Post-operative care and Pulmonary Hypertension

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Objective

- Postoperative pulmonary hypertension in congenital heart disease
- The patient with pulmonary hypertension undergoing general surgery
“The past”: 50’s – 60’s

**Table 3**

*Hemodynamics in the Operating Room and in the Postoperative Period after Closure of Ventricular Septal Defect in Eight Patients with Moderate or Severe Pulmonary Vascular Disease*

<table>
<thead>
<tr>
<th>Time of observation During</th>
<th>Cardiac index</th>
<th>Heart rate</th>
<th>Stroke index</th>
<th>Arterial press., mm. Hg</th>
<th>Atrial press., mean mm. Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Before repair</td>
<td>114</td>
<td>..</td>
<td>113/3 (LV) 107/4 (RV)</td>
<td>5</td>
</tr>
<tr>
<td>0–30</td>
<td>4.5</td>
<td>108</td>
<td>42</td>
<td>86/70 76/66</td>
<td>14</td>
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<tr>
<td>31–60</td>
<td>2.8</td>
<td>114</td>
<td>24</td>
<td>90/73 104/89</td>
<td>9</td>
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<tr>
<td>61–90</td>
<td>2.8</td>
<td>132</td>
<td>22</td>
<td>86/68 118/104</td>
<td>13</td>
</tr>
<tr>
<td>Day 1</td>
<td>3.0</td>
<td>126</td>
<td>24</td>
<td>100/84 84/65</td>
<td>7</td>
</tr>
<tr>
<td>Day 2</td>
<td>2.1</td>
<td>123</td>
<td>17</td>
<td>86/73 88/65</td>
<td>7</td>
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<tr>
<td>15</td>
<td>Before repair</td>
<td>80</td>
<td>..</td>
<td>94/60</td>
<td>7</td>
</tr>
<tr>
<td>0–30</td>
<td>..</td>
<td>86</td>
<td>..</td>
<td>102/63 94/59</td>
<td>12</td>
</tr>
<tr>
<td>Day 1</td>
<td>..</td>
<td>122</td>
<td>..</td>
<td>113/69 96/69</td>
<td>10</td>
</tr>
<tr>
<td>Day 2</td>
<td>..</td>
<td>119</td>
<td>..</td>
<td>115/70 100/74</td>
<td>11</td>
</tr>
<tr>
<td>Day 3</td>
<td>..</td>
<td>101</td>
<td>..</td>
<td>113/68 104/70</td>
<td>9</td>
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<tr>
<td>16</td>
<td>Before repair</td>
<td>..</td>
<td>..</td>
<td>73 (LV) 73 (RV)</td>
<td>7</td>
</tr>
<tr>
<td>0–30</td>
<td>..</td>
<td>108</td>
<td>..</td>
<td>99/69 91/66</td>
<td>13</td>
</tr>
<tr>
<td>Day 1</td>
<td>..</td>
<td>147</td>
<td>..</td>
<td>95/67 92/78</td>
<td>16</td>
</tr>
<tr>
<td>Day 2</td>
<td>..</td>
<td>120</td>
<td>..</td>
<td>72/29 88/73</td>
<td>12</td>
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</tbody>
</table>

Theye RA and Kirklin JW: Circulation, 1963

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Total No. of patients</th>
<th>PHE</th>
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<tbody>
<tr>
<td></td>
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<td>No.</td>
</tr>
<tr>
<td>TAPVC</td>
<td>90</td>
<td>36</td>
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<td>Truncus arteriosus</td>
<td>47</td>
<td>14</td>
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<tr>
<td>TGA</td>
<td>97</td>
<td>14</td>
</tr>
<tr>
<td>VSD</td>
<td>414</td>
<td>59</td>
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<tr>
<td>HLHS</td>
<td>50</td>
<td>4</td>
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<tr>
<td>AV canal</td>
<td>182</td>
<td>11</td>
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<tr>
<td>Total</td>
<td>880</td>
<td>138</td>
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</table>

