Anesthesia and Pulmonary Hypertension
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Abstract
Anesthesia and surgery are associated with significantly increased morbidity and mortality in patients with pulmonary hypertension due mainly to right ventricular failure, arrhythmias, postoperative hypoxemia, and myocardial ischemia. Preoperative risk assessment and successful management of patients with pulmonary hypertension undergoing cardiac surgery involve an understanding of the pathophysiology of the disease, screening of patients at-risk for pulmonary arterial hypertension, analysis of preoperative and operative risk factors, thorough multidisciplinary planning, careful intraoperative management, and early recognition and treatment of postoperative complications. This article will cover each of these aspects with particular focus on the anesthetic approach for non-cardiothoracic surgeries. (Prog Cardiovasc Dis 2012;55:199-217) © 2012 Elsevier Inc. All rights reserved.

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Introduction
Advances in the understanding of the pathogenesis and pathophysiology of pulmonary hypertension (PH) and the availability of new drug therapies for pulmonary arterial hypertension (PAH) have led to improved survival and increased awareness of this life-threatening condition. It has been known for many years that non-cardiac surgery, particularly Cesarean section for parturient woman with Eisenmenger’s Syndrome (ES), has been associated with high mortality of up to 70%. PH is also well known to complicate heart disease, and morbidity and mortality with cardiac surgery in such patients are increased. Conversely, data regarding the risk factors and outcomes of PH patients undergoing non-cardiac surgery have been scarce, probably because PH may have been occult or overlooked pre-operatively, whereas the presence of PH before cardiac surgeries is often identified with routine pre-operative testing. Data are now mounting about the risks of anesthesia and surgery in patients with PH, and this article will focus on the peri-operative management of patients with PH undergoing non-cardiothoracic surgery.

To date, there have been five retrospective studies reporting outcomes following non-cardiac surgery in patients with PH. Each of the studies varied in the diagnostic methods and definitions of PH used, the causes and severity of PH, and whether or not a control population was included. Perioperative morbidity occurred in 15%–42% of patients, and included post-operative respiratory failure (7%–28%), heart failure (10%–13.5%), hemodynamic instability (8%), dysrhythmias (12%), renal insufficiency (7%), sepsis (7%–10%), ischemia/myocardial infarction (4%), delayed tracheal extubation (8%–21%), longer ICU and total hospital length of stays, and a trend towards greater 30 day readmissions (16.7% and 7.8% in PH vs non-PH patients, respectively; p = 0.08, OR 2.4). In-hospital mortality was as low as 1% in a study that included mostly patients with PH related to left heart failure, however mortality rates in the
remaining four studies were between 7% and 10%. Interestingly, perioperative mortality with non-cardiac surgery was the same (7%) in a study that included only patients with mild–moderate pre-capillary PH, as it was in another study of patients with severe PAH (Eisenmenger’s syndrome), however both studies were small. It now seems clear that patients with PH of any etiology and severity, not just the rare disease PAH, have increased risk of perioperative morbidity and mortality with both cardiac and non-cardiac surgeries. Importantly, however, is that the perioperative management of patients with PH varies drastically, depending upon the etiology and severity of the disease. Successful management of the perioperative patient with PH is complex and requires a thorough understanding of the pathophysiology of PH and right ventricular (RV) function along with multiple steps that need to be taken, including recognition of the disorder, especially in patients at-risk for developing PAH (e.g. connective tissue disease, portal hypertension, congenital heart disease, and HIV infection), identification of the underlying cause(s), assessment of the severity of disease, assessment of the risks versus benefits of anesthesia and surgery, development of an anesthetic plan, and vigilant monitoring in the critical care setting for the early recognition and treatment of any postoperative complications.

Understanding pulmonary hypertension: definitions and classification

PH is defined with direct, invasive measurement via right heart catheterization as an elevated mean pulmonary artery pressure (MPAP) > 25 mm Hg. It is important to understand that PH is a disorder associated with many potential etiologies in which there is elevation of the pulmonary artery pressure (PAP) that results from an increase in: 1) resistance to blood flow within the pulmonary arteries (i.e. pulmonary vascular resistance, PVR), 2) pulmonary venous pressure from left heart disease, 3) pulmonary blood flow or 4) a combination of these elements.

Hemodynamic classification of PH

In hemodynamic terms (Table 1), PH related to increased PVR ≥ 3.0 Wood units (WU) without significant elevation of the left atrial pressure (LAP) or its surrogate, pulmonary capillary wedge pressure (PCWP) (i.e. PCWP ≤ 15 mmHg), is referred to as “pre-capillary” PH because the location of pressure elevation lies proximal to the pulmonary capillary bed within the pulmonary arteries. “Post-capillary” PH (also
known as “pulmonary venous”, “passive”, or “congestive” PH) is the hemodynamic profile resulting from left atrial pressure (LAP) elevation related to any cause of left heart failure (LHF). In pure post-capillary PH, the elevated LAP is passively transmitted backwards into the pulmonary veins and arteries, leading to elevated pulmonary artery pressure (PAP), and it is characterized by a PCWP > 15 mmHg with normal PVR and transpulmonary gradient (TPG; TPG = MPAP − PCWP). “Mixed” PH (i.e. mixed pre- and post-capillary), also known as “reactive” PH, results from chronic pulmonary venous hypertension that is nearly always related to left heart failure (LHF) and leads to pulmonary arterial vasconstriction and vascular remodeling and rise in PVR. This type of PH is characterized by an increased PCWP > 15 mmHg (often > 18 mmHg), PVR to ≥ 2.5–3.0 WU and a TPG of ≥ 12–15 mmHg. In these cases, the elevation in MPAP is out of proportion to the degree of PCWP elevation, hence the popular term “PH out of proportion to left heart disease” that is also often used to describe this condition. Mixed PH may further be described as “vasoreactive” or “fixed,” depending on the reversal of TPG and PVR with vasodilators and diuretics (or a left ventricular assist device). Rarely, increased pulmonary blood flow from a systemic-to-pulmonary shunt or high cardiac output state (e.g. anemia, sepsis, portal hypertension, thyrotoxicosis, chronic hemodialysis for end-stage renal disease, and some chronic myeloproliferative disorders) leads to PH without an elevation in PCWP or PVR. The severity of PAP elevation on the basis of the MPAP is characterized as mild (25–40 mmHg), moderate (41–55 mmHg), or severe (> 55 mmHg). Key measures for evaluating PH are right atrial pressure (RAP), central venous pressure (CVP), PCWP, cardiac output (CO), cardiac index (CI), mixed venous O2 saturation, and pulmonary and systemic vascular resistance calculations. The CVP and CI are very important parameters to assess during RHC, as markedly elevated CVP and reduced CI are indicative of right ventricular failure and poor survival in patients with PAH.

