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TRANSFORMING PATIENT SAFETY THROUGH EDUCATION AND ADVOCACY

Pulmonary Hypertension and RV Failure

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Introduction: Pulmonary hypertension (PH) and the associated RV dysfunction is increasingly being encountered in the perioperative period. Managing these patients is challenging, but a thorough understanding of the pathophysiology of PH and the associated RV dysfunction allows the practioner to anticipate, prevent and successfully manage many of the perioperative risks. The normal systolic, diastolic, and mean pulmonary artery pressure (PAP) is 25 mmHg, 10 mmHg, and 15 mmHg, respectively; the normal range for pulmonary vascular resistance (PVR) is 0.9 to 1.4 Wood units (or 90 to 120 dynes · s · cm^{-5}). The PVR is the quotient represented by PVR = (ΔP)/flow, where ΔP represents the mean PAP (mPAP) minus the left atrial pressure (LAP). This gradient commonly is referred to as the transpulmonary gradient (TPG). If the TPG is elevated, there is an increase in the PVR. On the contrary, if the TPG is not elevated, the increase in PAP is caused by an elevated LAP (implicating elevated LA pressure as a result of cardiac pathology). Flow is the blood flow through the pulmonary circulation i.e. cardiac output (CO). Thus, PVR = (mPAP - LAP) ÷ CO, or mPAP = LAP + (CO X PVR). Therefore, only 3 physiological factors increase in mPAP: (1) increase in LAP (due to cardiac pathology), (2) an increase in CO (congenital heart disease [CHD] with left-to right shunt, fluid overload, and hyperdynamic states), and (3) an increase in PVR (pulmonary parenchymal/airway disease, hypoxia, interstitial lung disease, thromboembolic disease, and idiopathic pulmonary artery hypertension). Because of pulmonary vascular remodeling, even factors 1 and 2 eventually leads to an increased PVR, and the associated increased mPAP will reflect both an increased LA pressure as well as increased PVR. For example, a patient with mitral valve stenosis who has an increased mPAP solely because of an increased LAP (without increased PVR, i.e., "reversible" PH). These patients, mitral valve replacement is usually uncomplicated and has little risk of RV failure. In comparison, patients with mitral stenosis and increased mPAP because of increased LAP as well as increased PVR (secondary to pulmonary vascular remodeling, i.e., "fixed" PH), may have severe RV failure after mitral valve replacement and difficulty in weaning from CPB. Acute–on-chronic increases in PVR are common the perioperative period, and can lead to acute decompensation in RV function. These factors include, amongst others, hypoxia, hypercarbia, acidosis, hypothermia (shivering), increased sympathetic tone (pain, anxiety), and exogenous or endogenous pulmonary vasoconstrictors such as catecholamines, serotonin, thromboxane, and endothelin. Early recognition and reversal of these causes of acute deterioration could be lifesaving.

Definition of PH: Normal mPAP at rest is 14± 3 mmHg, with an upper limit of 20 mmHg. The significance of mPAP between 21-24 mmHg is unclear. The European Society of Cardiology and the European Respiratory Society define pre-capillary -PH is as persistent increase in mPAP ≥ 25 mmHg at rest as assessed by right heart catheterization (RHC) in the setting of a normal PCWP of ≤15 mmHg, a PVR of ≤3 Wood units, and normal or reduced CO. They define post-capillary PH is defined as a persistent increase in mPAP ≥25 mmHg at rest as assessed by RHC in the setting of an increased PAWP ≥15 mmHg, PVR ≥3 Wood units, and normal or a reduced CO. The definition of PH according to the American College of Cardiology/American Heart Association 2009 Expert Consensus Document on PH, is a measurement by RHC, of a resting mPAP ≥25 mmHg, a PCWP/LAP ≤15 mmHg, and a PVR ≤3 Wood units.

