Perioperative Management of Pulmonary Hypertension

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Disclosures

• No financial disclosures
At the conclusion of the activity participants should be able to:

- Describe the steps required to develop an anesthetic plan for patients with pulmonary hypertension
- Discuss the treatment of the perioperative complications which may occur in patients with pulmonary hypertension
- Discuss the importance of teamwork in developing a multidisciplinary approach to the perioperative management of the patient with pulmonary hypertension
Increasing Incidence of Pulmonary Hypertension

Hyduk, MMWR 2005; 54:1
Pulmonary Hypertension

46 year old woman diagnosed with idiopathic pulmonary arterial hypertension (PAH) 6 years ago

On sildenafil and bosentan therapy

NYHA class 3

TTE: RVSP 70, mild-mod RVE and dysfunction

Scheduled for laparoscopic cholecystectomy after acute cholecystitis
The 7 Steps

Æ Recognition of pulmonary hypertension
Æ Assessment of severity of pulmonary hypertension
Æ Perioperative risk assessment
Æ Preoperative optimization of the patient
Æ Choice of anesthetic technique
Æ Choice of monitoring
Æ Treatment of decompensated pulmonary hypertension
Clinical Presentation of Idiopathic Pulmonary Arterial Hypertension

- Dyspnea
- Chest pain
- Syncope
- RVH
- Not right heart failure (edema, ascites, JVD, hepatomegaly)
Etiologies of Pulmonary Hypertension

Æ PAP = LAP + (CO x PVR)

Æ Etiologies of pulmonary hypertension
  Æ Increased left atrial pressure
  Æ Left ventricular failure
  Æ Valvular heart disease (mitral, aortic)
  Æ Cardiac shunts (congenital heart disease)
  Æ Increased PVR (non-cardiac etiologies)
Non-Cardiac Etiologies

- Pulmonary disease
  - Emphysema
- Chronic hypoxia
  - Pickwickian, OSA
- Pulmonary arterial obstruction
  - Pulmonary thromboembolism
- Idiopathic pulmonary arterial hypertension (IPAH)
  - Primary pulmonary hypertension (PPH)
Acute Pulmonary Vasoconstriction

Æ Hypoxia
Æ Hypercarbia
Æ Acidosis
Æ Sympathetic tone
Æ Vasoconstrictor agents
The 7 Steps

Æ Recognition of pulmonary hypertension
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Æ Choice of monitoring
Æ Treatment of decompensated pulmonary hypertension
Echocardiography in PH

Echocardiography in PH

- Calculation of sPAP: $\Delta P = 4V^2$
- Mitral stenosis
- Left ventricular dysfunction
- Cardiac shunts
- Estimation of RAP and CO
- RV function

The 7 Steps

- Recognition of pulmonary hypertension
- Assessment of severity of pulmonary hypertension
- Perioperative risk assessment
- Preoperative optimization of the patient
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- Choice of monitoring
- Treatment of decompensated pulmonary hypertension
Risk of Surgery in Patients with Pulmonary Hypertension

Æ Depends on etiology of pulmonary hypertension, severity of pulmonary hypertension, and adequacy of compensatory mechanisms (RAP, CO, SvO₂, RV function, functional status)
Cycle of RV Failure

Pulmonary Hypertension

↑RV Afterload

RV Hypertrophy

↑RV Contractility

Normal CO

↑PVR

↓RV Output

↓LV Output

↓Blood pressure

↓RV Coronary perfusion
Risk of Surgery in Patients with Pulmonary Hypertension

Æ Depends on etiology of pulmonary hypertension, severity of pulmonary hypertension, and adequacy of compensatory mechanisms

Æ Depends on surgical factors
Surgical Factors

- Rapid blood loss procedures
- RV preload
- Major surgery or blood transfusion
- Systemic inflammatory response syndrome produces pulmonary vasoconstriction
- Pulmonary dysfunction
- Pulmonary embolization
- Orthopedic procedures
Risk of Surgery in Patients with Pulmonary Hypertension

- Mortality for non-cardiac surgery with significant PH is reported in the range of 7-50%
- 70% mortality for Cesarean section in patients with systemic pulmonary pressures
- 35% mortality for liver transplantation; 80% mortality with mean PAP > 45 mm Hg
Non-Cardiac Surgery

Ramakrishna, JACC 2005; 45:1691

145 patients with pulmonary hypertension undergoing non-cardiac surgery

42% had one or more major perioperative morbid events

7% mortality

Only 27% NYHA class 3 or 4

Mean RVSP 48 mm Hg
## Multivariate Predictors of Morbidity

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of pulmonary embolism</td>
<td>7.3</td>
</tr>
<tr>
<td>NYHA functional class ≥ 2</td>
<td>2.9</td>
</tr>
<tr>
<td>Intermediate/high-risk surgery</td>
<td>3.0</td>
</tr>
<tr>
<td>Duration of anesthesia &gt; 3 h</td>
<td>2.9</td>
</tr>
</tbody>
</table>

