Preoperative Considerations in Patients With Pulmonary Hypertension: Your Patient Needs Surgical Clearance

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Patients with pulmonary arterial hypertension (PAH) are at increased morbidity and mortality risk when facing the need to undergo surgical interventions. The most common complications include those arising from right ventricular (RV) failure and respiratory failure—not surprising given the complex cardiopulmonary pathophysiology of this disease. While data are limited regarding the optimal preoperative approach to these patients, it is imperative to focus on the following key components: ensuring or establishing the patient's World Health Organization (WHO) classification, pulmonary hypertension (PH) group or subgroup; assessing the status and stability of RV function; optimizing the treatment regimen; and communicating a management plan for intra- and perioperative management to all members of the interdisciplinary clinical team. This article will focus on each of these steps in the preoperative algorithm, highlighting the need for further studies in this area.

Pulmonary arterial hypertension is a condition associated with increased pulmonary vascular resistance, resulting in progressive RV dysfunction.[1,2] Moderate to severe disease is associated with decreased functional capacity and an increased risk for mortality. The risk of surgery is markedly increased in patients with PAH, and for this reason elective surgery should generally be avoided or at least discouraged in this population when possible.[3,4] It is important to recognize that the type of surgery will impact the PAH patient's risk. Procedures associated with rapid blood loss, venous air embolism, systemic inflammatory response, carbon dioxide insufflation (eg, laparoscopic surgery), fat or cement emboli (eg, orthopedic surgery), and loss of pulmonary vasculature (eg, lung resection) are associated with higher risk.[4] Results of an international prospective registry including 114 patients emphasized the particular risk of emergency surgery with an observed mortality rate of 15% compared to 2% in nonemergency procedures.[5] However, even nonemergent surgery may be unavoidable in many PAH patients, necessitating a specialized preoperative risk assessment and careful preparation for the procedure.

The preoperative assessment in patients with PAH necessarily involves confirming or establishing the patient's diagnosis according to the WHO classification system,[6] and continues with thorough assessment of current stability with particular focus on measures of right heart function. The preoperative treatment regimen should be optimized to improve or maintain right heart function as well as overall functional capacity. Logistical planning for surgery includes reviewing feasibility of the current medication administration intraoperatively and postoperatively (especially in patients who will not be able to continue oral medications or who may need inhaled nitric oxide [iNO]), communication with the surgeon and anesthesiologist regarding intraoperative fluid management and monitoring, along with a clear delineation of responsibilities for postoperative care. A comprehensive plan also includes establishing a health care proxy for potential postoperative decision making and establishing goals of care should complications occur requiring discussions to address code status.

The value of preoperative medical and anesthesia consultations to address and optimize comorbidities including coronary artery disease, diabetes mellitus, and chronic renal insufficiency, as well as appropriate preoperative testing, is established; there are many other detailed reviews addressing these topics.[7,8] This review for PAH clinicians will primarily address assessing preoperative surgical risks, with focus on PH patients facing "semielective," noncardiac, nonobstetric surgery.

IMPACT OF PAH ON SURGICAL OUTCOMES

Multiple published reports have documented the impact of PAH on morbidity and mortality during pediatric, obstetric, cardiac, and noncardiac surgeries.[3,9-13] The threshold for pulmonary artery pressure associated with this increased morbidity and mortality risk has not been strictly established; however, in a study of patients undergoing coronary artery bypass surgery, a mean pulmonary artery pressure (mPAP) measurement of >30 mm Hg was a predictor of increased postoperative mortality.[12] Ramakrishna and colleagues utilized a Doppler echocardiographic estimated right ventricular systolic pressure (RVSP) of ≥35 in their retrospective investigation of 143 patients to evaluate the impact of PH on outcomes in noncardiac surgery.[3] Patients with PH related to left heart disease and those not diagnosed with PH prior to surgery were among those excluded from the analysis of morbidity and mortality within the

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Table 1: Incidence and Type of Early (≤30 Days) Morbidity in Patients With Pulmonary Hypertension (n = 145) After Noncardiac Surgery. Reprinted with permission.[3]