Classification of PH: PH has undergone several relassifications over the alst 20-years. The most recent classificaction system is shown in Table 1. It has 5 major categories, which include pulmoanry arterial disease (PAH), left heart disease, lung disease/hypoxemic states, chronic thrombo-embolic pulmonary hypertension (CTEPH), and unclear/multifactorial category.

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Table 1

1. Pulmonary arterial hypertension (PAH)
1.1. Idiopathic PAH
1.2. Heritable
1.2.1. BMPR2
1.2.2. ALK1, 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 PH of the newborn
1.6. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
2. PH caused by left-heart disease
2.1. Systolic dysfunction
2.2. Diastolic dysfunction
2.3. Valvular disease
3. PH caused by lung diseases and/or hypoxia
3.1. Chronic obstructive pulmonary disease
3.2. Interstitial lung disease
3.3. Other pulmonary diseases with mixed restrictive and obstructive patterns
3.4. Sleep-disordered breathing
3.5. Alveolar hypoventilation disorders
3.6. Chronic exposure to high altitude
3.7. Developmental abnormalities
4. CTEPH
5. PH 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. Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

Abbreviations: ALKI, activin receptor-like kinase type 1; PH, pulmonary hypertension; CTEPH, chronic thromboembolic PH.

production of vasoconstrictor and mitogenic compounds such as endothelin-1, angiotensin-2, serotonin, and thromboxane A2 and a deficient production of vasodilators such as prostacyclin

Pathogenesis: PH is a syndrome resulting from a pathologic increase in PVR, which leads to restricted flow through the pulmonary arterial circulation and, ultimately, RV failure. The etiology is often multifactorial and complex, a schematic of wg hich is shown in ***Figure 1***. The loss of vascular luminal cross-section because of vascular remodeling is the main cause for the increased PVR. Excessive vasoconstriction may be a significant contributing factor in about 20% of patients. The pan-vasculopathy that predominantly affects small resistance pulmonary arteries and involves intimal hyperplasia, medial hypertrophy, adventitial proliferation, thrombus in situ, varying degrees of inflammation, and plexiform arteriopathy. Mutations in 3 genes in the transforming growth factor-superfamily receptor pathway, namely, BMPR-2, activin receptor–like kinase-type 1(ALK-1), and endoglin, have been implicated in the pathogenesis of heritable PAH. The markedly reduced penetrance in families with PAH suggests that some form of "second hit" is required in addition to the mutation to lead to the manifestation of clinical disease. Endothelial dysfunction contributing to PAH involves increased

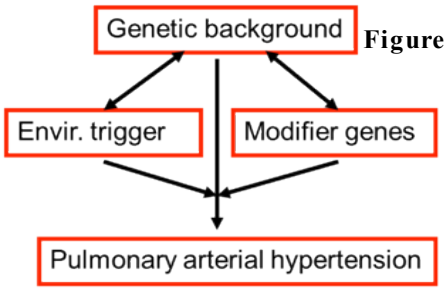

Figure 1

Spasm:
↓NO, ↑thromboxane, 5HT, abnormal Ca^{2+} handling and opening of VDCC
Inflammation
Thrombosis
Platelet aggregation
Sm. muscle hypetrophy
Intimal/adventitial prolif.