Bando K et al. J Thorac Cardiovasc Surg 1996
“Recent”

“…important factor on postoperative morbidity and mortality …”

Risk factors for length of stay in the CCU

- Diaphragmatic palsy
- Chylothorax
- Sepsis
- Renal failure
- **Pulmonary hypertension**
- Arrhythmia
- Cardiopulmonary resuscitation

Brown KL et al, Crit Care Med 2003
Children <18 years of age
Cardiothoracic surgery Jan 1, 1994-Dec 31, 1998

N=1349
- 164 neonates
- 511 infants

Severe pulmonary hypertension: n=27 (2%)
- 2 death within 30 days of surgery
- 3 death within 1 year of surgery

Most common heart defect: AVSD (14%, 12/85)
Other estimates ...  

*Perioperative pulmonary hypertension in paediatric patients: current strategies in children with congenital heart disease*

mPAP >25 mm Hg immediately after weaning from the CPB with normal systemic pressure

15/224 (6.7%) of patients fulfilled inclusion criteria

“most of the patients were infants with Downs syndrome and larger atrioventricular septal defect.”

Gorenflo M et al, Cardiology 2010
“Current”

Postoperative Mortality in Children After 101,885 Anesthetics at a Tertiary Pediatric Hospital

- Incidence of anesthesia-related death
  1/10,000 anesthetics performed

- 50% involved children with pulmonary hypertension

Van der Griend BF et al., Anesth Analg 2011
Cause of death

Schlingmann TR et al., Congenit Heart Dis 2012
Today

- Prevalence - Incidence
  - Difficult to determine
    - Specific patient population of the institution
    - Specific congenital diagnosis
      - Total anomalous pulmonary venous drainage
      - Truncus arteriosus
      - Transposition of great arteries (intact atrial septum)
    - Chromosomal abnormalities
Changes

- Surgery at younger age
- More robust surgical candidates
- Improved surgical techniques
  - Changes in cardiopulmonary bypass
  - Post bypass ultrafiltration
Pre-existing factors

Intraoperative factors

Postoperative factors

Postoperative Pulmonary Hypertension
Patient 1

- Late diagnosis:
  - Supracardiac TAPVD
  - Mild obstruction

- Uneventful in OR
Patient 1

Arterial Pressure

iNO ...... weaned off within 36 hrs
Patient 1

“In all cases mean percentage arterial medial thickness was greater than is normal at 5 hours.”

“... in all six cases mean percentage vein wall thickness was significantly increased and in two cases intimal proliferation occurred in preacinar veins.”

Haworth SG, Br Heart J 1982
Patient 2

PVRi baseline: 18.2 WU/xm²
PVRi 100%&20ppm iNO: 15.5 WU/xm²
PVRi Sildenafil: 17.2 WU/xm²

PVRI
Wood Units/mm²
Baseline: 7.5
O₂&iNO: 7.9
PGI₂: 2.4
Patient: 2

- Initially unable to come off bypass
  - ASD creation
  - iNO
  - Epoprostenol, epinephrine and vasopressin
  - RVP just subsystemic
Patient 2

- Impaired adaptation to post-op increase in PVR

- Pre-op: Maintenance of cardiac output - intracardiac shunt
Dilemma

- No comprehensive assessment of post-operative hemodynamics
  - Estimation by echocardiography
  - Less PA lines

Let’s remove it – and ignore the numbers ...
Dilemma

- No comprehensive assessment of post-operative hemodynamics
  - Estimation by echocardiography
  - Less PA lines

- No guidelines for therapy
  - Consensus: mPAP >25 mmHg, >50% systemic
  - Plus: low cardiac output
Hemodynamics

\[ PVR = \frac{(PAP - LAP)}{CO} \quad \text{and} \quad PAP = LAP + (CO \times PVR) \]