### Hemodynamic definitions of pulmonary hypertension

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<th>Definition</th>
<th>Hemodynamic Characteristics</th>
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<tr>
<td>PH</td>
<td>MPAP &gt; 25 mmHg</td>
<td>ALL</td>
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<tr>
<td></td>
<td>CO normal, reduced, or high*</td>
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<tr>
<td>Pre-capillary PH</td>
<td>PCWP/LVEDP ≤ 15 mmHg</td>
<td>1. PAH</td>
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<tr>
<td></td>
<td>TPG ≥ 12–15 mmHg</td>
<td>3. PH due to lung disease and/or hypoxemia</td>
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<tr>
<td>Post-capillary PH</td>
<td>PCWP/LVEDP &gt; 15 mmHg, PVR ≤ 3 WU</td>
<td>4. CTEPH</td>
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<tr>
<td></td>
<td>TPG &lt; 12 mmHg</td>
<td>5. PH with unclear or multifactorial mechanisms</td>
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<tr>
<td>Mixed PH</td>
<td>PCWP/LVEDP &gt; 15 mmHg, PVR &gt; 3 WU</td>
<td>2. PH owing to LHD</td>
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<tr>
<td>“Reactive”†</td>
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<tr>
<td>“Non-reactive”/“fixed”‡</td>
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All values measured at rest. PH = pulmonary hypertension; MPAP = mean pulmonary artery pressure; WHO = World Health Organization; CO = cardiac output; PCWP = pulmonary capillary wedge pressure; LVEDP = left ventricular end diastolic pressure; PVR = pulmonary vascular resistance; TPG = transpulmonary gradient; WU = Wood Units; PAH = pulmonary arterial hypertension; CTEPH = chronic thromboembolic PH; LHD = left heart disease.

* High CO can be present in cases of portal hypertension (PoPH; portopulmonary hypertension), hyperthyroidism, anemia, sepsis, systemic-to-pulmonary shunts (pulmonary circulation only), etc.

† PVR and TPG reverse with vasodilators and/or normalization of PCWP/LVEDP.

‡ PVR and TPG remain elevated despite normalization of PCWP/LVEDP with vasodilators, diuretics, and/or ventricular assist devices.

### WHO clinical classification of pulmonary hypertension

Table 2 outlines the updated World Health Organization (WHO) clinical classification of PH from the Dana Point meeting in 2008. It is important to note that WHO Group 2 PH from LHF is managed very differently than PAH and other etiologies of pre-capillary PH, and it can easily be distinguished hemodynamically with heart catheterization by the presence of elevated PCWP and/or LVEDP. Thus, the measurement of left ventricular filling pressure (PCWP and/or directly measured LVEDP) becomes the most critical aspect of defining the nature of PH and its treatment, and for this reason pressure tracings during heart catheterization should be reviewed independently by the interpreter for accuracy (end-expiratory rather than digitized mean PCWP).

Although many principles in the peri-operative management of RV failure and PH are common to any etiology of PH, there are critical differences that should be understood and recognized when it comes to the use of PAH therapies. One of the most important aspects relates to the effects of pulmonary vasodilators therapies in certain types of PH. While pulmonary vasodilators can have favorable responses and have been proven to be...
Table 2
WHO clinical classification of pulmonary hypertension (Dana Point, 2008).

1. Pulmonary arterial hypertension (PAH)
   1.1 Idiopathic PAH (IPAH)
   1.2 Heritable
      1.2.1 BMPR2
      1.2.2 ALK, endoglin (with or without hereditary hemorrhagic telangiectasia)
      1.2.3 Unknown
   1.3 Drug and toxin induced
   1.4. Associated with:
      1.4.1 Connective tissue diseases
      1.4.2 HIV infection
      1.4.3 Portal hypertension
      1.4.4 Congenital heart diseases
      1.4.5 Schistosomiasis
      1.4.6 Chronic hemolytic anemia
   1.5. Persistent pulmonary hypertension of the newborn
1'. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
2. Pulmonary hypertension owing to left heart disease
   2.1. Systolic dysfunction
   2.2. Diastolic dysfunction
   2.3. Valvular disease
3. Pulmonary hypertension owing to lung diseases and/or hypoxemia
   3.1. Chronic obstructive pulmonary disease
   3.2. Interstitial lung disease
   3.3. Other pulmonary diseases with mixed restrictive and obstructive pattern
   3.4. Sleep-disordered breathing
   3.5. Alveolar hypoventilation disorders
   3.6. Chronic exposure to high altitude
   3.7. Developmental abnormalities
4. Chronic thromboembolic pulmonary hypertension (CTEPH)
5. Pulmonary hypertension with unclear multifactorial mechanisms
   5.1. Hematologic disorders: myeloproliferative disorders, splenectomy
   5.2. Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
   5.3. Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
   5.4. Other: tumor obstruction, fibrosing mediastinitis, chronic renal failure on dialysis
5.4. Other: tumoral obstruction, pulmonary embolism (adenopathy, tumor, chronic renal failure on dialysis)
   5.5. Other: pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis)

beneficial in treating patients with PAH, they can have deleterious consequences when used in patients with non-PAH PH. For example, pulmonary vasodilator therapies can lead to a rise in pulmonary venous pressure and precipitate pulmonary edema when they are administered to patients with post-capillary PH from heart failure with preserved ejection fraction (HFpEF) or heart failure with reduced ejection fraction (HFrEF) (WHO Group II PH) perhaps with the exception of phosphodiesterase type-5 inhibitors (PDE5I), which are showing some promise in this group. In addition, systemically administered pulmonary vasodilators when given to hypoxic patients with parenchymal lung disease can increase perfusion to poorly ventilated lung regions and increase ventilation–perfusion mismatching, resulting in worsened hypoxemia.

Pre-operative evaluation and management

When contemplating surgery in a patient with PH, the perioperative evaluation should include an assessment of risk that takes into consideration the type of surgery, patient’s functional status, severity of disease including right ventricular function, and the patient’s comorbidities. In addition, patients without a history who are at high risk for PH (e.g. scleroderma spectrum of diseases, obesity and obstructive sleep apnea, and HFpEF) should be screened for symptoms and signs of PH, particularly if they are being considered for intermediate- or high-risk surgery.

High-risk surgical procedures include those that are associated with the potential for rapid blood loss, significant perioperative systemic inflammatory response (e.g. cardiopulmonary bypass), venous air embolism, carbon dioxide (CO2) (e.g. laparoscopic surgery), fat or cement emboli (e.g. orthopedic surgery), and loss of lung blood vessels (e.g. lung resection). Emergency procedures, ASA class ≥ 2, intermediate or high risk surgery, longer duration of surgery and anesthesia (> 3 h), coronary artery disease (CAD), chronic renal insufficiency, history of pulmonary embolism (PE), NYHA functional classification ≥ II, and PAP have all been identified as independent predictors of morbidity and/or mortality in patients with PH undergoing non-cardiac surgery (Table 3). Additionally, markers of RV strain, including right-axis deviation (RAD) (p = 0.02), RV hypertrophy (RVH) (p = 0.04), RV index of myocardial performance index (RVMPI) ≥ 0.075 (p = 0.03), RV systolic pressure/systolic blood pressure ratio ≥ 0.66 (p = 0.01), as well as the intra-operative use of vasopressors (p = < 0.01), were predictors of post-

Table 3
Risk factors for morbidity and mortality in non-cardiac surgery.

Patient factors
- History of PE, CAD, CKD
- NYHA/WHO FC ≥ II
- RAD on ECG
- Echo parameters: RAD ≥ 0.75
- Hemodynamics: higher PAP, RVSP/SBP ratio > 0.66

Operative factors
- Emergency surgery
- Intermediate or high risk operations
- Higher ASA class
- Longer duration of anesthesia
- Intra-operative vasopressor use

This table summarizes the risk factors identified from studies of patients with pulmonary hypertension undergoing non-cardiac surgery.

