MANAGEMENT OF PULMONARY HYPERTENSION AFTER CARDIAC SURGERY

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NORMAL PULMONARY CIRCULATION

- low pressure
- low resistance
- large reserve of low perfused pulmonary capillaries
- thin walled and is able to accommodate large changes in volume or preload

however

- limited contractile reserve to compensate for an increase in impedance or afterload
RV PERFUSION

• **diastole** and **systole** because of low wall tension.

• When PAP becomes systemic the **perfusion of the RV** is markedly diminished leading to a spiral decrease in overall cardiac output.
INCREASE IN AFTERLOAD:

• Decrease in RV stroke volume and output
• Bulging of the IVS into the LV leading to decrease LV filling and to further decrease LV output.
• An elevation of RV pressure and volume
• Dilation and thus may cause TR,
• Reduces forward cardiac output and ultimately end organ perfusion
RV AFTERLOAD

- pulmonary input impedance:
- pulmonary arterial compliance + pulmonary vascular resistance.
- Normally in pediatric cardiology, pulmonary vascular resistance has been used as the sole measure of right ventricular afterload.
- PVR measures the static component of impedance.
- Compliance measures the dynamic component.
- Pulmonary artery compliance is crucial to the success of the RV in maintaining cardiac output.
- Compliance of the pulmonary vasculature: how the blood volume is ejected and can be estimated SV/PP.
- Recent measures of pulmonary vascular input impedance have been shown to have added value in the measure of RV afterload.
PH CRISIS

- 2% -7% (post op)
- 4.5%: 156 patients undergoing 256 noncardiac procedure and catheterization (5% of cath & 2.7% all)
- 8% of 30-day mortality following repair
INCIDENCE

- Performing corrective surgery at a younger age
- Better surgical technique
- Changes in CPB practice
- PH therapy
DEFINITION

- Sudden increase in PAP : PAP/Systemic > 0.75
- Rise in CVP >20%
- Decrease in MAP >20%
- Decrease in O2sat<90%
- Evidence of LCOS
- Accompanied by bronchoconstriction
MANAGEMENT OF RIGHT HEART FAILURE IS COMPLICATED DUE TO THE COMPLEX INTERACTION BETWEEN THE RV AND THE LV

• The mainstays of treatment for acute RV failure include:
  • (1) RV afterload reduction
  • (2) improvement of RV contractility
  • (3) maintenance of systemic blood pressure to ensure coronary artery filling and to decrease IVS shift
  • (4) maintain adequate but not excessive preload
• Both hypovolemia and hypervolemia may impair RV function and perfusion. In many conditions, over aggressive volume administration may lead to worsening right heart failure, right ventricular dilation, and impairment of left ventricular output. Adequate right ventricular volume is required, but a too aggressive strategy may impair output
MANAGEMENT OF ACUTE RIGHT VENTRICULAR FAILURE

• In a patient with acute elevations of PAP and afterload, there is decreased in RV contractility with RV dilation in an effort to increase RV volume and improve cardiac output by the Frank–Starling mechanism.

• In patients with chronic PH, the RV compensates with myocardial hypertrophy that reduces wall stress. Despite the hypertrophic mechanism the RV can easily be overwhelmed and result in failure. RVH is associated with an increase in myocardial demand leading to a supply demand mismatch.

• Thus, patients with chronic PAH who have an upper-respiratory infection, pneumonia, marked changes in preload, or medication noncompliance can rapidly develop right ventricular failure. As these compensatory mechanisms unravel, RV stroke volume continues to decrease leading to an under filled LV with a drop in systemic blood pressure. This leads to a decrease in aortic and coronary perfusion and RV ischemia. This circular abnormality mandates rapid changes in preload, ventricular function, and afterload.
• The primary aim is:
  • decrease PVR and PAP
  • if not possible, to avoid stimulation of the pulmonary circulation and support right ventricular function through the balance between PVR&SVR and maintenance of cardiac output
In critical patients, CVP monitoring may provide important clues as to RV filling. The majority of patients with right heart failure will present with fluid overload and require diuretics. Although no optimal value of CVP has been determined a reasonable target of CVP is between 6 and 12 mmHg. For most patients with acute right heart failure, inotropic medication is a mainstay of therapy. There is no perfect inotropic agent as most inotropes will have effects on the systemic circulation, which may impair right ventricular perfusion.