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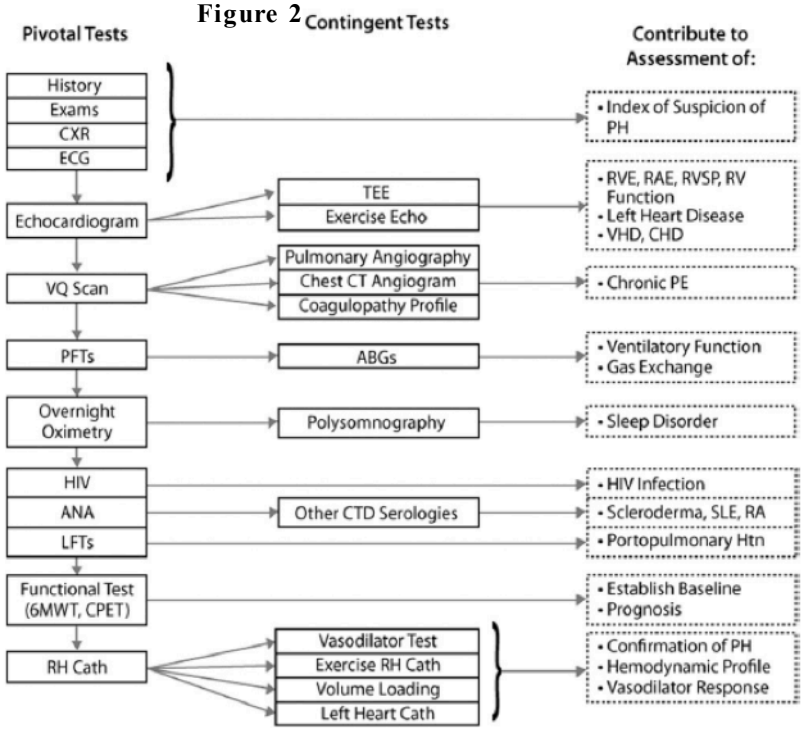
and NO. These mechanisms may be partcularly germane to PH assiociated with appeptite suppressant and in cases of newborm PH associated with SSRI use during pregnancy. Prostacyclin is a potent vasodilator and inhibits platelet activation, and has antiproliferative properties. In patients with PAH, there is a reduced ratio of thromboxane A2:prostacyclin, favoring thrombosis, proliferation, and vasoconstriction. Decreased endothelial NO synthase has been observed in PAH patients. Vasoactive intestinal peptide (VIP) causes vasodilatation and lung VIP levels are decreased in patients with PAH. Hypoxia causes vasodilatation of systemic vessels and vasoconstriction of the pulmonary vasculature,in part through the action of endothelin and serotonin. Acute hypoxia further inhibits the function of voltage-gated KATP channels of the PA smooth muscle, resulting in membrane depolarization, an increase in cytoplasmic calcium concentration, and vasoconstriction.

Diagnosis and investigation: The most common presenting symptoms are dyspnea on exertion, fatigue, chest pain, syncope, palpitations, and lowerextremity swelling. Signs of PH and RV failure include tachypnea, tachycardia, distended neck veins, left parasternal lift, an audible tricuspid regurgitation murmur, ascites, and lowerextremity edema. The American Heart Association proposes divding the investigation into two sets of tests: pivotal and contingency tests, and these are shown in ***Figure 2.*** An electrocardiogram, chest x-ray, and echocardiogram may display signs suggestive of PH . An echocardiogram should be considered once PH is suspected by history, clinical examination, and risk factors. Possible causes of PH that can be excluded or confirmed by echocardiography are congenital and acquired valvular disease, LV systolic and diastolic dysfunction, large pulmonary embolus, congenital disease with shunts. It ia important to rule out CTEPH as 50% of patients with a diagnosis of CTEPH have no prior history of acute pulmonary embolism. The screening test of choice to exclude CTEPH is radionuclide perfusion scanning. A normal or very low probability scan essentially excludes CTEPH, whereas a high probability scan warrants further evaluation with a pulmonary angiogram. A spiral CT scan, although excellent in excluding an acute PE, is less sensitive than perfusion scanning in excluding CTEPH. RHC should be performed in all cases diagnosied with PH to confirm the diagnosis and assess the hemodynamic profile, inclusing esponse to an acute vasodilator therapy. PVR is a more accurate diagnostic criterion to define PH because it reflects the influence of the TPG and CO and only is elevated if the vascular obstruction occurs within the precapillary pulmonary circulation.

Figure 2



Therapy: *Medical therapy*: Treatment goals include improvement in symptoms, functional capacity, lowering mPAP and normalizing CO, slowing the rate of progression of the underlying disease, and improvement in survival.