Morbidity	Patients* (n)	Frequency (%)
Respiratory failure	41	28
Cardiac dysrhythmia	17	12
Congestive heart failure	16	11
Renal insufficiency	10	7
Sepsis/hemodynamic instability	10	7
Hepatic dysfunction	6	4
Ischemia/myocardial infarction	5	4
Stroke	1	1

*Patients may have had one or more morbid event(s).

first 30 postoperative days. The observed mortality was 7%, with one of the deaths occurring intraoperatively in the setting of RV failure. Table 1 describes the most frequent morbidity events from that study with respiratory failure, dysrhythmias, and congestive heart failure at the top of the list. New York Heart Association functional class (NYHA FC) ≥2 and presence of systemic hypertension were associated with increased morbidity in a univariate analysis, while history of pulmonary embolism and NYHA FC ≥2 were considered predictors of short-term morbidity in the multivariate model.

These results were consistent with the findings of Kaw et al, who examined 173 patients who underwent right heart catheterization (RHC) and noncardiac surgery.[13] The definition of PH utilized in this study was mPAP >25 mm Hg. Of the 96 patients with PH, 26% suffered a morbidity/mortality event with congestive heart failure, hemodynamic instability, and respiratory failure most commonly observed. Mean pulmonary artery pressure, American Association of Anesthesiology Class, and chronic renal insufficiency were found as independent risk factors. Table 2 contains a summary of patient and operative risk factors based on published data, derived largely from retrospective studies and highlighting the need for prospective investigations in this area. These studies strongly demonstrate the significant negative impact of PH on perioperative outcomes and emphasize the importance of a thorough preoperative characterization and assessment of risk in this patient population.

IMPORTANCE OF CONFIRMATION AND CHARACTERIZATION OF PAH

Recent registry reports have shown that the delay from onset of symptoms until the diagnosis of PAH may exceed 2 years.[16] This suggests that some patients may have their PAH diagnosed at the time of their preoperative assessment. Others may have been given a presumptive diagnosis of PAH based on an echocardiogram finding but have not undergone a thorough evaluation to determine the WHO group.[17] Although most of the perioperative management approaches share a similar fundamental basis for different etiologies of PH, establishing and/or confirming the patient's WHO group diagnosis preoperatively by utilizing the recommended diagnostic approach[2] provides guidance regarding the use of PAH vasodilator therapy in the perioperative period. While pulmonary vasodilators have been proven effective in managing patients with PAH, the results are far less predictable when administered in non-PAH PH patients and may result in deterioration or death.[2,18] Of particular concern is the risk of pulmonary edema when PAH vasodilator therapy is utilized in patients with heart failure with preserved ejection fraction (HFpEF; WHO Group 2) or worsening ventilation-perfusion matching resulting in hypoxemia in patients with significant parenchymal lung disease and PH (WHO Group 3). Once PAH diagnosis is confirmed and subgroup classification is established, the preoperative evaluation continues with evaluation of current stability, with a particular focus on right heart function.

Table 2: Risk factors for morbidity and mortality in noncardiac surgery[3]

Patient factors
• History of pulmonary embolism, coronary artery or chronic kidney disease
• NYHA/WHO FC ≥II
• Right axis deviation on ECG
• Echo parameters: RVH, RVIMP ≥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
• Intraoperative vasopressor use

Abbreviations: NYHA=New York Heart Association, WHO=World Health Organization, RAD=right axis deviation, RVH=right ventricular hypertrophy, RVIMP=right ventricular index of myocardial performance, PAP=pulmonary artery pressure, RVSP=right ventricular systolic pressure, SBP=systolic blood pressure, ASA=American Surgical Association

ASSESSMENT OF PH STABILITY AND OPTIMIZING THERAPY

The stability assessment of PH patients typically begins with history and physical examination, where discovery of recent deterioration in functional status, elevated jugular venous pressure, increasing fluid retention, or occurrence of syncope may provide initial indications of failing right heart function. Further information is gathered through blood testing regarding anemia, renal function, and brain natriuretic peptide (BNP) or N-terminal pro-BNP (NT-proBNP) levels. Brain natriuretic peptide levels are sensitive indicators of heart failure and correlate with degree of cardiac stress and dysfunction. While decreasing renal function, increasing age, obesity, and female gender have all been associated with elevated baseline plasma BNP levels,[19] changes from the patient's previous baseline may have significant clinical utility. Elevations of plasma BNP from baseline in patients with PAH portend a higher risk of mortality, and decreases in circulating BNP levels have been associated with improved survival, suggesting a role for BNP as a monitoring tool to guide adequacy of vasodilator therapy.[20]