- an agent that may lower PAP but also lead to systemic hypotension may decrease coronary profusion, worsen septal shift and thus right ventricular function.
• Therapeutic Measures

**THERAPY SHOULD BE INDIVIDUALIZED.**

**THE MAIN MEASURES:**

- **ANALGESIA AND SEDATION,**
- **VENTILATION,**
- **INTRAVENOUS,**
- **INHALED DRUGS**
• **1. Anatomic Considerations**

FIRST OF ALL, **RESIDUAL ANATOMICAL PROBLEMS** SHOULD BE EXCLUDED AS THIS MAY BE RESPONSIBLE FOR INCREASED RVP AS IN THE CASE OF RESIDUAL SHUNTS OR RVOTO. THUS, ANATOMIC INVESTIGATIONS SHOULD BE PERFORMED SUCH AS TTE & TEE OR CATHETERIZATION PARTICULARLY IF A POTENTIAL INTERVENTION IS ANTICIPATED OR THE PATIENT IS NOT IMPROVING.
• a right-to-left shunt used as a “pop off” for the right side. Preserving a calibrated ASD or fenestrated ventricular defect in the patch is a common measure, but some authors advocate the use of a valve patch when a VSD is closed ("flap" fenestration of the VSD patch).

• This may be beneficial to maintain cardiac output but to the detriment of cyanosis. Oxygen delivery is maintained by increasing oxygen delivery. Delayed chest closure may be useful to decrease the constraints on a dilated dysfunctional RV.
2. Sedation and Analgesia

AGITATION AND STRESS ARE POTENTIAL TRIGGERS FOR PHC: SHOULD BE AVOIDED.

WELL-CONTROLLED ANALGESIA AND SEDATION SHOULD BE GUARANTEED WHILE ENSURING SPONTANEOUS BREATHING IN STABLE PATIENTS WHO WOULD BE CANDIDATES FOR EXTUBATION.

HOWEVER, UNSTABLE PATIENTS WITH FREQUENTLY OR POORLY TOLERATED PHC SHOULD BE KEPT DEEPLY SEDATED AND EVENTUALLY ON MUSCLE RELAXANTS AS REQUIRED.

THIS IS USUALLY ACHIEVED WITH A COMBINATION OF OPIOIDS AND BENZODIAZEPINES ADMINISTERED AS CONTINUOUS INFUSIONS AND TITRATED TO EFFECT.

OTHER ALTERNATIVES ARE AVAILABLE AND DEPEND ON SPECIFIC INSTITUTIONAL PROTOCOLS: DEXMEDETOMIDINE, PROPOFOL, AND CLONIDINE TO MENTION SOME. THE PRINCIPLE OF USING MINIMAL EFFICIENT DOSES SHOULD BE RESPECTED AS MUCH AS POSSIBLE.
It is essential to adequately ventilate patients with pulmonary hypertension and to avoid overdistention or atelectasis known to be potential triggers for increased PVR. It is important to remember that PVR is normal at normal FRC.

**3. VENTILATION AND PH**

Pulmonary vascular resistance rises in association with very large or very small lung volumes. Pulmonary vascular resistance is lowest at functional residual capacity.
ALKALOSIS

Alkalosis induces pulmonary vasodilatation, whereas acidosis induces vasoconstriction. It is known after the work of Chang et al that the triggers are mainly the pH (hydrogen ion concentration) and not the carbon dioxide levels. The current approach is to maintain a normal or slightly alkalotic pH (as to avoid aggressive ventilation) and only in rare instances to raise pH over 7.5.

Morris et al. showed that hyperventilation to increase pH has some deleterious effects such as an increase in SVR that may not be tolerated in the postoperative period. Use of sodium bicarbonate or THAM may be considered in some patients in order to induce alkalosis without the potential deleterious effects of hyperventilation.
4. OXYGENATION

It is well known that hyperoxia provokes pulmonary vasodilation and that hypoxia induces pulmonary vasoconstriction. It is therefore important to maintain an adequate oxygenation ($PO_2$ 80–100 mmHg) during a PHC and with patients at risk to develop these problems. This is obtained with the administration of oxygen and again adequate ventilation ensuring a proper lung volume. However, the effect of oxygen seems not so clear in the setting of PH after cardiac surgery as well as in the so-called fixed lesions. One must also remember that high levels of inspired oxygen may be deleterious and induce lung damage.
The effects of pH and PO2 on pulmonary vascular resistance
5. VASODILATOR DRUGS