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Low-level aerobic exercise is encouraged. Avoidance of high altitudes and oxygen supplementation on commercial aircraft for patients with room air saturations is advised. Oxygen therapy is indicated if oxygen saturation < 90% on room air. Ideally, pregnancy should be avoided. Routine anticoagulation with coumadin may improve survival. Digoxin and diuretics are used for RV for failure. Calcium channel blockers are indicated in a small, select group of patients with idiopathic PAH who show acute vasodilator responsiveness. Prostanoids are the mainstay for many patients. The 3 prostanoids available for treatment of PAH include intravenous epoprostenol (ie, prostacyclin/PGI2), subcutaneous treprostinil, and inhlaed iloprost, each with its own adnavatgees and disadvantages. Several studies have shown improved symptomatology, exercise tolerance, hemodynamics, quality of life, and survival. Although tachyphylaxis with the need for frequent dose adjustments occurs, the beneficial effects of prostanoids can be sustained for years, and, as a result, many patients have been removed from heart-lung transplantation lists. The endothelin antagonists, including drugs such as bosentan and sitaxsentan, are another important class of therapy. They are increasingly used as first-line oral therapy. The phospdiesterases (PDE) are another important class of agents. PDE 3 and 5 are enzymes that inactivate cAMP and cGMP, respectively, the principal second messengers of prostacyclins and NO. PDE inhibitors such as milrinone and sildenafil, act to augment cAMP- and cGMP-mediated intracellular signaling, leading to vasodilation and decreased PVR. Sildenafil improves exercise capacity, quality of life, and hemodynamics. Oral sildenafil has been used successfully to manage acute RV dysfunction in heart transplant recipients,to wean patients from NO, to reduce time on mechanical ventilation, and to prevent the sequelae of CPB on pulmonary endothelial cell function.85,86 More recently, it has been shown that sildenafil is absorbed via the sublingual route. Although not yet studied definitively, this may have implications for emergent perioperative care. The PDE-3 inhibitor, milrinone, acts similarly and can be administered intravenously or by inhalation. Recent studies have shown symptomatic benefit (without survival benefit) from combination therapies. The addition of sildenafil to inhaled iloprost or subcutaneous treprostinil is well tolerated and appears effective.
Invasive therapy: Observations have shown that patients with Eisenmenger syndrome (right-to-left shunting through an atrial or ventricular septal defect) and PAH generally have superior survival rates compared with idiopathic PAH, mainly because of decompression of a pressure-overloaded RV, improved LV filling, and a resulting increase in CO. Atrial septostomy is considered as a palliative procedure and/or a bridge to lung/heart-lung transplantation in patients with intractable RV failure despite maximal medical therapy. The intraatrial shunt causes a decrease in systemic arterial oxygen saturation that is compensated for by increases in CO and systemic oxygen delivery. Pulmonary endarterectomy (PEA) is indcated for carefully selected patients with CTEPH. The goal is to remove enough material to lower PVR and increase CO. Bilateral lung transplantation (and occasional heart-lung transplanation) is the final option for a minority of patients in whom medical therapy has failed; however, death rates on waiting lists are high because of a global shortage of donor organs. Although effective medical therapy has reduced the rate of transplantation in patients with PAH, approximately 4% of lung and combined heart and lung transplants performed annually worldwide are still for PAH patients. Extracorporeal support is indicated in patients with PAH are acute RV failure and hypoxemia caused by a massive PE, bridge-to-lung transplant, support after lung transplant, treatment of severe reperfusion edema after PEA, and for RV failure unresponsive to conventional medical therapy.Patients with end-stage RV failure because of PAH have done poorly with ventricular assist devices as tegh increased flow in a compromised pulmonary vascaular bed further increasespulmonar vessel injury, leaqding to pulmonary hemorrhage, hemoptysis, and death.

Prognosis: Advanced functional class, rapid symptom progression, poor exercise capacity, RV dysfunction, low CO, elevated brain natriuretic peptide, and an associated diagnosis of scleroderma as re associated with a poor outcome. The best survival rates are seen in patients with congenital heart disease associated PH. Idiopathic PAH has a median survival of 2.8 years A recent meta-analysis of 21 trials with 3,140 patients reported improvements in the exercise capacity and a 43% reduction in mortality.