PE = pulmonary embolism, CAD = coronary artery disease, CKD = chronic kidney disease, NYHA = New York Heart Association, WHO = World Health Organization, RAD = right axis deviation, ECG = electrocardiogram, RVH = right ventricular hypertrophy, RVMPI = right ventricular myocardial performance index, PAP = pulmonary artery pressure, SBP = systolic blood pressure, ASA = American Surgical Association
operative mortality on univariate analysis in one study by Ramakrishna et al. In a study by Kaw et al., which included 96 patients with PH and 77 patients without PH who underwent diagnostic heart catheterization and hemodynamic classification prior to non-cardiac surgery, 25 of 27 patients (92.5%) who had peri-operative complications were patients with PH. The only death in the study occurred in a patient whose MPAP was >45 mm Hg undergoing an intermediate-risk operation, and he/she developed post-operative congestive heart failure (CHF). Patients with pre-capillary PH had greater post-operative morbidity (41%) compared to patients with pure pulmonary venous or mixed PH from LHF (16% and 24%, respectively), although these differences were not statistically significant. Moreover, PA pulse pressure (p = 0.003) and PVR (p = 0.008) were associated with worse perioperative outcomes on univariate analysis, and recent reports have suggested that assessments of increased pulmonary vascular stiffness, decreased pulmonary compliance, which may be measured noninvasively by cardiac output divided by pulmonary artery pulse pressure, relative area change on cardiac magnetic resonance imaging (MRI) may be an indicator of poor outcomes in patients with PH. These results suggest that patients with an increased pulmonary artery pulsatile load are at greater risk for right ventricular pulmonary artery mismatch. It is notable, however, that in the study by Kaw and colleagues, the perioperative morbidity was high even among patients with purely pulmonary venous hypertension.

**Evaluation**

The pre-operative evaluation should include a thorough history and physical examination with special attention to signs and symptoms of right ventricular dysfunction. While dyspnea and generalized fatigue are the most common symptoms in patients with PAH, angina, near syncope and syncope are symptoms of advanced PAH disease. Syncope is a particularly ominous sign that portends a poor prognosis in PAH. Important exam findings to note include signs of right ventricular failure such as elevated jugular venous pressure (prominent V-waves are indicative of severe tricuspid regurgitation), right ventricular S3 gallop, hepatomegaly, abdominal swelling from ascites, and peripheral edema. Pulmonary crackles are indicative of either left-sided heart failure or interstitial lung disease rather than PAH.

Routine pre-operative tests include basic laboratory studies, electrocardiography, echocardiography, chest radiography, and consideration of right heart catheterization. If the etiology of PH has not already been established, additional studies should be considered in order to guide perioperative management. These include pulmonary function tests (PFT) and arterial blood gas analysis to evaluate for respiratory disease, ventilation/perfusion (V/Q) scan to exclude chronic thromboembolic PH (CTEPH), liver function tests, serologic studies for connective tissue disease and HIV infection to evaluate for diseases associated with PAH, and thyroid function testing.

Transesophageal echocardiography is an essential test to obtain pre-operatively, as it is the most useful and readily available noninvasive tool to evaluate right ventricular function in patients with PH. Anatomical and functional data, including both right and left ventricular size and function, valvular abnormalities, PAP estimate, and intracardiac shunts can be assessed. Depending on the severity of disease, patients with significant PH exhibit varying degrees of right ventricular enlargement and reduced systolic function. Intuitively, patients with marked right heart chamber enlargement and small, compressed left heart chambers have worse disease and are greater perioperative risk than patients with normal RV size and function. Objective measures of RV function that are useful include tricuspid plane annular excursion (TAPSE), right ventricular fractional area change, and the RV myocardial performance index. Paradoxical ventricular septal flattening occurring during systole is an indication of RV pressure overload, and it is a common finding in patients with significant PH. However, ventricular septal flattening during diastole indicates right ventricular volume overload, usually from RV failure and/or severe tricuspid regurgitation in patients with PH. Reduced LV systolic function and left atrial enlargement on echocardiography in patients with PH usually indicate that the PH is likely related to pulmonary venous hypertension. On the other hand, PH related to HFpEF can be a challenging diagnosis to make non-invasively and usually requires heart catheterization to assess the PCWP. However, many patients with significant pre-capillary PH from PAH, parenchymal lung disease, or CTEPH will have impairment of LV filling from ventricular interaction that manifests as Grade I LV diastolic dysfunction (impaired LV relaxation). On the other hand, moderate to severe LV diastolic dysfunction (i.e. pseudonormal or restrictive diastolic filling patterns) correlates with high left atrial pressure and strongly suggests that PH is related to left heart failure. The PA systolic pressure (PASP) can be estimated by using Doppler to measure the peak tricuspid regurgitant jet velocity. However, echo-Doppler estimates of PASP in PH patients can lead to both a significant under- or over-estimation of the true PAP when compared with catheterization. Agitated saline contrast not only aids in the estimation of PASP when the TR jet is incomplete and in the diagnosis of intracardiac congenital systemic-to-pulmonary shunts, but may also detect a patent foramen ovale, which can lead to right-to-left shunting in PH patients when the right atrial pressure is elevated. Echocardiographic predictors of a poor prognosis in patients with PAH include a severe right atrial enlargement, reduced TAPSE, higher Doppler global right ventricular index, left ventricular (LV) eccentricity index
(degree of interventricular septal flattening), and the presence of a pericardial effusion.34-36

**Pre-operative heart catheterization**

In cases where the patient has greater than mild PH by history and/or non-invasive assessment or if the patient is being considered for an intermediate- to high-risk operation, serious consideration should be given to performing a right heart catheterization for hemodynamic assessment of disease severity pre-operatively in order to guide perioperative management. In addition, RHC should be considered in patients who have evidence of significant PH (e.g. PASP > 50 mm Hg and/or RV enlargement) and who are at risk for both pre- and post-capillary PH, such as those with obesity, obstructive sleep apnea, scleroderma, or other risk factors for HFpEF (e.g. elderly, male gender, atrial fibrillation, left atrial enlargement), since the presence of pulmonary venous hypertension and severity of disease will alter perioperative management, particularly as it relates to the use of pulmonary vasodilators, inotidators and fluid management. Left heart catheterization should also be considered in patients suspected of having LHF, because many patients whose PCWP is not elevated actually have elevated LVEDP when measured directly, and they may be misclassified as having PAH.37 Depending on the urgency of surgery, the RHC can be done several weeks in advance so that PAH therapies in appropriate candidates can be initiated or optimized. For example, patients with idiopathic or associated PAH may benefit from pre-operative RHC followed by the initiation of intravenous prostanoid therapy if poor prognostic findings are demonstrated (e.g. high RAP, low CI, severely elevated PAP/PVR) prior to a higher risk surgery that cannot be delayed, such as orthopedic surgery. Patients with severe pulmonary venous hypertension may be optimized with appropriate diuresis, systemic vasodilators, and inotidators. In some cases, based mainly upon discussions between the PH specialist and anesthesiologist, a RHC may be done on the day of surgery with plans to defer surgery if severe hemodynamics are found versus retain the PA catheter to guide intra-operative management or remove the PA line if the hemodynamics are reassuring.