PH may be treated with intravenous or with inhaled vasodilators. Various intravenous vasodilators such as tolazoline, prostacyclin, phenoxybenzamine, phentolamine, and nitrodilators have been used in the past to reduce PAP. However, their lack of selectivity and inconsistent efficacy are a limiting factor; these drugs carry a risk of systemic hypotension among others, which may be undesirable after cardiac surgery.
INHALED NITRIC OXIDE (INO)

Inhaled nitric oxide (iNO) improves right ventricular systolic function by decreasing its afterload while increasing left ventricular preload, restoring aortic pressure and coronary perfusion.

In patients with poor left ventricular function, iNO should be used cautiously since the preload increase may be deleterious.
Wessel et al showed that pulmonary endothelial dysfunction was present after CPB; thus, the response to acetylcholine was attenuated, but the response to inhaled nitric oxide was maintained. These authors hypothesized that a dysfunctional endothelium with reduced endogenous nitric oxide release may contribute to postoperative PH.

Journois et al demonstrated that inhaled nitric oxide was a useful therapy for PHC refractory to conventional treatment. According to Miller et al. even low doses of nitric oxide (2 ppm) appear to be effective in such patients. Beghetti et al. showed that the effect of low-dose nitric oxide was maintained over several days at concentrations carrying little risks of toxicity. Nitric oxide has been used with success in several different CHD where increased PVR may complicate the postoperative course such as MS, TAPVC, Glenn anastomosis, and the Fontan circulation.
It also appears useful after cardiac and/or lung transplant. However, a beneficial effect in patients with cavopulmonary anastomosis is not consistently reported and despite an increase in cGMP levels. Inhaled nitric oxide augments right ventricular function after LVAD implantation, perhaps through an increase in pulmonary venous return and left atrial pressure, thus facilitating pump flow. Patients who remain dependent on NO and have rebound PH upon its withdrawal are candidates to therapy with sildenafil as a strategy to wean the NO.
INHALED PROSTACYCLIN

Inhaled prostacyclin is increasingly used as delivered by aerosol and may overcome the necessity of a special device to deliver NO.

Several series have been published with epoprostenol or iloprost and prospective studies are underway, but one of the major problems is to define the dose to be delivered as well as the exact dose delivered when the drug is administered in ventilated patients.
block the degradative action of PDE5 on cyclic GMP in the smooth muscle cells; **PDE-5 is increased in PH.** Specific PDE-5 inhibitors, such as sildenafil, promote an increase in cGMP levels and thus promote pulmonary vasodilation and remodeling. **Sildenafil is as effective a pulmonary vasodilator as inhaled NO.** Sildenafil may also be useful in the setting of inhaled NO therapy withdrawal in postoperative PH or in the presence of PH related to CLD.

Intravenous sildenafil has been shown to potentiate the increase in cGMP in response to NO in children with increased PVR related to CHD or in the postoperative state. Nevertheless, sildenafil infusion has been associated with increased intrapulmonary shunting and augmentation of hypoxemia related to ventilation/perfusion mismatch in the postoperative CHD patient. However, a recent study of intravenous sildenafil has shown improvement in oxygenation index in PPHN in patients treated with or without inhaled NO. In a double-blind, multicenter, placebo controlled, dose-ranging, parallel-group trial in postoperative PH, one of three doses of intravenous sildenafil, or placebo, was given, for a minimum of 24 h. Although the sponsor terminated the study after 15 months owing to slow patient accrual, intravenous sildenafil reduced PAP and shortened time to extubation and ICU stay in children with postoperative PH.

**PHOSPHODIESTERASE TYPE 5 (PDE-5) INHIBITORS**
After surgical correction of patients with preoperative PH or under significant risk for postoperative PH spells, most centers initiate milrinone and a low dose (less than 5 mg/kg/min) of dopamine or dobutamine for right ventricular dysfunction. Low doses of epinephrine may be added for further inotropic effect. Right ventricular function may be compromised following CHD repair because of CPB and direct injury by the surgical procedure itself. Increased PVR further compromises right ventricular function; as a result the right ventricle becomes dilated and induces an “intrapericardial tamponade” effect on the left ventricle. This in turn results in secondary diastolic dysfunction of the LV which further reduces cardiac output leading to aortic hypotension and coronary hypoperfusion of the right ventricle.