Perioperative RV failure in patients with PAH: Acute decompensation of patients with PH during the perioperative period is relatively common, can be lethal, and occurs as a result of acute RV failure. However, it is

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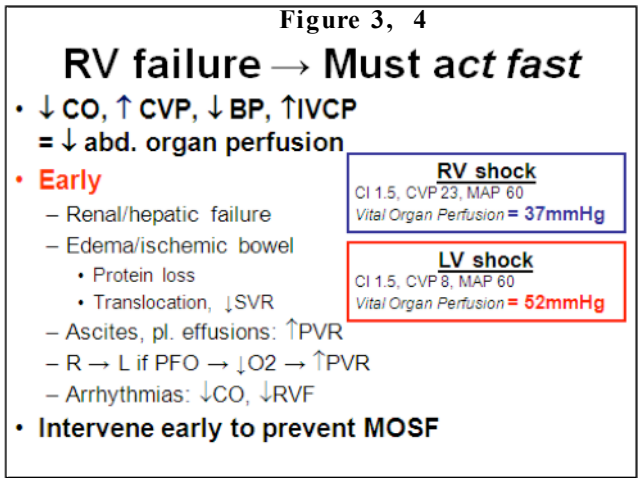
often preventable. Eisenmenger syndrome undergoing a cesarean section have been said to have a perioperative mortality of up to 70%. It is unlikely however, with todays knowlege and therapy, that this is still the case. Patients with PAH who require surgery should likely be managed in a centre and by a team experienced with the disease. Patients with PAH undergoing liver transplantation may have a mortality as high as 80%. The degree of preoperative RV dysfunction and elevation in PVR, together with the type of surgical procedure, are the major predictors of perioperative risk. High-risk surgical procedures include those that could cause significant perioperative systemic inflammatory response; rapid blood loss; high possibility of venous air, CO2, fat, or cement emboli; loss of lung blood vessels; and (reversible) factors leading to acute increases in PVR (eg, acidosis, hypoxia, shivering, pain, and anxiety). All attempts must be made to optimize PVR before surgery, including maximizing medical therapy and preventing conditions that may cause acute deterioration. Patients on chronic intravenous prostacyclin therapy ideally should continue their therapy throughout the perioperative period because discontinuation can precipitate an acute pulmonary hypertensive crisis. Changing to inhaled therapy under controlled conditions may be considered in order to mitigate the potent antiplatelet effect of intravenous prostacyclin, and potentially allow for neuraxial blockade. In selected patients not on PAH-specific therapies, a preoperative RHC, vasodilator trial, and PAH-specific therapy may be indicated. Patients with an unacceptable high risk for perioperative decompensation (even after optimization of medical therapy) should not have surgery or should be considered for noninvasive alternatives to surgery.