Acute vasoreactivity testing is routinely performed during the diagnostic right heart catheterization in patients with PAH in order to identify “vasoresponders” who are candidates for calcium channel blocker monotherapy.38,39 Pre-operative vasoreactivity testing may also be useful for perioperative planning in order to determine the degree of vasoreactivity and to predict the perioperative effectiveness of vasodilators such as inhaled nitric oxide. If the PVR does not decrease at all during testing, the pulmonary vascular disease is largely fixed/non-responsive and limits our perioperative interventions. Inhaled nitric oxide (iNO) is the preferred agent for acute vasodilator testing, but adenosine, epoprostenol, and inhaled iloprost can also be used. The efficacy of iNO depends on the baseline PVR and vasoreactivity, with greater response in patients with higher PVR, greater degree of vascular reactivity and worse RV function.40-42 Responsiveness to iNO may also reflect improved V/Q mismatch and improvement in hypoxic pulmonary vasoconstriction (HPV) in patients with parenchymal lung disease and a component of hypoxic PH (e.g., interstitial lung disease that is prevalent in the scleroderma patient population).

Dyspnea at rest, syncope, hemodynamic findings of severe RV failure (low CI, high RAP > 15 mmHg), metabolic acidosis, and marked hypoxemia are all signs of advanced, unstable disease and serious consideration should be given to cancelling or postponing the surgery until/unless improvement and stabilization can be achieved.

**Pre-operative hemodynamic optimization**

All attempts to lower PVR and improve RV function should be done prior to surgery, including maximizing medical therapy for PAH and heart failure, and preventing conditions that may cause acute deterioration. Examples include the initiation or augmentation of PAH specific therapies for patients with WHO Group I PH; administration of oxygen, bronchodilators, antibiotics, and steroids for patients with chronic obstructive pulmonary disease (COPD); use of BIPAP for patients with obstructive sleep apnea (OSA) and, diuretics, systemic vasodilators and other appropriate HF therapies for patients with WHO Group II PH. As a guide for management, Table 4 outlines the hemodynamic goals, which should be strived for throughout the perioperative period. If a patient has newly identified PH and the surgery cannot be delayed in order to establish the etiology and best treatment, a PDE5I such as sildenafil 20–40 mg three times daily, can be started pre-operatively as it has acute vasodilatory effects, right ventricular inotropy and has been safely administered to a broad spectrum of PH disease etiologies, although this has not been studied specifically for most non-PAH PH etiologies.

<p>| Table 4 |</p>
<table>
<thead>
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<th>Perioperative hemodynamic goals.</th>
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<tr>
<td>• MAP ≥ 55 to 60 mmHg</td>
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<tr>
<td>• SBP ≥ 80 mmHg</td>
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<tr>
<td>• SvO2 saturation 92% to 100%</td>
</tr>
<tr>
<td>• RAP &lt; 10 mmHg</td>
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<tr>
<td>• MPAP &lt; 35 mmHg</td>
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<tr>
<td>• PVR/SVR ratio &lt; 0.5 (if possible)</td>
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<tr>
<td>• PCWP 8 to 12 mmHg</td>
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<td>• CI ≥ 2.2 L/min/m²</td>
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This table summarizes optimal perioperative hemodynamic conditions. Not all of these hemodynamics are achievable in patients with pulmonary hypertension, however they represent goals for the medical management of patients during the perioperative period. MAP = mean arterial pressure, SBP = systolic blood pressure, SvO2 = systemic venous oxygen saturation, RAP = right atrial pressure, MPAP = mean pulmonary arterial pressure, PVR = pulmonary vascular resistance; SVR = systemic vascular resistance, PCWP = pulmonary capillary wedge pressure, CI = cardiac index.
Multidisciplinary planning for surgery

Owing to the complexity of most PH treatment protocols, pre-operative coordination among the patient’s care team is vital and can take considerable time. The perioperative management of PH patients frequently involves a multidisciplinary team approach that includes physician subspecialists such as anesthesiologists, cardiologists, and pulmonary/critical care physicians, in addition to allied healthcare team members (nurses, respiratory therapists, and pharmacists). For all except the lowest risk PH patients and procedures, one of the most critical aspects of the pre-operative planning involves the identification of a highly qualified anesthesiologist with experience in managing patients with PAH, complex hemodynamics, and transesophageal echocardiography (TEE), such as a cardiovascular or critical care anesthesiologist. Generally speaking, patients with PH, particularly those with PAH, should be referred to a tertiary care center for procedures requiring anesthesia. Moreover, in patients with severe PH, RV failure, and chronic hypoxemia requiring moderate or deep sedation for procedures (e.g. endoscopy, TEE, teeth extraction), consideration should be given to having the procedure done with an experienced anesthesiologist present. Also extremely important is the post-operative “hand-off” from the intra-operative team (surgeon and anesthesiologist) to the post-operative team (usually the critical care physician and PH specialist).

Chronic PAH therapies, including PDE5I, endothelin receptor antagonists (ERA), and prostanoids, should be continued throughout the perioperative period. Patients on chronic inhaled prostacyclin analogues should receive treatment before surgery, and if they are unable to continue inhaled therapy after surgery (e.g. intubated), consideration should be given to the administration of iNO, intermittent nebulized prostacyclin, continuously inhaled Flolan, versus intravenous prostanoids. Although prostanoids cause platelet inhibition, their use does not cause significant bleeding complications with surgery. Coumadin should be discontinued before the procedure without the need for bridging with heparin unless there is another indication (e.g. history of PE, hypercoagulable state, mechanical heart valve, etc.). Patients should receive prophylactic anticoagulation perioperatively to prevent deep vein thrombosis and pulmonary thromboembolism.

Intra-operative management

General principles: RV–PA mechanical coupling

As with both pre- and post-operative management, the primary intra-operative goal for patients suffering from PH is to maintain optimal mechanical matching between the RV and pulmonary circulation. Ultimately, this requires an understanding of intra-operative events that can affect RV afterload, inotropy, and oxygen supply/demand relationships.

RV afterload

It is conceptually clear that chronic PH opposes ejection from the RV leading to chamber dilation, hypertrophy, increased wall stress, and reduced ejection fraction. Less apparent, however, is the fact that a variety of common intra-operative events can acutely alter both
the magnitude and nature of this load. For example, the seemingly simple transition from spontaneous respiration to positive pressure mechanical ventilation produces cyclic changes in RV afterload that affect volume and pressure (Fig 1). This effect can be amplified by patient position (Trendelenburg, prone), the addition of positive end-expiratory pressure (PEEP), and surgical manipulations such as pneumoperitoneum (see below). Ultimately, ventilatory changes in afterload can have clear effects on RV preload, stroke volume and ejection fraction (Fig 1). The relationship between lung volume and PVR during mechanical ventilation is U-shaped with PVR being minimal at functional residual capacity and increased at both large and small lung volumes. At low lung volumes, alveolar hypoxia and hypercarbia cause HPV whereas hyperinflation of the lungs leads to compression of the intra-alveolar vessels with marked increases in PVR. Likewise, PEEP > 15 mm Hg increases PVR. In addition to the acute pulmonary vascular effects of hypoxia and/or hypercarbia, patients can also be subjected to venous emboli arising from air, thrombi, or particulate matter forced into the circulation (particularly during orthopedic surgery) intra-operatively. Finally, surgical procedures involving the lung can have direct effects on both the pulmonary circulation and myocardial contractile reserve that persist postoperatively.