For patients at risk for hypoxemia and hypoventilation, relatively simple preoperative maneuvers such as pulse oximetry monitoring, including nocturnal testing during sleep and/or polysomnography, may be of benefit. Improving hypoxemia with supplemental oxygen and adding continuous positive airway pressure (CPAP) in indicated patients may help improve exercise capacity, volume status, and daytime alertness while also establishing the therapeutic regimen that will minimize complications in the postoperative period. Preoperative thoracic computed tomography (CT) scanning and pulmonary function tests (PFTs) are not routinely performed in patients with established PAH; however, they may be useful in some patients for evaluating recent changes in function. In particular, patients with worsening hypoxemia and/or nontypical PAH symptoms such as cough, sputum production, or pleuritic chest pain warrant consideration of thoracic CT scanning. Patients with a history of smoking or interstitial lung disease may benefit from PFTs as significant worsening of FEV1/FVC ratio suggests obstructive lung disease, and diminishing total lung capacity (TLC) may indicate worsening restrictive lung disease. Moderate to severe obstructive or restrictive ventilatory defects discovered during PFTs deserve further evaluation, usually including a pulmonary consult, to determine if the surgery should be canceled or postponed for treatment of the lung disease.

The 6-minute walk test is often pursued in the preoperative assessment. A lower 6-minute walk distance (6MWD) has been correlated with a worse prognosis compared to a higher 6MWD in patients from registry data[2]; however, the available data in preoperative risk studies have not supported a specific walk distance predictive of morbidity.[3] Cardiopulmonary exercise testing (CPET) may better define the functional capacity and risk in patients with PAH as it provides a dynamic assessment of cardiac reserve. However, there are no established parameters for exercise level that are clearly predictive of postoperative outcome. Historically, CPET has been utilized in patients with chronic heart failure to make determinations of timing of transplantation, and parameters such as peak oxygen uptake are a recognized part of the general risk stratification of patients with PAH. In vascular surgery patients, the preoperative exercise capacity in metabolic equivalents (METs) has been used to risk stratify patients; those capable of performing less than 1 MET during CPET are recommended for further testing and/or medication therapy while those capable of >1-4 METs are considered functional enough to proceed without further testing.[21,22] The most prudent recommendation may be to facilitate ambulation to maintain conditioning in patients prior to surgery without setting a specific functional goal, or routinely delaying a procedure to complete a pulmonary rehabilitation program, since this approach is not supported by the literature.

A transthoracic echocardiogram serves as a core test for preoperative evaluation of patients with PAH as it provides a noninvasive evaluation of right heart function. Patients with normal right atrial and RV sizes and preserved RV function are better risk surgical candidates. Markers of poor prognosis on echocardiogram in PAH include reduced tricuspid annular plane systolic excursion (TAPSE), severe right atrial enlargement, abnormal right ventricular index of myocardial performance (RVIMP or Tei Index), presence of pericardial effusion, and increased left ventricular eccentricity index.[23,24] Along with its utility, the limitations of the echocardiogram must be acknowledged. The echocardiogram provides only an estimate of RVSP by extrapolating from the tricuspid regurgitant jet velocity, which may under- or overestimate the actual pulmonary artery pressure when evaluated with RHC.[25] Also, while improvement in these echocardiographic parameters is considered a positive sign in patients on treatment, the timing and degree of change that may correlate with an improved postoperative outcome has not been determined. Ramakrishna and colleagues' study emphasized this point as they observed no association between selected parameters on echocardiogram and postoperative morbidity; however, RV hypertrophy, RVIMP $\geq$0.75, and RVSP to systolic blood pressure ratio of $\geq$0.66 were all significantly associated with increased early mortality.[3]