Ramakrishna, JACC 2005; 45:1691
Risk of Surgery in Modern PH Centers

Meyer, Eur Respir J 2013; 41:1302

- 114 patients undergoing major surgery at 11 PH centers
- All patients on medications for PAH
- 43% of patients NYHA class 3 or 4
- PAP 45 mm Hg
- 39% urgent or emergent surgery
- 82% GA, 18% spinal anesthesia
- 7 patients (6%) had major complications
- 4 patients (3.5%) died
Risk of Surgery in PH Centers

Risk factors for major complications

- RAP > 7 mm Hg (OR 1.1)
- 6MWD < 400 m (OR 2.2)
- Use of vasopressors (OR 1.5)
- Emergency procedure (OR 2.4)

Mortality 15% vs. 2%
The 7 Steps

Æ Recognition of pulmonary hypertension
Æ Assessment of severity of pulmonary hypertension
Æ Perioperative risk assessment
Æ Preoperative optimization of the patient
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Æ Choice of monitoring
Æ Treatment of decompensated pulmonary hypertension
Therapy of Pulmonary Hypertension

- Treatment of the underlying disease
- Oxygen supplementation
- Treatment of right heart failure
- Pulmonary vasodilator therapy
Vasodilators

Æ Beta-agonists: Isoproterenol
Æ Alpha-antagonists: Phentolamine, tolazoline
Æ Arterial dilators: Hydralazine, diazoxide
Æ Venodilators: Nitroglycerin
Æ Balanced dilators: Nitroprusside
Æ Calcium blockers: Nifedipine, diltiazem
Therapy of Pulmonary Hypertension

Prostacyclin-cAMP pathway:
- Arachidonic acid
- Endothelium
- Cyclooxygenase
- PGI synthase
- PGH$_2$

Nitric oxide-cGMP pathway:
- Endothelin converting enzyme
- L-Arginine
- NO synthase
- NO

Endothelin pathway:
- Proendothelin
- Endothelin receptor antagonist
- ETB

Smooth muscle cells:
- Adenylate cyclase
- PDE 3,4 inhibitor
- PGI$_2$

Intercellular crosstalk:
- PDE 3,4
- Guanylyl cyclase
- PDE-5
- cGMP
- GMP
- Inositol 1,3,5 triphosphate
- Vasoconstriction

Reduce vessel tone
Inhibit proliferation
Continuous Intravenous Prostacyclin


Æ 27 patients with IPAH treated with prostacyclin for more than one year

Æ PVR decreased an average of 53%

Æ All patients had symptomatic improvement
Survival in IPAH

McLaughlin, Circulation 2002; 106:1477
Bosentan Therapy for IPAH

Sildenafil Therapy in PH

Galiè, NEJM 2005; 353: 2148
Inhaled Nitric Oxide
Inhaled Prostacyclin (Flolan©)

Æ Equivalent pulmonary vasodilation to inhaled nitric oxide

Khan, J Thorac Cardiovasc Surg 2009;138:1417
Inhaled Prostacyclin (Flolan®)

Æ Continuous nebulization into ventilator circuit with initial rate of 0.05 mcg/kg/min

Æ Infusion pump and electronically-driven nebulizer (Aeroneb)
  - Nebulizer is expensive

Æ Infusion pump and flow-driven nebulizer (Miniheart)
  - Continuous gas flow may adversely affect ventilator
Inhaled Prostacyclin (Flolan®)

Æ Glycine buffer is sticky and will occlude valves and filters
  Æ Double filters on expiratory limb with changes every 30-60 minutes
  Æ Monitor peak inspiratory pressure
  Æ Be prepared for Ambu bag ventilation with nebulizer

Æ Rebound pulmonary hypertension with discontinuation
The 7 Steps

- Recognition of pulmonary hypertension
- Assessment of severity of pulmonary hypertension
- Perioperative risk assessment
- Preoperative optimization of the patient
- **Choice of anesthetic technique**
- Choice of monitoring
- Treatment of decompensated pulmonary hypertension
Hemodynamic Goals in PH

- Maintain preload
- Maintain SVR (systemic afterload)
- Maintain contractility
- Maintain heart rate and sinus rhythm
- Avoid increased PVR
Anesthetic Techniques

Æ General anesthesia
   Æ ↓ Preload, ↓ afterload, ↓ contractility

Æ Neuraxial blocks
   Æ ↓ Sympathetic tone, ↓ preload, ↓ afterload

Æ Regional anesthesia
   Æ Ideal for peripheral procedures and for postoperative pain
In theory there is no difference between theory and practice. In practice there is.
Induction Techniques