Acute decompensation caused by RV failure frequently is misdiagnosed. Unlike cardiogenic shock from acute LV failure alone (with systemic hypotension, end-organ hypoperfusion, and relatively normal RA pressures), acute RV failure causes increases in RA pressure and systemic venous pressure. Acute RV shock therefore has a worse prognosis than acute LV shock; the reasons for this are shown in **Figure 3**. As shown, in two hypothetical patients with similar cardiac outputs, the patient with RV failure has a "double hit" compared to the patient with LV shock i.e reduced inflow and reduced outflow. This double hit on the vital organs in acute RV failure can rapidly (within hours) manifest as multiple organ system failure. In addition, the elevated RA pressure may cause hypoxemia in susceptible patients by causing a right-to-left shunt across a patent foramen ovale. It is important to note that tricuspid regurgitation (TR) is common in acute and chronic RV failure, and, hence, thermodilution CO measurements may be misleading. TdCO accuracy depends on the severity of the TR (in severe TR, it underestimates CO), but there is also a flow dependency of TdCO in TR (in acute TR, there is an underestimation of Td CO when the CO is high, an overestimation when the CO is low, and a minimal effect when the CO is midrange). TdCO also may be inaccurate in the presence of anatomic shunts; if there is a left-to-right shunt, thermodilution will measure pulmonary rather than systemic blood flow because the cold indicator will be diluted by shunted blood. If there is a right-to-left shunt (Eisenmenger), thermodilution will measure systemic rather than pulmonary blood flow because some of the cold indicator will pass through the shunt. However, the PAP measurements still may be useful to monitor the effect of pulmonary artery vasodilators or vasopressors. Some of the interventions and drugs that improve RV function (ie, alpha adrenergic agonists, phosphodiesterase inhibitors, and calcium sensitizers) may have potentially deleterious effects on the systemic vascular resistance (SVR), particularly if the decrease in SVR is larger than the increase in RV CO. Similarly, systemic vasopressors used to maintain systemic blood pressure and RCA perfusion may cause elevation in PVR.

Figure 3, 4



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The treatment principals of perioperative RV failure (**Figure 4**) include:

Principles of managing perioperative RV failure

- **Rx precipitating cause if present**
  - PE thrombolysis, reverse hypoxemia, acidosis
- **Hemodynamic support**
  - Optimize rate/rhythm
  - Optimize preload
  - Optimize RV function
    - Maximize the TSG
  - Minimize RV afterload

1. *Optimize RV rate and rhythm*. Sinus rhythm is optimal filling of a hypertrophied and dilated right ventricle. Because of the association of RV failure with TR, higher heart rates may be desirable to reduce end-diastolic volume. Stroke volume is limited by the increase in RV afterload, it is best to avoid bradycardia. If there is significant RV ischemia, excessive tachycardia may not be tolerated either. A loss of sinus rhythm may lead to acute hemodynamic decompensation, and early synchronized cardioversion should be considered. In cardiac pacing is possible, atrial or atrial-ventricular sequential pacing leads to improved RV diastolic filling compared with ventricular pacing alone. It is crucial to optimize electrolytes and magnesium, and to consider amiodarone early to control or prevent atrial fibrillation.

2. *Optimize of RV filling*. Perioperative CVP monitoring is important; in general, when the CVP is low, the RV must be "coping" even if the PAP and PVR are elevated (ie, the right ventricle must have been"primed" [hypertrophied] and exposed to a progressively higher PAP and PVR over time). On the other hand, an elevated CVP may imply a failing right ventricle with or without TR. The compromised right ventricle will tolerate neither hypovolemia nor overfilling; therefore, an optimal position has to be determined and maintained on the compromised failing RV Frank-Starling curve. Because the RV is mainly a "volume chamber," it is less preload dependent than the LV; thus, for a given increase in preload, a smaller increase in stroke volume is expected. However, because it is thin walled, the RV is much more afterload dependent than the LV and the RV CO decreases significantly with an acute increase in mPAP. Past teachings have often suggested that the RV be filled aggressively to passively increase pulmonary blood flow and CO. This may hold true with normal PVR (Fontan physiology, which is not the case in PH) but not in circumstances in which the PVR is high. Excess volume loading will result in acute RV distention, increased TR, right-to-left shift of the interventricular septum, impairment of LV end-diastolic filling and pericardial constraint (due to distended RV). These factors all causes a reduced stroke volume, reduced systemic blood pressure, inadequate RCA perfusion, and an ensuing downward hemodynamic spiral. This is especially true once the CVP reaches values of 15 to 20 mmHg. It is difficult to determiine optimal RV filling. This can be assessed with cautious fluid boluses (250 mL of lactated Ringer's solution) or by an autotransfusion by elevation of the patient's legs. Ongoing fluid boluses are indicated if elevation of the legs causes a modest (2-5 mmHg) elevation in CVP and corresponding elevation in PCWP and mean arterial pressure; an elevation of only the CVP (with minimal/ no change in PCWP or mean arterial pressure) likely indicates RV distention and precludes further fluid boluses. A relatively underfilled RV is likely the lesser of 2 evils.