Right heart catheterization is the only method of obtaining direct assessment regarding cardiac hemodynamics and cardiac output, and for this reason should be considered in patients with PH as part of their preoperative evaluation if other noninvasive tests do not reliably provide status of right heart function. Right heart catheterization can confirm WHO Group diagnosis, and in particular differentiate HFpEF from PAH. The importance of obtaining an accurate pulmonary capillary wedge pressure (PCWP) in this setting deserves emphasis. Utilizing methods that include careful analysis of the pressure tracing, measuring wedged oxygen saturation, and/or deflating the balloon slightly and further advancing the catheter may be necessary to confirm a true and accurate PCWP. Without a true PCWP, the left ventricular end diastolic pressure may be overestimated and the patient misclassified as HFpEF when in fact the correct diagnosis is PAH. If a left heart catheterization is indicated to assess coronary patency or uncertainty regarding the PCWP remains unresolved, confirmation with direct measurement of left ventricular end diastolic pressure will establish the correct diagnosis.

Performing a preoperative RHC will also help guide the use of preoperative diuretics for patients with high right atrial pressures and the postoperative inotropes for patients with a low cardiac index. In selected patients, RHC with vasodilator challenge utilizing iNO may be performed to assess the potential utility of iNO postoperatively to acutely reduce RV afterload. Right heart catheterization will also provide information that helps providers decide that a potential surgical procedure is too high risk and needs to be avoided.[4]

In patients who are clinically high risk due to NYHA FC IV status and history of syncope, demonstrating high-risk hemodynamic parameters such as low cardiac index and high right atrial pressure[2] leaves PAH clinicians with few options: mainly to cancel surgery or delay until clinical and/or hemodynamic stability might be achieved.

If a delay in surgery is feasible, as in some orthopedic procedures, and therapeutic adjustments are sought, the initiation or addition of phosphodiesterase type-5 inhibitor (PDE-5i) therapy and initiation of or dose increases in parenteral prostacyclin may be considered, although these are not evidence-based recommendations. The potential advantage to PDE-5i therapy, such as sildenafil 20 mg 3 times daily or tadalafil 40 mg once daily, compared to endothelin receptor antagonist therapy as a preoperative choice, is the purported acute vasodilatory and positive RV inotropic effects of the PDE-5i class. Prostacyclin therapy may have similar acute vasodilatory effects as well as positive RV inotropic effects, and increases in dose of a parenteral or inhaled prostacyclin may also be a desirable choice. Any therapeutic changes may result in adverse side effects, including lowering of systemic blood pressure and gastrointestinal symptoms such as nausea and diarrhea, so these should also be considered when medication initiation or dosing changes are made close to the date of any planned surgery. Again, these treatment suggestions are general (and largely hypothetical) recommendations. Further research will hopefully address this area and provide more practical evidence-based algorithms.

LOGISTICS: IMPORTANCE OF THE HEALTH CARE PROXY, MEDICATION PLANNING, AND THE INTERDISCIPLINARY TEAM APPROACH

Effective communication preceding surgery between patients and their PH provider team is imperative to help set expectations, discuss potential alternatives to the proposed procedure, determine the ideal hospital for the procedure, and establish the patient's treatment goals. Given the elevated morbidity and mortality risks, devoting time to establishing a health care proxy to make decisions as the patient's surrogate when necessary is appropriate. Also, specifically discussing potential circumstances, such as a cerebrovascular accident or severe sepsis, in which the patient may wish to be declared DNR (do not resuscitate) and/or limit certain types of aggressive care is also recommended.

Just as good communication between the PH clinician and the patient is essential to optimizing the treatment regimen, communication among the members of the multidisciplinary team is key to optimizing surgical outcomes. The members of the perioperative care team will typically include PAH clinicians (physician, nurse practitioner, physician assistant, respiratory therapist), surgeon, anesthesiologist, medical consult specialist as well as intensivists, nurses, and allied health care professionals (such as respiratory therapists and pharmacists) responsible for postoperative care. Involvement of a cardiac anesthesiologist is generally recommended for patients with PAH who are considered high risk and for high-risk surgical procedures. The practical issues that need to be addressed among specialists include arranging a preoperative anesthesia consult, preparing for management of comorbidities (eg, obtaining the home CPAP machine for patients with sleep apnea), developing a plan for postoperative medication delivery, and determining which clinicians will be responsible for each aspect of postoperative care. The latter 2 of these issues warrant further discussion.