Æ Propofol: ↓preload, ↓afterload, ↓contractility

Æ Ketamine: ↑PVR (but not if ventilation is maintained)

Æ High dose narcotics: No direct effect but respiratory depression (↑PaCO₂)

Æ Etomidate: Ideal agent
Maintenance of Anesthesia

Æ Nitrous oxide: ↑PVR (?not in kids)
Æ High-dose narcotics: Emergence problems
Æ Isoflurane/sevoflurane: ↓SVR and PVR proportionally
Æ Combined narcotic-volatile agent techniques work well
Æ Increasing role for dexmedetomidine
Æ Avoid bradycardia
Ventilation and PVR
The 7 Steps

Æ Recognition of pulmonary hypertension
Æ Assessment of severity of pulmonary hypertension
Æ Perioperative risk assessment
Æ Preoperative optimization of the patient
Æ Choice of anesthetic technique
Æ Choice of monitoring
Æ Treatment of decompensated pulmonary hypertension
Intraoperative Monitoring

Æ Standard ASA monitors
Æ Arterial catheter
Æ Intraoperative TEE
   Æ RV function, RV volume, LV volume
Æ Pulmonary artery catheter
   Æ Not used for wedge pressure measurement
      Æ Risk of pulmonary artery rupture
Æ Progression of pulmonary hypertension
   Æ Guide surgical and anesthetic decision making
Æ Treatment of systemic hypotension
PA Catheters in Eisenmenger’s Disease

Æ Pulmonary artery pressure equals systemic blood pressure
Æ Pulmonary artery wedge pressure equals CVP
Æ Thermodilution CO not accurate
Æ PA catheters pass into systemic circulation
The 7 Steps

- Recognition of pulmonary hypertension
- Assessment of severity of pulmonary hypertension
- Perioperative risk assessment
- Pre-operative optimization of the patient
- Choice of anesthetic technique
- Choice of monitoring
- Treatment of decompensated pulmonary hypertension
Cycle of RV Failure

**Pulmonary Hypertension**
- $\uparrow$ RV Afterload
- $\uparrow$ RV Hypertrophy
- $\uparrow$ RV Contractility
- Normal CO

**Normal CO**

$\uparrow$ PVR

$\downarrow$ RV Output

$\downarrow$ LV Output

$\downarrow$ Blood pressure

$\downarrow$ RV Coronary perfusion
Treatment of RV Failure

Æ Molloy, Am Rev Respir Dis 1984; 130:870

Æ Right ventricular failure model in dogs due to pulmonary hypertension from pulmonary embolism

Æ Resuscitation with

Æ Volume: 0% survival
Æ Isoproterenol: 0% survival
Æ Norepinephrine: 100% survival
RV Decompensation

Æ RV ischemia

Æ RV coronary flow normally in systole and diastole; in pulmonary hypertension, only in diastole

Æ Increased oxygen consumption

Æ Cycle of ischemia and failure
RV Decompensation

Æ Role of the interventricular septum

Æ High LV pressure normally pushes the septum towards the RV free wall, producing RV ejection
## Etiologies of Hypotension

<table>
<thead>
<tr>
<th></th>
<th>CVP</th>
<th>PAP</th>
<th>CO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decreased preload</strong></td>
<td>↓↓↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td><strong>Decreased contractility</strong></td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td><strong>Decreased SVR</strong></td>
<td>→</td>
<td>→</td>
<td>↑ or →</td>
</tr>
<tr>
<td><strong>Increased PVR</strong></td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
</tbody>
</table>
Management of Hypotension

Is CVP decreased?  Yes  Volume
  ↓No
Is PAP decreased?  Yes  Inotropes
  ↓No
Are there reversible causes of increased PVR?
  ↓No
  ↓Yes
Is cardiac output decreased?  Treatment
  ↓No
  ↓Yes
Systemic  Inotropes and/or
vasoconstrictors  Pulmonary vasodilators
Management of Hypotension

Is CVP decreased? Yes Volume
- No

Is PAP decreased? Yes Inotropes/
- No Vasoconstrictors

Are there reversible causes of increased PVR? No
- Yes

Is cardiac output decreased? Treatment
- No

Systemic Inotropes and/or
Vasoconstrictors Pulmonary vasodilators
Management of Hypotension

Is CVP decreased?  Yes  Volume
  ↓ No
↓ No

Is PAP decreased?  Yes  Inotropes/
  ↓ No  Vasoconstrictors
↓ No

Are there reversible causes of increased PVR?  ↓ Yes
  ↓ No
↓ Yes

Is cardiac output decreased?  Treatment
  ↓ No  ↓ Yes
↓ Yes

Systemic vasoconstrictors  Inotropes and/or
Pulmonary vasodilators
Active Pulmonary Vasoconstriction