3. *Maintain RV myocardial performance*. This includes maintenance of RV coronary perfusion pressure and RV inotropic therapy. Normally, RV coronary perfusion occurs during systole and diastole. However, as the PVR and RV pressure rises, the RCA flow changes to be mainly in diastole (similar to left coronary artery perfusion). RV subendocardial ischemia, caused by myocardial oxygen supply-demand imbalance, is common in PH. To avoid this, systemic hypotension, excessive increases in RV pressure, contractility, and heart rate must be avoided. It is important to immediately increase the systemic blood pressure and, subsequently, RCA perfusion pressure when acute RV failure is diagnosed. This can be achieved by optimizing the volume status and use of vasopressors (i.e. norepinephrine and vasopressin). Accumulating clinical experiences as well as animal data suggest that vasopressin causes less of an increase in RV afterload than does norepinephrine and reduces the dose of norepinephrine required

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to maintain the systemic blood pressure. The choice of type of anesthesitic technque (general versus regional) and the type of anesthetic agents is *much* less improtant than understanding the physiological perturbations induced by the anesthetic. Anticipating and mitigating the physioological effects will prevent acute decompenstion, allowing many types of anesthesia for these patients. In this regard, volatile agents, propofol, thiopental, narcotics, ketaime and etomidate can all be used in the appropriate manner. RV contractilty may have to be enhanced in acutely failing RV with either beta-adrenoreceptor agonist therapy (e.g. dobutamine), PDE-3 inhibitor (milrinone), or a calcium-sensitizer (levosimendan). All the classes also reduce PVR. The may be used in combinnation. However, when given in larger doses, they may also acutely reduce SVR. If the increase in RV CO does not offset the reduction in SVR, the systemic BP may decrease, and the RCA perfusion will be compromised. This may aggrevate the situation instead of improving RV function. It is therfore crucial to start these agents at a low- dose to avoid the deletrious effects on SVR. Dobutaine effects are short-lived and may be easier to titrate than milrinone. The combination of low-dose dobutaime and low-dose milrinone are synergistic and may optimize cardiac function with less side effetcs than higher doses of each agent alone. Levosimendan is a cardiac inotrope that binds to troponin C, sensitizing the cell to calcium, which increasese contractility without increasing intracellular calcium. Epinephrine, norepinephrine, and dopamine, due to their multi-receptor profiles, are less atractive agents.

4. *Maintain the transeptal gradient (TSG) and RV geometry*. At normal RV systolic pressure (25 mmHg) and LV systolic pressure (125 mmHg), there is a large gradient from the left ventricle to the right ventricle (TSG = 100 mmHg), causing the normal interventricular septum to bulge into the RV. This provides a "scaffold" against which the RV-free wall contracts. Septal function accounts for about 50% of normal RV systolic. Therefore, conditions that reduce the LV pressure (systemic hypotension) or increase the RV pressure (PH) will reverse the TSG and severely compromise RV function. These conditions are common in patients with RV dysfunction due to PH, and the periopetrative period creates many opportunities to aggrevate the TSG changes (e.g. any cause of reduced SVR). This causes the RV to become more globular (the RV "bulges" into the left ventricle and impairs LV filling). The missalignment of the oblique arrangement of the RV septal myofibrils (due to dilation and shift) causes RV dysfunction. In order to maintain the TSG, the PVR needs to be reduced, and the systemic blood pressure needs to be aggresively maintained.

