioperative management is divided into the following three phases: (1) preoperative

evaluation and preparation; (2) intraoperative management—anesthesia induction, maintenance, emergence, and extubation; and (3) postoperative care.

There is limited research evidence in the literature that describes the potential for morbidity and mortality perioperatively in patients with PH undergoing noncardiac surgery. Hypotension, respiratory compromise, and right ventricular failure are potential complications that may occur intraoperatively or postoperatively. The noncardiac surgical procedure will significantly affect the risk of morbidity. Low-risk surgical procedures include dermatologic, endoscopic, cataract, and breast surgeries. Intermediate-risk procedures include carotid endarterectomy, orthopaedic, prostate, thoracic, head and neck, and gynecologic surgeries. Emergent major surgeries associated with the potential for large fluid shifts and/or blood loss such as surgery of the aorta, other vascular surgery, and liver transplantation are considered high risk. Potential complications that may occur intraoperatively or postoperatively in noncardiac surgery include hypotension, respiratory compromise, or right ventricular failure.[13]

Many clinical risk factors have been identified in patients with PH that increase the risk of perioperative complications. Several research studies have evaluated the risk factors as well as morbidity and mortality rates in patients with PH undergoing noncardiac surgeries. Ramakrishna et al conducted a retrospective study with 145 patients undergoing noncardiac surgery. Findings include 7% early mortality (less than or equal to 30 days postoperatively) with the most frequent contributors to death being acute respiratory failure (60%) and right ventricular failure (50%).[14]

Kaw et al conducted a case study of patients with PH undergoing noncardiac surgery. PH patients preoperatively had an increased risk of overall morbidity and mortality (26% vs 2.6%, $P < .05$).[15] The perioperative health care team should complete a risk assessment to determine the need for invasive monitoring. Placement of a pulmonary artery catheter should be considered in patients with PH undergoing intermediate- to high-risk procedures and in patients with symptomatic PH or right ventricular failure.[16]

Preoperative Evaluation and Preparation

The goal of preoperative evaluation in patients with PH is to determine if the patient suffers from right ventricular failure or has other high-risk indicators. Many of the objective and subjective findings of PH resemble those of heart failure and the most common patient complaints are dyspnea and fatigue. A complete history and physical, chest x-ray, electrocardiogram (EKG), transthoracic echocardiogram, and WHO functional class should be performed and evaluated, usually by a cardiologist consultant. A complete history and physical examination can assist the clinician in determining severity of PH. Clinical symptoms of advanced PH include the following: dyspnea at rest; decreased cardiac output; metabolic acidosis; hypoxemia; third and fourth heart sound of right ventricular origin; large “a” wave in jugular pulse; prominent “v” waves in jugular pulse with holosystolic murmur indicating tricuspid regurgitation; diastolic murmur of pulmonary regurgitation; right heart failure (hepatomegaly, peripheral edema, and ascites); cool extremities; and syncope. A history of syncope is an extremely poor prognostic sign.[17] The anesthetic management will be based on the severity of the patient’s symptoms and diagnostic findings.

An EKG should be performed on all patients with PH before anesthesia. With advanced PH, right ventricular hypertrophy will appear on the EKG as right axis deviation, possibly a predominant R wave in lead V1, a deep S in V6, inverted T waves in right precordial leads V2 and V3m, and peaked P waves. Atrial dysrhythmias, atrial flutter, and atrial fibrillation may contribute to further deterioration in advanced PH.[6] A prominent pulmonary artery will be visible on the preoperative chest x-ray along with right atrial and right ventricular dilatation.[18] A transthoracic echocardiogram is performed to assess valvular structures, size and function of both right and left ventricle, and measure pulmonary artery pressure. Transthoracic echocardiogram findings of advanced PH include elevated right ventricular pressure, right ventricular dilatation, septal bowing into left ventricle hypokinesis, and the presence of a pericardial effusion. The transthoracic echocardiogram generally underestimates the MPAP.[16]

A right heart catheterization is a diagnostic procedure that directly measures MPAP, cardiac output, PVR, and pulmonary capillary wedge pressure. At rest the normal MPAP is between 12 to 16 mm Hg. A resting MPAP greater than or equal to 25 mm Hg is diagnostic of PH. Pulmonary artery catheters are recommended in patients undergoing intermediate- to high-risk surgical or diagnostic procedures and in patients with symptomatic PH or a history of right ventricular function. If coronary artery disease or mitral or aortic valvular disease is suspected, a concomitant left-sided catheterization is indicated. A hemodynamic profile that includes an elevated right atrial pressure and reduction in cardiac output is of great concern. This is an indication of right ventricular failure and surgery should be avoided unless minor.[18]