ÆHypoxia
ÆHypercarbia
ÆAcidosis
ÆSympathetic tone
ÆVasoconstrictors
Management of Hypotension

Is CVP decreased? Yes Volume
↓ No

Is PAP decreased? Yes Inotropes/
↓ No Vasoconstrictors

Are there reversible causes of increased PVR?
↓ No

Is cardiac output decreased? Treatment
↓ No
↓ Yes

Systemic Inotropes and/or
vasoconstrictors Pulmonary vasodilators
Systemic Vasoconstrictors

Æ Kwak, Anaesthesia 2002; 57:9

Æ 27 patients with pulmonary hypertension who developed hypotension following induction of anesthesia

Æ Randomized to norepinephrine infusion vs. phenylephrine infusion to increase systolic BP by 50%

Æ Phenylephrine failed to increase SBP by 50% in one-third of patients
Vasopressin

Æ Systemic vasoconstriction via the V1 receptor
   Æ No pulmonary, renal, cardiac, or cerebral vasoconstriction
Æ Pulmonary vasodilation via a NO-dependent mechanism
Æ Effective for rescue therapy of PH
MANAGEMENT OF HYPOTENSION

Is CVP decreased?  Yes  Volume
↓No
↓No

Is PAP decreased?  Yes  Inotropes/
↓No  Vasoconstrictors
↓No

Are there reversible causes of increased PVR?
↓No
↓Yes

Is cardiac output decreased?  Treatment
↓No  ↓Yes

Systemic  Inotropes and/or
vasoconstrictors  Pulmonary vasodilators
## Inovasodilators

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Milrinone (1 hour)</th>
<th>Milrinone (2 hours)</th>
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<tbody>
<tr>
<td>MPAP</td>
<td>34</td>
<td>28</td>
<td>27</td>
</tr>
<tr>
<td>CI</td>
<td>2.6</td>
<td>2.8</td>
<td>3.1</td>
</tr>
<tr>
<td>PVR</td>
<td>701</td>
<td>462</td>
<td>379</td>
</tr>
<tr>
<td>MAP</td>
<td>78</td>
<td>75</td>
<td>74</td>
</tr>
</tbody>
</table>

Wang, Adv Ther 2009; 26:46
Inovasodilators

Æ Hachenberg, J Cardiothorac Vasc Anes 1997; 11:453

Æ Patients undergoing MVR for mitral regurgitation

Æ Randomized to PDE 3 inhibitor (enoximone) or to inovasodilator (dobutamine with NTG)
<table>
<thead>
<tr>
<th></th>
<th>Pre-Enoximone</th>
<th>Enoximone</th>
<th>Pre-Dob/NTG</th>
<th>Dob/NTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP</td>
<td>32</td>
<td>23</td>
<td>34</td>
<td>22</td>
</tr>
<tr>
<td>CO</td>
<td>3.9</td>
<td>5.7</td>
<td>4.2</td>
<td>5.3</td>
</tr>
<tr>
<td>MAP</td>
<td><strong>77</strong></td>
<td><strong>72</strong></td>
<td><strong>74</strong></td>
<td>73</td>
</tr>
</tbody>
</table>

Hachenberg, J Cardiothorac Vasc Anes 1997; 11:453
MANAGEMENT OF HYPOTENSION

Is CVP decreased?  Yes  Volume
↓No

Is PAP decreased?  Yes  Inotropes/
↓No  Vasoconstrictors

Are there reversible causes of increased PVR?  ↓Yes
↓No

Is cardiac output decreased?  Treatment
↓No  ↓Yes

Systemic Pulmonary vasodilators
vasoconstrictors Inhaled
Postoperative Management

- Most challenging aspect of the case
- Emergence issues
  - Dexmedetomidine
- ICU monitoring
- Continue chronic pulmonary vasodilator therapy throughout the perioperative period
The 7 Steps

- Recognition of pulmonary hypertension
- Etiology of pulmonary hypertension
- Assessment of severity of pulmonary hypertension
- Perioperative risk assessment
- Preoperative optimization of the patient
- Choice of anesthetic technique
- Choice of monitoring
- Treatment of decompensated pulmonary hypertension
Tips for the Anesthesiologist (I)

Æ Risk-benefit analysis before anesthesia
Æ Optimize the patient before surgery
Æ Maintain outpatient pulmonary vasodilators
  Æ Role for perioperative sildenafil
Æ Avoid vasodepressant drugs
  Æ Use etomidate for induction
Æ Vasoconstrictors for hypotension
  Æ Vasopressin
Tips for the Anesthesiologist (I)

Æ Avoid pulmonary vasoconstriction
Æ Adequate oxygenation and ventilation
Æ Avoid high tidal volume ventilation
Æ Adequate pain control
Æ Avoid treating pulmonary artery pressure in the absence of other indications
Æ Call a friend: Rpearl@stanford.edu
THANK YOU!