The perioperative medication plan first needs to ensure that the patients' current and potential future medication needs are adequately covered in terms of in-hospital availability. Not all hospitals have the range of PAH medications on formulary and/or available, and this may be a factor in determining whether a hospital is suited to perform the necessary procedure. Medication planning also needs to consider feasibility of dosing of oral medications such as PDE-5i and endothelin receptor antagonists in patients who may be unable to tolerate oral intake and/or dosing of inhaled prostacyclins in patients who may be ventilator dependent and unable to utilize their usual prostacyclin inhalation delivery system postoperatively. Alternatives to oral and inhaled medications might include temporizing use of iNO, which is not universally available, and inhalation prostacyclin via the mechanical ventilator, with which some centers may not have experience. A more significant risk procedure might also justify initiation of a parenteral prostacyclin as part of preoperative treatment optimization and for perioperative maintenance. Whatever medication treatment plan is developed, establishing lines of responsibility for important aspects of postoperative care is important.

For some institutions with experienced PAH programs, an agreement for postoperative management to be done by the PAH team with the surgical team focusing on the surgical issues has been suggested.[4] This allows the clinicians with the greatest knowledge of the individual patient and with the PAH expertise to make the likely required adjustments to medication dosing, choose appropriate inotropic and/or vasopressor support, and manage mechanical ventilation when required. Not all institutions will necessarily follow that approach, and some larger institutions have intensivists with appropriate experience in their critical care units that is ideally suited to manage the challenges presented in postoperative patients with PAH. In surgical procedures beyond minimal risk, the presence of highly experienced PAH specialists is an important reason to consider scheduling surgery at or transferring to a tertiary care center. While no evidence-based recommendation can be made regarding ideal approach to postoperative care, effective communication pertaining to these issues prior to surgery will serve to minimize conflict and confusion among interdisciplinary team members.

CONCLUSION

The risks of postoperative morbidity and mortality are clearly elevated for patients with PAH. While retrospective studies have identified factors such as NYHA

Table 3: Questions to be answered preoperatively for the PH patient

1. Is the planned surgery elective and might the morbidity and mortality risks be avoided by choosing a nonsurgical management strategy?
2. Is the type of PH well characterized or is further testing required to confirm WHO group or subgroup diagnosis?
3. Has the patient been recently evaluated with history, examination, BNP/blood testing, echocardiogram or MRI, and possibly right heart catheterization to assess right ventricular function?
4. If right ventricular function is not optimized (eg, volume overload/edema/ascites, TAPSE <2 cm, elevated BNP, cardiac index <2), can the surgery be safely delayed while additional treatment options are initiated? Is there time to initiate a pulmonary rehabilitation program?
5. Has the medical center for the proposed surgery been matched with regard to availability of essential PH medications, anesthesia, and surgical expertise to manage potential intra- and perioperative challenges in patients with PH?
6. Is there an intra-, peri-, and postoperative plan and lines of responsibility communicated to involve all members of the patient's PH multidisciplinary care team?
7. Is there a health care proxy clearly identified and has there been substantial conversation regarding goals of care and complications that might result in changes in DNR status?

FC ≥2, RV hypertrophy, and RVIMP ≥0.075 as preoperative risk factors associated with increased risk, further prospective research is much needed to guide our management of these individuals. A methodical approach to this issue, including a thorough patient assessment and detailed preoperative planning, is imperative to optimize outcome. The best response to the question, "Can I send my patient with PAH for surgery?" may ultimately be, "Have the key preoperative questions been adequately addressed" (Table 3). The process necessitates consideration of nonsurgical alternatives, establishing WHO group, assessing status of right heart function, optimizing the treatment regimen, and communicating potential intraoperative concerns and medication plans to all members of the multidisciplinary care team. Despite the elevated risks facing PAH patients with surgery, careful planning and close collaboration of specialists may provide the best possible outcome.

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