It is important to appreciate that while RV afterload is often summarized as PVR, this steady-state variable (i.e., defined by mean pressure and mean flow) is largely dictated by small vessels and may not adequately incorporate the added pulsatile load presented to the RV by anesthetics or intraoperative manipulation of large elastic vessels. Furthermore, intra-operative events such as positive pressure ventilation, position, or surgical techniques may augment the underlying impact of vasoconstriction and vascular remodeling on pressure and flow wave reflection, thus imposing a greater reflective component to RV afterload as well. For example, as shown in Fig 2, while compressing the left branch of the PA – as may be done during surgery in the chest – has only a modest acute effect on the absolute value for maximal RV pressure, it does produce a distinct qualitative change in the RV pressure waveform, indicative of changes in load not summarized by PVR. While the highest pressure is attained early in systole at baseline, during left PA compression the highest pressure is late in systole suggesting the enhanced contribution of reflected waves (“late phase load”). Consistent with a predominant effect on large vessels, there is a relatively greater increase in characteristic impedance (Zc), an index of large vessel pulsatile load, than PVR. However, also evident in Fig 2 is the fact that simultaneously measured PA pressure does not as clearly reflect the qualitative shift to a late-phase load evident in the RV pressure waveform. The potential clinical implication of this observation is that when a PA catheter positioned more distally in the circulation is used to monitor pressure intra-operatively, its ability to appreciate acute qualitative changes in RV pressure that reflect more than just alterations in PVR may be dampened or lost.

**RV inotropy**

Two main aspects of intra-operative care can affect myocardial contractile performance via both direct and

![Fig 2. Right Ventricular and Pulmonary Arterial Pressures Before and During Compression of the Left Pulmonary Artery. Top panel. Right ventricular (RV) and pulmonary arterial (PA) pressures before and after compression of the left PA in an experimental animal (swine). Changes in both the amplitude and morphology of the pressure waveforms are evident along with calculated changes in pulmonary vascular resistance (PVR) and characteristic impedance (Zc). Bottom panel. Changes in the RV pressure—volume relationship produced by compression of the left PA are depicted.](image-url)
indirect mechanisms: 1) depression by anesthetics and 2) acute changes in sympathetic/parasympathetic tone.

Anesthetic-induced myocardial depression

Many of the drugs used both for induction and maintenance of anesthesia have well-described direct effects on inotropy.\(^{48,49}\) In general, anesthetic drugs have been found to directly affect either calcium cycling by the myocyte, or the sensitivity of contractile proteins to the amount of calcium released into the cytoplasm during systole. In addition, anesthetics tend to have depressive effects on the autonomic nervous system that can indirectly influence contractility. The direct negative inotropic effects of inhaled anesthetics in particular are dose related, and potency for this response varies among different drugs; halothane – now rarely used – produces the greatest effect. To date, the literature focuses primarily on the effects of anesthetic drugs on the LV and suggests that the overall hemodynamic impact of decreased contractility is offset to some degree by a simultaneous decline in afterload. However, studies evaluating the effects of inhaled anesthetics such as isoflurane, sevoflurane, and desflurane on the RV have provided a different picture.\(^{46,50,51}\) For example, as shown in Fig 3, while isoflurane has similar potency for depressing contractility in both ventricles, it has disparate effects on afterload, particularly when pulsatile components are assessed. Ultimately this produces different dose-dependent effects on the total work each ventricle has to perform in order to move blood into the circulation. Complicating things further are data showing regional differences in the negative inotropic effects of volatile anesthetics on the RV, i.e. greater relative depression of the outflow than inflow tract.\(^{51,52}\)

Experimental data also indicate that two commonly used intravenous anesthetics, propofol and etomidate, can have direct depressive effects on myocardial contractility, albeit at relatively high concentrations.\(^{48,53}\) The clinical significance of these observations remain somewhat controversial, particularly as they apply to patients with PH.\(^{54}\) Alternatively, concerns have been raised about the use of ketamine, not because of negative inotropic effects (direct effects are modest), but due to the possibility of sympathetic stimulation and pulmonary vasoconstriction.\(^{54}\) However, there are clinical data to suggest that when ventilation is maintained to prevent hypercarbia and optimize acid–base balance, this effect is negated.\(^{55}\) and that ketamine may, in fact, have pulmonary vasodilating properties.\(^{56}\)

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**Fig 3. The Comparative Dose-related Effects of Isoflurane on Biventricular Function.**\(^{50}\) Preload recruitable stroke work (PRSW) was used as an index of contractility, and steady-state (frequency independent) and characteristic impedance (frequency dependent) regarded as indices of afterload. The disparity of effects on each ventricle is evident, with there ultimately being a marked difference in relationship between total chamber work ($W_T$) and cardiac output (CO). (Data adapted from Price et al.\(^{17}\)).
Sympatho-vagal balance

Neuraxial anesthesia (spinal, epidural) has been safely used in patients with PH and may have advantages in some populations, (i.e. obstetrics). Nonetheless, autonomic nervous fibers are more sensitive to blockade by local anesthetics than sensory or motor fibers, and there is always the possibility that the level of autonomic blockade could include cardiac innervation arising from the upper thoracic portion of the spinal cord. At the same time, since cardiac parasympathetic innervation originates in the cranial region, function of these fibers can remain intact. Ultimately, an acute shift in sympatho-vagal balance can occur. While relatively well tolerated in normal patients, the consequences may be more profound in those dependent upon high sympathetic tone for inotropic and/or chronotropic augmentation.

Acute changes in myocardial oxygen supply/demand

Relative to the RV stresses imposed by everyday life (i.e., exercise, fever), perhaps the most unique challenge encountered intra-operatively is the combination of increased RV afterload and transient systemic hypotension. Between the direct cardiovascular effects of anesthetic drugs, the indirect impact of withdrawing sympathetic tone, effects of mechanical ventilation, and intraoperative manipulation of the heart and/or great vessels, periods of transient hypotension are common during anesthesia and surgery. While these effects are generally treated rapidly and have less global impact on the LV – where vasodilation and myocardial depression tend to decrease mechanical work and oxygen consumption – similar unloading is not as prominent for the RV; most anesthetic drugs produce less pulmonary than systemic vasodilation, and as noted above, the imposition of positive pressure ventilation tends to augment afterload during the ventilatory cycle. Changes in coronary perfusion patterns in the setting of PH and RV hypertrophy and the propensity for RV ischemia even in the absence of significant coronary disease have been well described. Of particular note is the transition to greater dependence upon diastolic coronary flow as RV pressures and systolic wall tension rise. It is in this context of increased load and altered coronary perfusion patterns that systemic arterial hypotension may have greater impact on the RV than LV in the setting of PH.

Fundamentals of anesthetic management

There are obviously a variety of anesthetic techniques available — local, conscious sedation, regional (i.e., axillary block for surgery in the upper extremity), neuraxial (spinal, epidural), general. The decision of which one to use is dictated by a combination of the planned surgery, patient preference, and comorbidities. For the PH patient, there is the added dimension of a low tolerance for any degree of hypoxia and/or hypercarbia, which can complicate sedation, and the possibility of intra-operative events that may acutely worsen PH and disrupt what was a compensated state at baseline. For example, while many orthopedic procedures are amenable to neuraxial anesthesia, during surgery such as hip replacement there is substantial risk of intra-operative pulmonary emboli that can potentially precipitate instability and necessitate emergent tracheal intubation under suboptimal conditions. As such, a controlled general anesthetic with careful airway management and elective tracheal intubation is often preferred. Similarly, for patients with PH secondary to chronic hypoxia from intrinsic lung disease, obesity, or obstructive sleep apnea, careful consideration of a technique that optimizes airway patency and gas exchange is essential.

