Post-op Management of Heart and Lung Transplants
Lundy J. Campbell MD

Topics to Cover
- Hemodynamic Instability
  - Causes / treatment
- Pulmonary HTN / RV failure
- Pulmonary vasodilators
- Mechanical ventilation
- ECMO
- Pain / sedation
- Delirium

Hemodynamic Instability
- Graft dysfunction / Reperfusion injury
- Post-bypass inflammatory response
- Depleted catecholamines
- Labile fluid status
- Elevated PVR
- Autonomic denervation

Graft Dysfunction (Heart)
- Primary graft dysfunction
- Secondary graft dysfunction
  - Hyper acute rejection
  - Pulm HTN
  - Surgical complications
PGD Definition (Heart)

- LVEF ≤ 40%
- Occurs within 24 hours
- Need for mechanical support

PGD Exclusion Criteria (Heart)

- Sepsis
- Hyper acute rejection
- Bleeding
- RV dysfunction with elevated PVR

Natural History PGD

- Increased 30 day mortality – 30%
- Increased 1 year mortality – 35%

- Note: Most common causes of 30 day mortality: MOF – 70%, PGD – 20%, Sepsis – 10%

Donor Factors Causing PGD (Heart)

- Brain death sequelae to organs
  - Impaired contractility
- Cold ischemia during transport
- Warm ischemia during surgery
- Reperfusion injury
- Donor risk factors
  - Age
  - Female
  - Cause of death
Recipient Factors for PGD (Heart)

- High PVR
- Activation of SIRS (Vasoplegia)
  - Mechanical circ support
  - Long X-clamp time
  - Large transfusion requirements
  - Pre transplant inotropic support
  - Pre transplant mechanical ventilation

PGD (Lung)

- Presents with refractory hypoxia
- Increased pulmonary capillary permeability
- Diffuse alveolar infiltrates in most severe form
- Lack of cardiogenic pulmonary edema

Primary Graft Dysfunction (Lung)

- Most frequent cause of early mortality
- Affects up to 30% of all transplants
- Leads to prolonged mechanical ventilation and ICU LOS
- Increased risk for poor functional outcomes and BOS
- 5 fold increase in early post-transplant mortality in severe cases

Lung PGD Grading (ISHLT)

<table>
<thead>
<tr>
<th>PGD Grade</th>
<th>Infiltrates c/w diffuse pulmonary edema</th>
<th>PaO2/ FiO2</th>
<th>Specific Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
<td>Any</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>+</td>
<td>&gt; 300</td>
<td>N/C or FiO2 &lt; 0.3</td>
</tr>
<tr>
<td>2</td>
<td>+</td>
<td>200-300</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>+</td>
<td>&lt;200</td>
<td>ECMO, iNO with FiO2 &gt; 0.5</td>
</tr>
</tbody>
</table>
Lung PGD Exclusion Criteria

- Cardiogenic pulmonary edema
- Pneumonia or aspiration
- Hyperacute rejection
- Pulmonary venous anastamotic obstruction

Lung PGD Donor Factors

- Extremes of age
- Female
- Elevated PASP at time of transplant
- Obesity
- Pre-existing PAH or IPF
- Brain-death induced lung injury

PGD Recipient Factors

- Blood product administration
- Single transplant
- CPB use

PGD Treatment

- Supportive
- Limit injury from mechanical ventilation
  - Minimal O2
  - Lung Protective Mode
- Limit fluids / Diuresis
- Use of iNO?
- ECMO
Hyper acute Rejection

- Occurs in minutes – hours post reperfusion
- Pre-formed recipient antibodies
  - ABO incompatibility
  - Complement Activation
- Profound Hypoxemia
  - Severe pulmonary edema

Donor Size Mismatch (Heart)

Oversized
- Donor/Recipient wt. ratio > 2
- Systemic HTN
- CNS issues, Coma
- Decrease BP to near pre-transplant levels
- May not fit into mediastinum

Undersized
- Donor Recipient wt. ratio < 1
- Increased cardiac demands
- Heart failure
- Increased mortality
- Note: Body weight not always a good predictor
Treatment of HD Instability

- Increase Contractility
- Improve SVR
- Reduce SVR

Increase Contractility

- Depleted catecholamine stores (donor / recip)
- Denervated heart
  - Epi
  - Norepi
  - Milrinone
  - Dobutamine
  - Isoproterenol
  - Levosimendan?

Monitoring

- Standard Monitors
- Arterial Line
- CVP Measurement
- PAC (w CCO and MVO2)
- TTE

Improve SVR

- CBP Vasoplegia
- Improve coronary perfusion
  - Phenylephrine
  - Norepinephrine
  - Epinephrine
  - Vasopressin
Reduce SVR

- Corticosteroid medications
- Blunted diuretic and natriuretic responses
- Failing LV
- Catecholamine dysregulation from low CO pre
- Pre-existing renal injury / dysregulation
  - Nitroprusside
  - Nicardipine
  - NTG
  - Clevidipine

Arrhythmia Post Heart Transplant

- Sinus node dysfunction common (45%)
  - Related to ischemia, swelling, denervation
- Typically transient
  - 2-5% need for permanent pacemaker
- Chemical Pacemaker
- Temporary Pacing (A vs. AV)
  - 90 BPM

Why “Rapid” HR

- Ischemia-reperfusion injury causes diastolic dysfunction
- Need higher filling pressures
- Change in Starling curve
- Don’t increase SV in response to preload increase

Arrhythmia Post Lung Transplant

- Typically supraventricular origin
- SVT 34-74%
- AF approx. 40%
Labile Fluid Status