5. *Reduce PVR*. Patients on chronic therapy for PH should continue their established treatment during the perioperative period. Anesthetic agents that increase PVR should be minimized. FRC must be carefully maintained **(Figure 5)** and any factors that cause a reduction in FRC must be avoided. In contrast to systemic arteries, pulmonary vessels constrict with hypoxia (Euler-Liljestrand reflex) and dilate with hyperoxia. Thus, perioperative hypoxemia, hypercarbia, atelectasis, pleural effusions, hypothermia, fluid overload, pain, and anxiety can all cause acute rises in PVR with resultant RV decompensation. Therefore, perioperative ventilation strategies of patients with PAH should incorporate high concentrations of oxygen, low tidal volumes (6 mL/kg of predicted body weight), a respiratory rate sufficient to achieve mild hypocarbia, and optimum levels of positive end-expiratory pressure (5-10 cmH2O). Early drainage of pleural effusions and recruitment maneuvers should be considered.Intravenous air or particulate material (precipitated drugs) should be avoided because of the potential for right-to-left embolization through an opened foramen ovale.

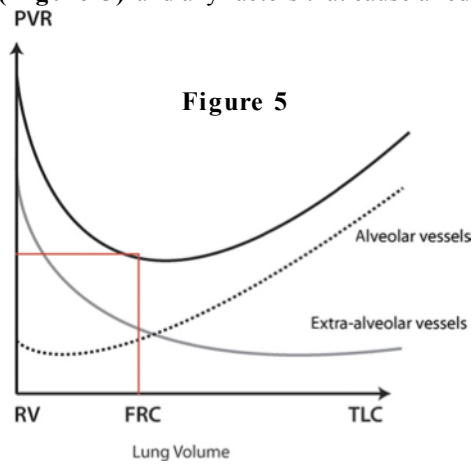

Figure 5

Apart from the previously mentioned physiologic considerations, the PVR be reduced by selective PA vasodilators. Unfortunately, none of the available intravenous PA vasodilators is selective enough not to cause accompanying systemic vasodilation, which potentially could lead to reductions in the RV coronary perfusion and RV ischemia. Hence, we need to use dugs that cause pulmonary artery dilation "selectively", either by virtue of their specificty for

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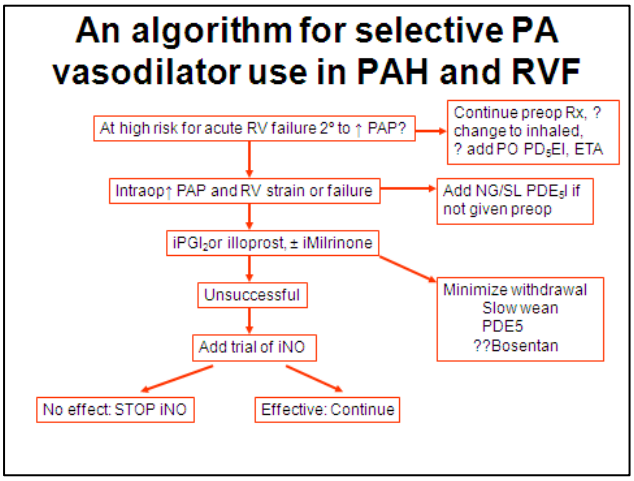
PA or by virtue of the method of delivery. Inhaled PA vasodilators cause preferential vasodilation in well-ventilated lung zones, with improvement in V/Q matching and arterial oxygen saturation. Inhaled agents decrease mPAP, have little effect on SVR, so TSG is not deletriously affected. Commonly used inhaled agents include various prostanoids (prostacyclin and iloprost), inhaled milrrinoe, and inhaled nitric oxide. The each have the advantages and limitations, and some of the agents used in combination may have be mechanistically additive. A proposed algorithm for using sel;ective PA vasodilators is shown **Figure 6.**

Conclusion: The perioperative management of patients with PH and associated RV dysfunction is complex and requires a thorough understanding of the PA/RV pathophysiology. Failure to diagnosis RV failure early and institute the correct therapy will lead to high perioperative morbidity and mortality. The anesthesiologist has to be aware of the potential treatment strategies including optimizing physiologic parameters, the use of selective pulmonary artery vasodilators, and inotropic and systemic blood pressure support. These patients should be managed by teams familiar with the disease.



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