Lowering the MPAP before surgery is important and all attempts should be made to do so. Oxygen, bronchodilators, vasodilators, and inotropes can be used to lower MPAP. Current PH treatments should be maintained throughout surgery. The withdrawal of PH-specific medications may cause rebound PH and right ventricular dysfunction. The anesthesia provider should embrace a multidisciplinary approach. Physician subspecialists including pulmonary or critical care physicians and cardiologists, as well as nurses, respiratory therapists, and pharmacists should be consulted depending on the severity of the PH and the complexity of the type of surgery. Anesthetic technique depends on the surgical procedure, patient preference, and patient comorbidities as well as preparation for the potential of intraoperative events that could potentially worsen PH[19] (Table 2).

Intraoperative Management

The intraoperative phase begins with induction of anesthesia and ends with emergence and extubation. The main goals of intraoperative management are reduction of PVR and maintenance of optimal matching of the RV and pulmonary circulation. This requires knowledge and understanding of pathophysiology and the pharmacologic effects of anesthetic agents that can "effect right ventricular afterload, inotropy, and oxygen supply/demand relationships."[20, p205] The focus of nonpharmacologic management is on avoiding triggers of PH exacerbation including hypoxemia, hypercarbia, acidosis, hypervolemia, and hypothermia.[19] An anxiolytic agent should be used with caution to ensure the

Table 2. Preoperative Evaluation High-Risk Clinical Predicators

History	EKG	Echo	Hemodynamics	Surgical	Laboratories
• WHO-FC ○ Class III or IV	• Right. axis	• Right atrial enlargement	• Right atrial pressure ≥12 mm Hg	• Intermediate- and/or high-risk surgery	• Brain natiruretic peptide >300 pg/mL
• ASA class >2	• Right ventricular hypertrophy	• Interventricular septal diastolic flattening	• Mean arterial pressure ≥55 mm Hg	• Emergency surgery	• Reduced creatinine clearance <60 mL/min

• Coronary artery disease
• Comorbidities
  ○ Pulmonary embolism
  ○ Obstructive sleep apnea
  ○ Chronic renal insufficiency
  ○ Untreated PH
		• Pericardial effusion
		• Right ventricular hypertrophy
		• TAPSE < 0.8 cm
		• Right ventricle perfusion index ≥0.75
		• RVSP: SBP ration >0.66
			• Cardiac index < 2.2 L/min/m^2	• Anesthesia >3 h
				• Intraoperative need for vasopressors	

ASA, American Society of Anesthesiologists; EKG, electrocardiogram; WHO-FC, World Health Association functional class; RVSP, right ventricular systolic pressure; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion.

patient maintains airway patency and adequate ventilation before induction. The patient should receive preoxygenation with 100% fraction of inspired oxygen (FiO_2) before induction and the depth of the anesthesia should be adequate before laryngoscopy and tracheal intubation to reduce vasoconstriction caused by stimulation of the sympathetic nervous system. Adequate anesthesia depth should be maintained throughout the surgical procedure and monitored. Fluid management should be guided by hemodynamic measurements and euvolemia maintained near baseline if possible. Consistency in lung volumes should be maintained with proper ventilation modalities as variations in lung volumes will affect PVR. The PVR is the lowest when lung volumes are near functional residual capacity.[19] Ventilation should be monitored and adequacy of ventilation assessed by arterial blood gas with a goal of pH greater than 7.4 and $PaCO_2$ 30 to 35 (avoiding respiratory acidosis). Hypothermia should be prevented by using effective warming techniques including forced air warming blankets and intravenous fluid warmers to prevent shivering and sympathetically mediated vasoconstriction.[19]

Certain unavoidable intraoperative events including transition to positive pressure ventilation, positioning, or surgical techniques can produce increases in RV afterload. Placing the patient in either the trendelenburg or prone position, adding positive end-expiratory pressure, and surgical manipulations can amplify this effect. If a pulmonary artery catheter is inserted, it must be carefully positioned and secured to assure meaningful readings and reduce risk of complications.[20] If PH persists despite employment of these nonpharmacologic measures, pharmacologic management is required.

