Critical Care of the Lung Transplant Patient: The Surgical Perspective

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Management of the Lung Transplant Patient in the Early Postoperative Period

- Surgical complications
- Acute rejection
- PGD
- Infections

POD# 0, 3, 7, 14, 30
Critical Care of the Lung Transplant Patient

1. Preoperative management → Donor lung, bridge to lung transplant: ventilator, ECMO
2. Intraoperative management
3. Postoperative Management
4. Principles of Primary Graft Dysfunction
5. ECLS and Lung Transplantation in an Advanced Lung Failure Unit
Injury to the Donor Lung: A Multifactorial Process

- Ventilator-associated lung injury
- Ischaemic times
- Excess fluid
- Local ischaemia (induced by vasopressors and cold flush)
- Aspiration or pneumonia
- Brain death
- Thrombosis

Activation of inflammatory cascade

Primary graft dysfunction after transplantation

Munshi L, Keshavjee S, Cypel M. *Lancet RM* Feb 2013
Clinical Problem - PGD
Risk Factors for PGD: Donor + Operation + Recipient Can All Contribute!

Recipient:
- IPF, PAH
- Bridge to transplant
- Elevated PA-pressures in OR
- Difficult surgery
- Cardiac - LV diastolic dysfunction

Primary Graft Dysfunction: Case

• 47 year old man
• Sarcoidosis, RVSP 83
• Bilateral lung transplant
• Difficult dissection, technically challenging operation
• Required cardiopulmonary bypass support
• Came off bypass easily
Chest X-rays On Arrival in ICU and POD#1
What are these x-rays telling us?
Primary Graft Dysfunction: Case

- 47 year old man
- Sarcoidosis, RVSP 83
- Bilateral (sequential) lung transplant
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Chest X-rays On Arrival in ICU and POD#1
What are these x-rays telling us?
# Definition of Primary Graft Dysfunction

**International Society for Heart and Lung Transplantation**

<table>
<thead>
<tr>
<th>Grade</th>
<th>( \text{PaO}_2/\text{FiO}_2 )</th>
<th>Infiltrates</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&gt;300</td>
<td>Absent</td>
</tr>
<tr>
<td>1</td>
<td>&gt;300</td>
<td>Present</td>
</tr>
<tr>
<td>2</td>
<td>200-300</td>
<td>Present</td>
</tr>
<tr>
<td>3</td>
<td>&lt;200</td>
<td>Present</td>
</tr>
</tbody>
</table>

- Assessed at: T0, T24, T48, T72 hours
- Automatic Grade 3: ECMO or iNO and \( \text{FiO}_2 > 0.5 \)
- Nasal prongs or \( \text{FiO}_2 < 0.3 \): Grade 0 or 1

Primary Graft Dysfunction: A Multifactorial Injury

- A relatively common early complication
  - Severe PGD (PGD3) in 20 - 30%
  - Increased : 20%
  - Negative long-term effects
    - Increased Chronic Lung Allograft Dysfunction (CLAD)
    - Link between early innate immune injury and late acquired immune response (rejection)

- Exclude:
  - Infections
  - Technical issues (e.g. pulmonary venous obstruction)
  - Volume overload
  - Cardiac issues

ICU Management during the first 72 h

Overall Goals

• THIS IS A LEAKY CAPILLARY SYNDROME LUNG INJURY!
• Careful fluid management to avoid lung edema, BUT preserving adequate end-organ perfusion
• Adequate pain management
• Early weaning of sedation → Early extubation
• Early mobilization
• Immunosuppression
• Antibiotic prophylaxis
Hemodynamic monitoring – You Need a Swan Ganz Catheter

CVP (RV pre-load)

PAS and PAD
PA flow=cardiac output

PVR (RV after-load)
Post LTx

PCWP (LV pre-load)

LV-RV Interaction

RV
Pre-load
After-load
Contractility

LV
Pre-load
After-load
Contractility
SVR
CVP (RV pre-load) < 8 mmHg
(fluids/furosemide, PEEP)

mPAP < 20 mmHg
CI = 2.2 - 2.5

PAOP (LV pre-load) < 10 mmHg
(fluids/furosemide, PEEP)

LV After-load: MAP 65-75 mmHg
(vasopressors, vasoldilators, sedation, PEEP)
Contractility (inotropes)