Regardless of technique, there are fundamental components of any anesthetic that must be considered in the patient with PH:

Basic preparation

For all PH patients, intravenous lines and syringes must be meticulously de-aired. The hypertensive pulmonary circulation is particularly sensitive to even small amounts of air that would generally be tolerated in a normal patient. In addition, patients with a patent foramen ovale are at risk for passage of air into the systemic arterial circulation as right atrial pressure may exceed that in the left atrium. Forced air-warming blankets, heat and moisture exchangers in the breathing circuit, and warmed IV fluids are all helpful in preventing hypothermia, which can inhibit physiologic HPV and lead to V/Q mismatching.

Airway management and ventilation

Whether administered by nasal cannula, face mask, laryngeal mask airway, or an endotracheal tube, all anesthetics should include supplemental oxygen. In addition to preventing hypoxemia, oxygen acts as a direct pulmonary vasodilator, and is frequently administered in high concentration. When using anesthetic techniques other than general, it is extremely important to assure airway patency and easy access to the airway should ventilation become compromised in any way. For general anesthesia, the initial induction represents a period of vulnerability since ventilation can become uncontrolled, and there is the potential for intense sympathetic stimulation if laryngoscopy is performed prior to achieving a deep level of anesthesia. As such, application of 100% oxygen by mask to fill the lung functional reserve capacity (FRC) prior to induction of anesthesia, and careful attention to anesthetic depth prior to laryngoscopy and tracheal intubation are especially important in patients with PH. An additional challenge is presented by the PH patient with obstructive sleep apnea or intrinsic lung disease with low FRC and diffusing capacity. In these situations, the airway must be very carefully evaluated pre-operatively, and the risks of sympathetic stimulation from “awake
Volumes at normal functional residual capacity. Between 5 and 10 cm H2O, and maintenance of lung to 35 mmHg or less, PEEP hyperventilation when necessary to achieve a PaCO2 of 30 the patient with PH should entail the use of higher FiO2, possible hypoxia-induced pulmonary vasoconstriction. CO2 analysis is useful as a trend, it is not an accurate procedures to allow for rapid hemodynamic control and avoid and promote.

Table 5 Perioperative ventilatory conditions to avoid and promote.

<table>
<thead>
<tr>
<th>Avoid pulmonary vasoconstrictors:</th>
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<tr>
<td>• Hypoxemia</td>
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<tr>
<td>• Inspiratory pressure &gt; 30 mm Hg</td>
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<tr>
<td>• High PEEP (&gt; 15 mmHg)</td>
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<td>• Hypercapnia</td>
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<td>• Acidosis</td>
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<th>Promote pulmonary vasodilation:</th>
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<tr>
<td>• Improve oxygenation (e.g. FiO2 1.0)</td>
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<tr>
<td>• Permissive hypocapnia (PaCO2 ≥ 30–35 mmHg)</td>
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<tr>
<td>• Alkalosis (pH &gt; 7.4)</td>
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<tr>
<td>• Optimal ventilatory volume</td>
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This table summarizes the conditions to avoid or promote during mechanical ventilation in patients with pulmonary hypertension. PEEP = positive end-expiratory pressure, FiO2 = fraction of inspired oxygen.

intubation” with fiberoptic bronchoscopy balanced against the benefit of avoiding a period of poor ventilation and possible hypoxia-induced pulmonary vasoconstriction.

After the airway is secured, ventilator management of the patient with PH should entail the use of higher FiO2, hyperventilation when necessary to achieve a PaCO2 of 30 to 35 mmHg or less, PEEP < 15 mmHg (preferably between 5 and 10 cm H2 O), and maintenance of lung volumes at normal functional residual capacity.佩佩lac.

Table 5 outlines the perioperative ventilatory conditions to avoid and promote.

**Monitoring**

Invasive arterial pressure monitoring is indicated for most procedures to allow for rapid hemodynamic control and blood sampling for gas analysis. While standard end-tidal CO2 analysis is useful as a trend, it is not an accurate reflection of PaCO2 in patients with increased dead space ventilation. As such, arterial blood gas sampling can be beneficial for assuring adequate ventilation and normocarbia.

Pulmonary artery catheters are not generally indicated for low-risk procedures as the risks probably outweigh the benefits. However, as noted below, even seemingly simple minimally invasive procedures can impose acute intra-operative challenges to the RV, and these need to be considered when planning intra-operative monitoring and possible pharmacotherapy. An introducer catheter for central venous access may be placed at the start of a procedure so that CVP can be monitored and a PA catheter subsequently added intra-operatively, if needed. This also allows for venous blood sampling to assess oxygen saturation as an index of cardiac output adequacy. In cases where significant blood loss or changes in RV afterload are anticipated, PA catheter insertion prior to beginning the procedure may be helpful in guiding perioperative fluid and vasomodulating therapies.佩佩lac. During the intra-operative period, maintenance of euvolemia is particularly challenging because intravascular volume is constantly in flux due to the combination of blood loss and evaporation from the skin, breathing circuit, and surgical field (especially in open abdominal surgery). PA catheters with the ability to monitor continuous mixed venous saturation offer real-time assessment of oxygen extraction and global cardiac performance as well as monitoring trends. However, thermodilution measurement of cardiac output based either upon cold bolus injection via a PA catheter or continuous “reverse” heat pulses from a coil may have questionable utility in the setting of RV dilation, due to concurrent tricuspid regurgitation.佩佩lac. Accuracy of newer devices based upon arterial pulse contour analysis in PH patients remains unclear, but has been questioned.佩佩lac. A more accurate measurement may be obtained by the Fick method, but this technique is relatively slow and tedious, and provides only a snapshot that may not be of great value in guiding acute therapy intra-operatively. Recent studies suggest that a new “Bioreactance” method for continuously measuring cardiac output non-invasively in ambulatory patients with PH provides data that are remarkably similar to intermittent Fick measurements.佩佩lac. However, intraoperative accuracy of this device in PH patients remains to be determined.

An adjunct or alternative to intraoperative PA catheter monitoring is transesophageal echocardiography (TEE).佩佩lac. While routine use is not clearly indicated, in cases involving significant blood loss and rapid intravenous fluid administration, TEE can be helpful in evaluating right heart size and function, as well as stroke volume. In the setting of systemic hypotension, the combination of TEE and CVP can rapidly distinguish between hypovolemia and right heart failure. In addition, acute changes in systolic PA pressure can be estimated when a jet of tricuspid regurgitation is present, and estimation of the mean PA pressure has also been described.佩佩lac. Finally, continuous qualitative evaluation of biventricular function and ventricular interdependence can best be assessed with TEE during times of intra-operative stress.