Pharmacologic Management

The various medications used perioperatively can affect PVR either directly or indirectly through alterations of cardiac output and pulmonary blood flow. Anesthetic agents "can produce changes in PVR, RV afterload and potentially intracardiac shunting."[21, p1612] Myocardial contractility may be affected either directly or indirectly which includes myocardial depression from anesthetics or acute changes in sympathetic or parasympathetic tone.[12] Anesthesia-induced myocardial depression can be caused by both intravenous induction agents and inhalation agents used for anesthesia maintenance. Inhaled anesthetic agents have a direct negative inotropic effect, which are dose related. Although "neuraxial anesthesia (spinal, epidural) has been safely used in patients with PH, autonomic nervous fibers are more sensitive to blockade by local anesthetics than sensory or motor fibers."[20, p208]

The perfect drug for reducing PVR without reducing systemic vascular resistance does not exist. Most drugs that reduce PVR also reduce systemic vascular resistance, which can reduce coronary perfusion pressure. Elevated right ventricular pressure impedes coronary blood flow while increasing right ventricular oxygen demand. When combined with a reduction in coronary perfusion pressure, myocardial ischemia can result. Hypoxic myocardial cells are less able to contract effectively. Less effective heart pumping causes the ventricles to stretch, diastolic pressures to rise, and heart failure to progress. Treatment for RV dysfunction with increased PVR includes administration of vasodilator drugs. The pharmacologic treatment of choice in RV dysfunction with normal PVR is positive inotropic drugs.[21]

Medications to Support Hemodynamic Stability

Intravenous vasodilators including sodium nitroprusside and nitroglycerin have been the traditional treatment for PH in the patient under general anesthesia. Although both drugs decrease PVR, these drugs are nonselective and therefore often decrease systemic blood pressure, which can impair RV perfusion and cause ischemia.[19] In PH, RV perfusion occurs predominately in diastole, therefore, the risk of RV ischemia and failure is increased in the presence of systemic hypotension.[19] In addition, these drugs can reduce the protective effect of hypoxic pulmonary vasoconstriction secondary to dilation of pulmonary vessels that supply poorly ventilated alveoli.[19] Therefore, the administration of a selective pulmonary vasodilator may be needed.

Pulmonary vasodilators used in the management of PH include prostaglandins and inhaled nitric oxide (INO). Prostaglandins are effective in reducing pulmonary arterial pressure and PVR as well as increasing cardiac index and RV function, compared with nitroglycerin and sodium nitroprusside; however, prostaglandins are not selective for pulmonary circulation when administered

intravenously and may cause systemic hypotension.[19] Inhaled nitric oxide vasodilates the pulmonary vasculature without causing secondary systemic hypotension. The extremely short duration of action of INO allows this inhaled gas to relax the smooth muscles of pulmonary vessels perfusing the ventilated lung.[19] Therefore, blood flow is increased only in the ventilated areas of the lungs, leading to reduction in intrapulmonary shunting, which improves ventilation perfusion and increases arterial oxygenation. The rapid termination of INO's action by red blood cells prevents downstream relaxation of systemic vessels thereby preserving coronary perfusion pressure and oxygen delivery to the heart. The efficacy of INO is greater in patients with elevated PVR and depends on vascular reactivity.

Postoperative Management

The focus of postoperative management is to prevent complications. The postoperative management requirements will depend on the surgical procedure and the patient's WHO functional classification and collaboration with the pulmonologist or cardiologist may be necessary. To prevent worsening RV dysfunction and failure, careful attention to maintaining euvolemia, oxygen levels, and acid-base status are necessary.[22] Administration of PH medications should be continued postoperatively, which may require alternative medications or delivery routes depending on the patient's current status and ability to swallow.[22] In addition, pain control is essential to minimize sympathetic nervous system activation, which could worsen symptoms related to PH.

Conclusions

Patients diagnosed with PH scheduled to undergo noncardiac surgery require a thorough preoperative assessment and clearance from a cardiologist, or a pulmonary or critical care physician. In addition, the pharmacy department should be alerted to the potential need for selective pulmonary vasodilators to ensure availability. The severity of the patient's PH will determine the diagnostic and laboratory testing required. The anesthetic and perioperative management will likewise be determined by the patients' WHO classification, which indicates the severity of the disease. All health care providers involved in the perioperative management of the patient with PH must be knowledgeable about the steps that can be taken to maintain hemodynamic stability during the perioperative period. The perioperative health care team must work together to ensure that measures are taken to reduce the likelihood of an exacerbation of PH during the perioperative period.

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1.5 Contact Hours

Purpose of the Journal of PeriAnesthesia Nursing: To facilitate communication about and deliver education specific to the body of knowledge unique to the practice of perianesthesia nursing.

Outcome of this CNE Activity: To enable the nurse to increase knowledge on the care of the patient with pulmonary hypertension

Target Audience: All perianesthesia nurses.

Article Objectives

1. Describe the pathophysiology of pulmonary hypertension (PH).
2. Discuss the perioperative management of patients with PH.
3. Describe pharmacologic and nonpharmacologic interventions that can be used in the perioperative management of patients with pulmonary hypertension.

Accreditation

American Society of PeriAnesthesia Nurses is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center's Commission on Accreditation.

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