LV-RV interaction
PAD-PAOP, pO2, pCO2, MV settings, sedation, iNO

PVR (RV after-load)
Post DLTx
PGD 3

End organ perfusion monitoring:
SvO2, lactate, u/o, pH, HCO3-, temperature

Lung function monitoring:
P/F, Vd/Vt, compliance, CXR, EVLW (?)
Monitoring

Monitor and record the following parameters as indicated below or more frequently if clinically required:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (SAP, DAP) (q1h)</td>
<td>65 - 75 mmHg</td>
</tr>
<tr>
<td>HR (q1h)</td>
<td>60 - 100 b/min</td>
</tr>
<tr>
<td>CI (q4h)</td>
<td>2.2 – 2.5 L/min/m²</td>
</tr>
<tr>
<td>mPAP (PAS, PAD) (q1h)</td>
<td>≤ 20 mmHg</td>
</tr>
<tr>
<td>CVP (q1h)</td>
<td>&lt; 8 mmHg</td>
</tr>
<tr>
<td>PCWP (q4h)</td>
<td>&lt; 10 mmHg</td>
</tr>
<tr>
<td>Calculate - and look at - CI, PVR and SVR q 4h</td>
<td>&lt; 5 mmHg</td>
</tr>
<tr>
<td>PAD-PCWP (q4h)</td>
<td></td>
</tr>
<tr>
<td>SvO₂ (q8h)</td>
<td>&gt; 60%</td>
</tr>
<tr>
<td>pH, PaO₂, PaCO₂ (HCO₃) (q8h)</td>
<td>&gt; 7.30, &gt; 60 mmHg, 30 - 45 mmHg</td>
</tr>
<tr>
<td>Lactate (q8h)</td>
<td>≤ 2.5 mmol/L</td>
</tr>
<tr>
<td>U/O (q1h)</td>
<td>&gt; 0.5 ml/kg/hr</td>
</tr>
<tr>
<td>Temperature (q1h)</td>
<td>35 - 38 °C</td>
</tr>
</tbody>
</table>
Goals of Mechanical Ventilation Management

• Provide adequate support for gas exchange
• Minimize respiratory distress
• Protective - minimize ventilator-induce lung injury
• Optimize alveolar recruitment
• Facilitate bronchial toilet
• Facilitate early weaning
Initial mechanical ventilation settings

**Strategy**

- Pressure controlled ventilation
- Minimize tidal volume/distending pressure
- Minimize FiO₂
- Optimize PEEP

**Goals**

- Early weaning
- Vt ≤ 6 cc/kg (PBW D/R) Pplat < 30 cmH₂O
- SpO₂ ≥ 90%
- Maintain alveolar recruitment

**PEEP/FiO₂ table:**

<table>
<thead>
<tr>
<th>FiO₂</th>
<th>0.3</th>
<th>0.4</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.8-1</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEP</td>
<td>5</td>
<td>5-8</td>
<td>8-10</td>
<td>10-12</td>
<td>12-14</td>
<td>14-15</td>
</tr>
</tbody>
</table>

- Minimize respiratory rate:
  - RR < 25 breaths/min
  - pH > 7.30

- Maximize expiratory time:
  - I:E ≤ 1:2 (1:3, 1:4, etc.)
PGD Treatment

- Manage leaky capillary syndrome
- pRBCs (when needed) and 25% Albumin are agents of choice for intravascular volume expansion in the early phase
- Diuresis (euvolemia – NB nephrotoxic immunosuppressants and antibiotics)
- Protective ventilation
- iNO (10 ppm for oxygenation, 40ppm for PAP)
- PGE$_1$, other agents in the pipeline (targetting inflammation, free radicals, early innate and acquired immune responses)
- ECLS
Ventilator Management - Weaning

P/F ≥ 200:

1. Optimize analgesia
2. Assess CXR, endotracheal secretions (suctioning), and chest tube output/leak
3. Optimize hemodynamic management
4. Wean sedation: manage agitation / sedation
5. Wean iNO (5 ppm/hr, when iNO is 5 ppm proceed with slower wean)
6. Wean MV to assisted modality of MV (e.g. PSV) if tolerated, and target:
   1. 6-8 cc/kg PBW D/R
   2. RR < 25 breaths/min
7. Follow the spontaneous breathing trial (SBT) policy (twice daily)
8. After failure of > 3 SBT, after > 72 hours of continuous MV, or after failed extubation: consider tracheostomy → allows easier mobility, improved patient comfort, oral hygiene, and clearance of pulmonary secretions
Management

P/F < 200:
- Optimize sedation/analgesia
- Assess CXR, endotracheal secretions (suctioning), and chest tube output/leak
- Optimize hemodynamic management
- Manage / treat agitation
- Maintain controlled modality of MV with protective settings (see initial MV settings)
- Consider iNO – it works in this population to improve V/Q matching

P/F < 150:
- Contact lung transplant surgeon / team
- Consider neuro-muscular blocking agents

P/F < 100:
- ECLS
ECLS for Intraoperative Support in Lung Transplantation

• 40-50% patients require cardio-pulmonary support

• Traditionally CPB was used and associated with increased risk of complications:
  • Bleeding
  • PGD
  • Neurologic Complications
Outcomes of intraoperative extracorporeal membrane oxygenation versus cardiopulmonary bypass for lung transplantation