**Hemodynamics**

During anesthesia and surgery, pharmacological maintenance of systemic and coronary artery perfusion pressure is often needed to compensate for anesthetic or procedure-induced hypotension. The challenge of evaluating and maintaining euvolemia was previously discussed. Apart from hypovolemia, management of hypotension in PH patients should be primarily directed toward vasopressor therapy rather than downward titration of any IV pulmonary vasodilator the patient may be receiving. As noted above, chronic PH leads to remodeling of the right heart and changes in the pattern of coronary perfusion, making it particularly prone to ischemia in the setting of systemic hypotension. In general, the vasoconstrictors phenylephrine and vasopressin can restore adequate aortic root pressure without marked increases in PVR. Vasopressin in particular has been noted in experimental models to bind to peripheral V1 receptors and cause
systemic vasoconstriction while stimulating nitric oxide release and vasodilation in the pulmonary circulation, thus lowering the pulmonary to systemic vascular resistance (PVR/SVR) ratio. For patients with frank RV dysfunction, vasopressor agents with inotropic properties (e.g. norepinephrine or epinephrine) are generally preferred. RV afterload reduction using pulmonary dilator therapy can also be helpful to improve RV function. While systemically administered vasodilators such as IV prostanooids, sodium nitroprusside, and nitroglycerin reduce PVR (the former being most appropriate in PAH patients and the latter two reserved for patients with left heart failure), systemic effects limit their use in patients receiving anesthesia. Inhaled prostanooids and nitric oxide are more suitable for use in the operating room because of their pulmonary selectivity. iNO is rapidly inactivated by hemoglobin and has no systemic effects. It has the added potential benefit of increasing PaO2 by reaching well-ventilated regions of the lung and improving ventilation–perfusion matching, which can be beneficial not only in PAH patients but also in patients with parenchymal lung disease. Although there are reports of inhaled prostanooids and iNO being used successfully to reduce PVR in patients with left ventricular dysfunction, they should generally be used with caution in such patients because of the risk of precipitating pulmonary edema.

The immediate post-operative period

For patients that have undergone a general anesthetic, the risks and benefits of extubation in the operating room must be considered on a case-by-case basis. After a lengthy procedure requiring a large volume of intravenous fluid or in the presence of any indication of right heart failure, it is advisable to delay extubation until effective diuresis can occur. Post-operatively, PH patients require a well-planned pain management strategy to minimize sympathetic activation and increases in PVR and immediate post-operative monitoring in an intensive care unit. Epidural analgesia, peripheral nerve blocks, and non-opioid pain medications are useful post-operative pain management strategies. In addition to pain, immediate post-operative care should include close attention to body temperature since hypothermia and shivering can acutely increase PVR. Patients with OSA should have their home positive pressure airway device readily available in the post-anesthesia care unit. While recovering from general anesthesia, OSA patients may benefit from augmentation of their minute ventilation with CPAP or BIPAP. Arterial blood pressure and PA catheter monitoring can be very useful to follow acute hemodynamic changes.

Special Intra-operative Case Considerations

In addition to the general practices just described, certain surgical procedures present additional challenges for PH patients. The following is a brief overview of the perioperative implications of such procedures.

Orthopedics

Debilitating arthritis and trauma are common indications for orthopedic surgery in all patients including those with PH. Peripheral nerve blocks can provide excellent anesthesia for surgery on the feet and upper extremities, without the hemodynamic complexities of general anesthesia. Conscious sedation is usually used to augment patient comfort during surgery, but as noted above, particular attention must be paid to insure adequate ventilation during sedation since even mild hypercapnia and hypoxia can lead to significant increases in PVR. The highest risk orthopedic procedures for PH patients include hip and knee joint replacements, and hip fracture repairs. Joint replacements in the setting of PH of all etiologies carry a very high morbidity and mortality. Accordingly, the risks and benefits of this essentially elective surgery must be carefully weighed. In contrast, hip surgery in the setting of fracture is an urgent procedure with few acceptable alternatives.

Although pre-operative discussion prior to these procedures is often focused upon the type of anesthesia (regional versus general anesthesia), the greater risk is actually related to surgical technique. In addition to common risks such as bleeding, hip or knee replacement surgery can carry the added potential for pulmonary emboli due to preparation of the femoral canal for prosthesis insertion. The initial process of reaming the bone results in extremely high intramedullary pressures that transfer bone fragments, marrow, fat, air and inflammatory mediators into the circulation. In addition, the surgeon may elect to use bone cement to fix the prosthesis in place. During cementing, an exothermic reaction occurs in the compound causing it to expand in the intramedullary space; pressures as high as 5000 mmHg have been measured in cadaveric studies, increasing the potential for air and/or other medullary components to enter the circulation and create potentially lethal pulmonary emboli. Consistent with this prospect, intra-operative echocardiography studies indicate that cementing leads to a larger embolic load than uncemented arthroplasty, with emboli as large as 5 cm reported. Embolic loads have also been described during final reduction of the hip joint. Ultimately these embolic “showers” can lead to acute changes in RV afterload not only by physical effects on the pulmonary circulation, but also by release of pro-inflammatory mediators that may further increase PVR. Hypotension should be quickly treated with vasoconstrictors. Preemptive inotropic support can be considered in patients with severely compromised right heart function in anticipation of an embolic load. Dobutamine may be a preferable inotropic choice since it causes less systemic vasodilation than milrinone.

Laparoscopy

Some “minimally invasive” surgical procedures designed to be less stressful may, in fact, present significant physiological challenges to the PH patient.
Laparoscopy has become widely used for a variety of abdominal procedures, and is clearly beneficial in terms of post-operative pain and recovery time. Less well appreciated, however, is the fact that laparoscopy – which involves pressurized distension of the abdomen with carbon dioxide, diaphragmatic displacement, increased inspiratory pressures, mesenteric and aortic compression, and often hypercarbia – can have substantial acute impact on biventricular load and pump function. For the RV in particular, the combination of pneumoperitoneum and the increased inspiratory pressure required for mechanical ventilation and prevention of atelectasis has marked effects on both the magnitude and character of RV afterload. As shown in Fig 4, with the increasing airway pressures associated with pneumoperitoneum, there is not only a progressive rise in PA pressure, but a compression of the PA that results in decreased diameter, increased pulse wave velocity, and rapid augmentation of pulsatile components of RV afterload.

Clinical data based upon PA catheter measurements have indicated that even in otherwise healthy individuals, laparoscopy can have marked effects on cardiac output, particularly when the patient is in the “head up” position, and that these effects can lead to compromised hemodynamics in patients with pre-existing cardiac disease. Not surprisingly, the acute hemodynamic consequences of laparoscopy in patients with PH are less well described. Clinical data also indicate that the increases in PA pressure induced by laparoscopy may not be immediately reversed when the pneumoperitoneum is relieved. In that the abdomen is distended with pressurized CO2, it is relatively common for there to be a degree of subcutaneous emphysema — and hypercarbia as this CO2 is absorbed — in the immediate post-operative period. The persistent increase in PA pressure, probably from pulmonary vasoconstriction, has been linked to this hypercarbia, and while seemingly well tolerated in normal subjects, may have deleterious effects in patients with PH and poorly compensated RV function.