**\( \uparrow \) LAP**
- Left ventricular failure
  - Systolic/diastolic
  - Valvular disease

**\( \uparrow \) CO**
- Congenital heart disease
- Sepsis
- Anemia

**\( \uparrow \) PVR**

**Acute**
- Hypoxia
- Hypercapnia
- Acidosis
- \( \uparrow \) Sympathetic tone
- Exogenous/endogenous vasoconstrictors
- Pulmonary embolism

**Chronic**
- Parenchymal lung disease
- Chronic hypoxia
- Pulmonary artery obstruction
- Pulmonary arterial hypertension
Left ventricle

- Afterload reduction
  - Milrinone ...
Therapeutic options: Intervention

- Selective effects on pulmonary circulation
- Increases cGMP
  - ↓ intracellular calcium concentration
  - Smooth muscle relaxation
- Rapid inactivation
- No systemic vasodilatation
Therapeutic options
Prostacyclin

☐ Produced by endothelial cells

☐ Drug: Short half-time
  ■ Intravenous (Epoprostenol = Flolan®)
    ‣ Increased pulmonary shunt/reduction of PaO\textsubscript{2}
    ‣ Systemic vasodilation
  ■ Inhaled (Iloprost = Ventavis®)
Inhaled Nitric Oxide Versus Aerosolized Iloprost in Secondary Pulmonary Hypertension in Children With Congenital Heart Disease
Vasodilator Capacity and Cellular Mechanisms
Therapeutic options

PDE 5 inhibitor - Sildenafil

- Reduces the breakdown of cGMP
  - Vasodilation of corpus cavernosum
  - Hyperemia of the nasal mucosa
  - Vasodilation of the pulmonary vasculature

- Oral administration
  - Minimal side effects
Oral sildenafil

66 infants on iNO after closure of septal defects/cavopulmonary shunts
Stepwise dose increase
5-7 days

Nemoto, S et al., Eur J Cardiothorac Surg 2010
Therapeutic options
PDE 5 inhibitor - Sildenafil

- Intravenous application
  - Reduces pulmonary vascular resistance
  - Enhances pulmonary vasodilator effects of NO
  - Significant systemic vasodilation
  - Significant reduction in blood pressure
  - Desaturation – not improved by iNO

Stocker C et al, Int Care Med 2003
Therapeutic options
PDE 5 inhibitor - Sildenafil

- Intravenous application

Fraisse A et al., Int Care Med 2011
Therapeutic options: Prevention

- Choose the right patient

- Acute perioperative pulmonary hypertension
  - Avoid hypoxia
  - Avoid acidosis/hypercarbia
  - Avoid hypothermia

- Optimal airway pressures/lung volumes
- Adequate analgesia/sedation
iNO for prevention of post-op PH?

- N=124 infants
  - Large VSD/AVSD (75%)
  - Truncus arteriosus, TAPVD

- Randomized to
  - low-flow iNO (10 ppm)
  - Placebo

- Fewer pulmonary hypertensive crisis
- Shorter time on ventilator

Miller OI et al, Lancet 2000
Sildenafil for prevention of post-op PH?

- 2005-2008
- 38 children
  - Moderate-severe PH

**Sildenafil**
- 1 week before/1 week after surgery (n=15)
- Cardiopulmonary bypass/1 week after surgery (n=23)

Palma G et al., Tex Heart Inst J 2011
Endothelin Receptor Blocker
Animal study

Lambs with increased pulmonary blood flow
Pretreatment with PD 145065
Nonselective endothelin receptor blocker

Reddy VM et al, Circulation 1997
Tezosentan

- 274 patients with pulmonary hypertension
  - ≥18 years, cardiac surgery
  - Multicenter, double-blind, randomized, placebo-controlled trial
  - Intravenous tezosentan during surgery and up to 24 hours afterwards or matched placebo
- No reduction in RV failure

Denault AY et al., J Cardiothorac Vasc Anesth 2013
Rebound Pulmonary Hypertension

- Imbalance of vasodilator stimuli
- Increased production of vasoconstrictor stimuli
- Down-regulation of endogenous NO production
- Persistent or increased degradation of cGMP

Pulmonary hypertensive crisis

- Sudden increase in PA pressure/PVR
- Causing right heart failure
- Systemic hypotension
- Myocardial ischemia
- Bronchoconstriction

- Potentially fatal
Stimulus
Pain – hypothermia – suctioning – acidosis etc.