6. INOTROPIC AND VASOACTIVE DRUGS
The effect of the usual inotropes such as epinephrine or dopamine on the right ventricle as well as the potential deleterious effect on the pulmonary vascular resistance is still matter of debate. It is anyway tempting and justified to use catecholamines in this setting trying to find a balance between the potential beneficial and the detrimental effects. Epinephrine can improve cardiac function but is known to be deleterious to the myocardium if used at high doses and for a prolonged period of time.

However, it may still have a place at low dose. Norepinephrine through an increase in SVR may improve coronary perfusion and as such improve right ventricular function. The use of systemic vasoconstrictors is supported by an animal model of acute right heart failure, in which RV functional performance with increased cardiac output was achieved by administration of vasopressors, such as norepinephrine and epinephrine. The virtues of these drugs should be balanced against their side effects.
• In severe RV failure, the use of high dose milrinone and dobutamine in isolation may lead to clinical worsening. Animal studies have shown improved contractility with a combination of epinephrine/milrinone and dopamine/milrinone compared to dobutamine alone.

• Limitations of catecholamine agents include a potential increase in PVR and detrimental increase in heart rate.

• An ideal vasoactive agent will increase SVR greater than PVR and therefore maintain right coronary profusion.

• Some centers use vasopressin which increases SVR but may also lower PVR by the release of local nitric oxide. The normal RV, and even the hypertrophied RV in the patient with PH, responds poorly to acute increases in RV afterload. Therefore, a mainstay of therapy for right heart failure is reduction of RV afterload. Inhaled nitric oxide is a selective pulmonary vasodilator that increases CGMP, may augment the nitric oxide response and may also facilitate weaning of nitric oxide to prevent rebound PH. Further, PDE-5 inhibitors may also improve right ventricular performance.
PERFECT DRUG

The finality is that the perfect drug should:

- improve myocardial performance
- vasodilate the pulmonary vascular bed
- inducing tachycardia and increasing oxygen consumption.

Milrinone is a phosphodiesterase inhibitor that may have some of these properties and it is increasingly used in postoperative care. The role of type 5 phosphodiesterase inhibitors in the presence of PH has a major interest, but type 3 inhibitors such as milrinone have been by far more studied and largely used in pediatric practice. Some new therapies are under development.

Nesiritide or natriuretic hormone shows some synergistic effect with nitric oxide and sildenafil. The same principle applies to levosimendan, a calcium sensitizer that enhances contractility and has some vasodilatory properties without increasing myocardial oxygen consumption. Levosimendan has also been shown to have some pulmonary vasodilator effects in the presence of acute pulmonary hypertension, but so far data in children is scarce and further studies are also needed.
Therapeutic approach to PAH

**ENCOURAGE:**
- Anatomic investigations
- Opportunities for right-to-left shunt as a “pop-off”
- Sedation/analgesia or anesthesia
- Moderate hyperventilation
- Moderate alkalosis
- “Perfect” metabolic status
- Adequate inspired oxygen
- Normal lung volumes
- Optimal hematocrit
- Inotropic support
- Vasodilators
- Nutritional support

**AVOID:**
- Residual anatomic defects
- Intact atrial septum in right heart failure
- Agitation and pain
- Respiratory acidosis
- Metabolic acidosis
- Volume overload
- Alveolar hypoxia
- Atelectasis or overdistension
- Excessive hematocrit
- Low cardiac output and low coronary perfusion
- Vasoconstrictors/increased afterload
CONCLUSION

Management of pulmonary hypertension in the cardiac intensive care setting should be multifactorial and multidisciplinary as it remains challenging and still carries, even if decreased compared to the previous decade, a significant mortality and morbidity. An increased knowledge of the mechanisms as well as the introduction of new therapies has led to better prognosis.

Appropriate therapy requires firstly the identification of the potential cause. Besides the pharmacological approach, caregivers should consider the creation of anatomic paths to decompress the right ventricle, as the final cause of death remains ventricular failure.