- May have pre-existing renal dysfunction
- Hypovolemia
  - Ongoing bleeding
  - Stiff, poor compliance ventricle post-bypass
  - Diuretic use
- Hypervolemia
  - Over transfusion
  - AKI
- Nephrotoxic agents
  - Antibiotics, immunosuppression
- Early CRRT

Coagulopathy/Bleeding

**Causes**
- Extensive dissection
- Prior ECMO or mechanical support pre-transplant
- Prior surgery
- Prior infections
- Poor nutritional status
- CBP time
- Post-op ECMO

**Treatment**
- Judicious use of blood products
  - Avoid alloimmunization
  - Leukocyte reduced RBCs
- Use of rVIIa
- Profinine (II, IX,X)
- Kcentra (II, VII, IX, C, S)

Pulm HTN / RV Failure (Heart)

- Increased mortality due to RV failure post-op
- Over 6 Wood units: RV failure to 75%
- 20% w/o elevated PVR
- Usually due to transient pulm vascular hyper-reactivity post-bypass
  - Cold, pain, stress, hypoxia, hypercarbia
- Tx: Pulm vasodilators

Pulm HTN / RV Failure (Lung)

- Although replacing pulm vasculature
- RV function may already be down
- RV stunning during transplant
- Increased PVR during single lung perfusion
- Increased PVR from Pulmonary stenosis due to anastomotic complications
Pulmonary Vasodilators

• Milrinone
• Dobutamine
• Inhaled NO
• Inhaled prostacyclin
• Sildenafil

Nitric Oxide

• Endothelium-derived relaxing factor
• Vasodilation by increased cGMP in vascular smooth muscle
• Inhibits neutrophil sequestration, degranulation, free-radical formation

Inhaled Nitric Oxide

• Inhaled pulmonary vasodilator
• Match V/Q
• Doesn’t leave the pulmonary circulation
• Doesn’t cause systemic vasodilation
• Methemoglobinemia
• Concern for increased free-nitrite radical formation (especially if given early during reperfusion)

Inhaled NO: Does it work?

• Well known to reduce PASP and RV dysfunction
  – Elevated PASP may further damage lung
• Shown to prevent PGD in animal studies
• Not similar results in randomized, controlled clinical trials in humans
  – May be due to lung injury assoc with brain death?
Inhaled NO Increases PaO2 in Pigs post Lung Transplant

![Graph showing PaO2 after 4 and 24 hours of reperfusion with ventilation at Fio2 of 1 and blood flow to the native right lung (NL) or to the transplanted left lung (TL) alone. † indicates p < 0.001 versus TL at 4 hours in the control group; * indicates p < 0.05 versus TL at 4 hours in the control group.](image)

Inhaled NO Decreases PVR

![Graph showing PVR after 4 and 24 hours of reperfusion, ventilation at Fio2 of 1, and blood flow to the native right lung (NL) or to the transplanted left lung (TL) alone. † indicates p < 0.001 versus TL at 4 hours in the control group; * indicates p < 0.01 versus TL at 4 hours in the control group.](image)

Inhaled NO Decreases PMN Sequestration

![Graph showing percentage of peripheral blood PMN increase after 4 and 24 hours of reperfusion in the control and NO groups. * indicates p < 0.05 versus control group at 4 hours.](image)

Inhaled NO Does Not Change P/F in Humans

![Graph showing trend of P/F ratio from 1 to 12 hours of reperfusion with ratio at 1 hour taken as baseline. Circles and solid line: control group; triangles and dashed line: group with nitric oxide from onset of reperfusion.](image)
Inhaled NO Does Not Change PMN Sequestration in Humans

No Benefit from iNO
- Randomized, controlled trial of 84 lung transplant patients
- 20ppm iNO started 10 min after reperfusion
- No effect of iNO on hemodynamic variables
- No effect on P/F ratio or required FiO2
- ICU and hospital LOS similar

Mechanical Ventilation
- Effect on Preload and Afterload
- Low tidal volumes
- PEEP
- Minimize O2
- Extubation criteria
- Use of NIPPV

Extubation Criteria
- Relatively HD stable
- Adequate oxygenation/ventilation
- Reasonable O2 level
- Corrected bleeding/coagulopathy
- Relatively euvolemic
- Pain well controlled
- iNO weaned down
NIPPV Use

- Useful initially post-extubation
- Not a long-term solution
- Increased aspiration risk
- Difficult nutrition
- Skin breakdown

ECMO

- Pre-transplant to stabilize/rehab patient
- Post-transplant for graft failure
- VV
- VA
- Cannulation sites
- Risks
- Benefits

Pain Control

- Narcotics
  - Dilaudid
  - Oxycodone
  - Tramadol
- Epidural Analgesia
- Others
  - Ketamine
  - Gabapentin
  - Lidocaine
  - Tylenol

Sedation

- Needed if remain intubated, mechanical support
- Use minimum possible
- Daily sedation wakeup
- Avoid benzodiazepines
- Increased delirium risk
- Propofol
- Dexmedetomidine
Dexmedetomidine

- Dose
- Mechanism of Action
- Effects
- Side-Effects

Catecholamine Levels decrease with Increasing Dexmedetomidine Levels

Hemodynamic Effects of Increasing Dexmedetomidine Dose

Additional Hemodynamic Effects of Increasing Dexmedetomidine Dose
Delirium

- Hyper vs. hypoactive
- Ensure adequate sleep
- Control pain
- Avoid benzodiazepines
- Minimize sedation
- Day/night cycling
- Re-direction/Family involvement
- Exercise / ambulation
- Pharmacotherapy

Thank You