- PAP/PVR ↑
- Cardiac output ↓
- Hypotension
- SvO₂ ↓
- Hypoxic pulmonary vasoconstriction ↑
- R→L shunt (PFO)
- O₂ delivery ↓
- Bradycardia
-Death

PAP:SAP>0.75
Pulmonary hypertensive crisis

- Hyperventilation
  - Bag/Ventilator changes
- Hyperoxygenation
- Sedation/Muscle relaxant
- Correct acidosis
- Pulmonary vasodilators
Mechanical support

Efficacy of extracorporeal membrane oxygenation as a bridge to lung transplantation

Yoshiya Toyoda, MD, PhD, Jay K. Bhama, MD, Norihisa Shigemura, MD, Diana Zaldonis, MPH, BSN, Joseph Pilewski, MD, Maria Crespo, MD, and Christian Bermudez, MD

Extracorporeal Membrane Oxygenation in Nonintubated Patients as Bridge to Lung Transplantation


Growing Experience with Extracorporeal Membrane Oxygenation as a Bridge to Lung Transplantation

Pulmonary hypertension and non-cardiac surgery

- Paucity in pediatric literature

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**Carmosino MJ et al., Anesth Analg 2007**

<table>
<thead>
<tr>
<th>Procedures</th>
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<tr>
<td>Cardiac catheterization</td>
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<tr>
<td>Central venous access</td>
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<td>Airway</td>
<td>28</td>
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<td>Abdominal</td>
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<td>Thoracic</td>
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<td>Other</td>
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<table>
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<tr>
<th>Anesthetic type</th>
<th>n</th>
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<tbody>
<tr>
<td>Sedation</td>
<td>56</td>
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<tr>
<td>General volatile</td>
<td>148</td>
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<tr>
<td>General TIVA</td>
<td>52</td>
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<table>
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<tr>
<td>Natural unaided airway</td>
<td>54</td>
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<tr>
<td>ETT</td>
<td>192</td>
</tr>
<tr>
<td>LMA</td>
<td>7</td>
</tr>
<tr>
<td>Face mask</td>
<td>3</td>
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</table>

256 procedures
Pulmonary hypertension and non-cardiac surgery

- Few case series for adults
  - Ramakrishna G et al., JACC 2005
  - Minai OA et al., Conn Med 2006
  - Lai HC et al., Br J Anaesth 2007
  - Price LC et al., Eur Resp J 2010

- N=437
  - Major surgery: 85.4%
  - General anaesthesia: 89.3%
  - Morbidity: 29%
  - Mortality 5.7%
Pulmonary hypertension and non-cardiac surgery

- Risk factors/effect of anesthetics/opioids
  - Worsening pulmonary hypertension
  - Right ventricular ischemia
  - Pain – Increase of PVR
  - Rebound pulmonary hypertension
Pulmonary hypertension and non-cardiac surgery

- Hypotension with stable cardiac output
  - Reduced SVR: Norepinephrine (↓ PAP/BP ratio)
  - Alternatively: vasopressin
  - Dopamine/epinephrine: increase HR and myocardial oxygen consumption
  - Reduced CVP/PCWP/PAP: increase preload
  - Increased CVP/PAP: Correct hypoxia/acidosis, pulmonary vasodilators
Summary

- Postoperative pulmonary hypertension
  - Less frequent
    - Earlier repair
    - Better CPB strategies
  - Still present
    - Immanent in specific lesions
    - Higher awareness
  - Various treatment options
    - Mild-moderate alkalosis
    - iNO
    - Prostacyclin
    - Sildenafil