It is important to appreciate that not all procedures involving laparoscopy present the same physiological perturbations. For example, robotic-assisted procedures in the lower abdomen, used in particular for pelvic surgery such as radical prostatectomy or hysterectomy, can have different hemodynamic implications than upper abdominal procedures (i.e., cholecystectomy), largely due to patient position. Commonly, extreme Trendelenburg positioning (up to 45°) will be maintained for several hours, further augmenting the impact of pneumoperitoneum on inspiratory pressure, pulmonary compliance, and RV afterload. In a study of otherwise healthy patients, invasive monitoring revealed that right and left heart filling pressures were increased 2–3 fold. PH (defined as a PASP > 35 mmHg) was present in 75% of these normal patients. In this population, both right and left heart pressures proportionally increased, as did the mean arterial pressure. The CO was unchanged. Even moderate (30°) head down position led to a 50% increase in CVP. Right ventricular stroke work index increased 65%, although echocardiography indicated that there were no signs of right ventricular pressure overload in this healthy population. This technique has not been carefully studied in patients with PH, but it is expected that steep positioning in robotic-assisted laparoscopy would be poorly tolerated.

Thoracic surgery

Another minimally invasive surgical technique associated with acute challenges to mechanical coupling between the RV and pulmonary circulation is thoracoscopy for lung biopsy or resection. While the long-term benefits of thoracoscopy are becoming increasingly clear, particularly in elderly subjects or those with significant co-morbidities, the short-term stresses on the RV can be profound. Although thoracoscopy does not involve a sustained pressurization of the chest similar to that produced in the abdomen during laparoscopy, it does require non-ventilation and prolonged atelectasis of the operative lung. There are two features of this intentional lung collapse that are particularly relevant to
the PH patient: a) the increase in PA pressure and RV load produced by HPV and b) the potential for systemic hypoxia.

Following the initiation of single lung ventilation, there are an acute rise in airway pressure as the tidal volume is shifted to one lung, and a progressive redistribution of blood flow away from the non-ventilated lung as alveolar oxygen is absorbed and HPV occurs. While this redistribution of pulmonary blood flow has only a modest effect on PA pressure in normal subjects, the effect is more pronounced in those with pre-existing PAH (Fig 5). Accordingly, it has become relatively common to use iNO or intravenous (IV) epoprostenol intra-operatively to optimize vasodilation in the ventilated lung thus reducing PA pressure while maximizing ventilation/perfusion matching and lessening the risk of systemic hypoxia. Confounding this approach to some degree has been the increasing pre-operative use of IV pulmonary vasodilators that may affect HPV intra-operatively. In this setting (Fig 5), there may be benefit to also instituting inhaled pulmonary vasodilators during single lung ventilation to

Fig 5. Effect of Single Lung Ventilation on PAP and CVP in a Patient with PAH. The effect of initiating single lung ventilation (SLV) on pulmonary arterial (PAP) and central venous (CVP) pressure in a patient with pre-existing PAH.

Fig 6. Representative Tracings of Systemic and Pulmonary Arterial Pressures During Lung Lobectomy in a Patient with Pre-existing PAH. Representative simultaneous tracings of systemic arterial and pulmonary arterial (PA) pressures during lung lobectomy in a patient with pre-existing PAH who was receiving intravenous (IV) Flolan (epoprostenol) preoperatively. With the transition from double lung ventilation (DLV) to single lung ventilation (SLV), the IV Flolan dose was decreased and inhaled Flolan initiated in order to maximize vascular dilation of the ventilated lung and potentially lessen and deleterious effects of systemic Flolan on hypoxic pulmonary vasoconstriction. Following lung resection and resumption of the preoperative Flolan dose, PA pressure remained elevated relative to baseline.
allow for limiting or even discontinuing intravenous therapy, lessening potential inhibition of HPV and promotion of systemic hypoxia.

Finally, it is important to note that even when normal double lung ventilation is resumed upon conclusion of the procedure, PA pressure may not return to pre-operative levels despite increased doses of intravenous and/or inhaled pulmonary vasodilator, particularly if an anatomic resection (i.e. lobectomy) was performed (Fig 6).

Post-operatively, epidural analgesia is commonly used following lung resection and other non-cardiac surgery in the chest. As noted above, sympathetic blockade at the thoracic level can lead to dampening of cardiac sympathetic tone and systemic hypotension when high concentrations of local anesthetics are administered in the epidural space. Accordingly, in light of the fact that PA pressure may remain elevated following lung resection despite increased doses of pulmonary vasodilators, using a dilute local anesthetic solution, careful monitoring of systemic arterial pressure, and rapid intervention for hypotension are warranted.

Obstetrics

PH and pregnancy are well known to be a potential lethal combination. Outcome statistics are primarily derived from case studies and small case series, but perioperative mortality rates have been reported to be between 30% and 70%. A recent review of the literature sought to compare more recent outcome data (1997–2007) with previous reports (1978–1996). The more recent mortality rate declined among patients with IPAH to 17%, compared with 30% in previous decades. On the other hand, congenital heart disease associated PAH and other PH cases are still associated with mortality of 28%–33%. As such, avoidance of pregnancy or termination is still strongly advocated.

For pregnant patients presenting with newly diagnosed or established PAH who present at a stage where the risk of termination is similar to delivery of the fetus or who refuse to terminate pregnancy, successful maternal–fetal outcomes have been reported with an aggressive and multidisciplinary management approach. Vaginal delivery, often with an assisted 2nd stage, is preferred unless there is a recognized obstetrical indication for a Cesarean section (C-section). Advantages to vaginal delivery over C-section include less fluid shifts, decreased bleeding complications and a lower rates of infection. Slow epidural analgesia is strongly advised for the laboring parturient patient to minimize the risk of hypotension and also to avoid sympathetic stimulation associated with painful labor contractions. Invasive monitoring is necessary with an arterial line and either a CVP or PA catheter. If needed for inotropic support of a failing right ventricle, low dose dobutamine is often effective, however vasopressin is preferred if a pressor is needed.

Post-operative Management

An algorithm for the post-operative management of patients with PH and RV failure is proposed in Fig 7. Patients with PH warrant ICU monitoring in the post-operative period. Death, when it occurs, can be sudden and often occurs within the first few days after surgery. Frequent serial examinations should be performed in order to promptly identify and treat factors that may precipitate acute decompensated right ventricular failure (ADRVF).

Post-operative Management Algorithm for Patients with PH

![Post-operative Management Algorithm](image)

**Fig 7.** Post-operative Management Algorithm for Patients with PH and RV failure. This figure provides an algorithm for the management of patients with pulmonary hypertension in the post-operative period.
**Summary**

Anesthesia and surgery in patients with PH are associated with high perioperative morbidity and mortality, and elective surgeries should generally be avoided. Successful perioperative management requires a multidisciplinary approach involving the PH specialist,
anesthesiologists, critical care physicians, and allied healthcare team members. Pre-operative planning should include a careful risk assessment, taking into account the type of surgery as well as the etiology and hemodynamic severity of PH, patient functional status, and other medical comorbidities. If possible, optimization of hemodynamics and management of comorbidities should be attempted prior to surgery. Anesthetic agents, mechanical ventilation, and conditions related to specific surgeries have profound effects on pulmonary arterial and right ventricular coupling, and a thorough understanding of these physiologic effects, as well as having an experienced anesthesiologist, are of paramount importance for the successful perioperative management of patients with PH. Post-operative management must include vigilant hemodynamic monitoring with serial assessment, optimization of hemodynamics, avoidance of factors known to cause pulmonary vasoconstriction, and when necessary, the administration of inopressors and pulmonary vasodilators, the choice of which is based largely upon the etiology of PH. In the future, studies of patients with PH undergoing anesthesia and surgery should provide greater understanding of the risk factors and optimal perioperative management of these complex patients.

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