Tiago N. Machuca, MD, Stephane Collaud, MD, MSc, Olaf Mercier, MD, PhD, Maureen Cheung, MD, Valerie Cunningham, CCP, S. Joseph Kim, MD, PhD, Sassan Azad, CRA, Lianne Singer, MD, MSc, Kazuhiro Yasufuku, MD, PhD, Marc de Perrot, MD, MSc, Andrew Pierre, MD, MSc, Karen McRae, MD, Thomas K. Waddell, MD, PhD, Shaf Keshavjee, MD, MSc, and Marcelo Cypel, MD, MSc

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CPB</th>
<th>ECMO</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of MV (days)</td>
<td>7.5 (2-18)</td>
<td>3 (2.5-5)</td>
<td>0.005</td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>9.5 (3-210)</td>
<td>5 (3-9)</td>
<td>0.026</td>
</tr>
<tr>
<td>Hospital Stay (days)</td>
<td>27 (17-42)</td>
<td>19 (14-30)</td>
<td>0.029</td>
</tr>
<tr>
<td>ECLS post-op</td>
<td>5 (7.5%)</td>
<td>0</td>
<td>0.166</td>
</tr>
<tr>
<td>Dialysis requirement</td>
<td>12 (18%)</td>
<td>3 (9%)</td>
<td>0.37</td>
</tr>
<tr>
<td>Reoperation (bleeding)</td>
<td>18 (27%)</td>
<td>3 (9%)</td>
<td>0.04</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>10 (15%)</td>
<td>2 (6%)</td>
<td>0.32</td>
</tr>
</tbody>
</table>
12-month Survival After Lung Transplant

The graph shows the percent survival over months for two groups: ECMO and CPB. The line for ECMO is blue and the line for CPB is red. The graph indicates that ECMO has slightly better survival rates compared to CPB, but the difference is not statistically significant with a p-value of 0.29.

University Health Network
ECLS for Primary Graft Dysfunction (PGD)
Current Algorithm for Extracorporeal Lung Support (ECLS)

Hypercapnic failure

- Veno-Venous (low flow)

Hypoxemic failure

- Veno-Venous (high flow)

PAH (severe RV dysfunction)

- PA-LA iLA (pumpless)
- Veno-Arterial
- VV + Septostomy
Case 1

- 30Y, male with CF
- BLT
- After reperfusion of 1st lung patient become hypoxemic
- VA ECMO for intraoperative support
- Wean VA ECMO at the end of transplant
- Severe hypoxemia and respiratory acidosis develops next few minutes
- PAP 52/30 mmHg
- Moderate requirements for vasopressors and inotropes
- Pulmonary edema evident on bronchoscopy

- What’s next?
Some options…

• 1) Trial of iNO
• 2) Leave Chest Open
• 3) Initiate VV ECMO
• 4) Initiate VA ECMO
VV or VA ECMO for PGD?
VA ECMO Advantages

• Both respiratory and hemodynamic support

• Ability to decrease pulmonary flow and pulmonary pressure

• Ultimate protection in severe leaky capillary syndrome – IR injury

Marasco et al. 2011
VA ECMO Disadvantages Compared to VV

- More Bleeding
- More Stroke
- More Ischemic complications
- Poor central oxygenation if cardiac function is preserved
- Potential deleterious effect to bronchial circulation - healing and delayed edema clearance (full VA bypass)

Marasco et al. 2011
• Promptly corrects hypoxemia and respiratory acidosis
• No direct hemodynamic support*
• Decreased risk of embolic, neurologic, and bleeding complications
• Single cannulation site
• Avoids arterial cannulation
• Simple to wean
• Does NOT offload the lung circulation

Successful ECLS Bridge to LTx

1. Patient Selection
2. Avoid prolonged mechanical ventilation pre-ECLS
3. Provide adequate pump support
4. Avoid groin cannulation if possible
5. Ambulatory and non-intubated preferred, but avoid lung de-recruitment
6. Consider early tracheostomy and nutritional support
7. Need an engaged AND persistent multidisciplinary team
32 yo female with Cystic Fibrosis
Past Medical History

- Cystic Fibrosis
  Chronically infected with Pseudomonas
  Progressive drop in lung function over last year
  \((\text{FEV}_1 1.4\text{L})\)
  Frequent exacerbations \(\rightarrow\) IV antibiotics and steroid
- Considering lung transplant assessment but doing relatively well
- Exocrine pancreatic insufficient, CF related diabetes, DIOS
- Married, 3 yo daughter
Mar 2, 2016: Acute worsening of SOB, hypoxemia; FEV₁ dropped to 0.79L (23% Pred)

Mar 9, 2016 Developed H1N1 pneumonia treated with Tamiflu

Respiratory failure on BIPAP at outside hospital - developed worsening hypercapnia

Apr 7, 2016 Intubated and transferred to TGH for urgent lung transplant assessment /bridge to LTx
Assessment Summary

Cardiac Echo:
• Normal sized LV with moderate LV dysfunction
• LVEF estimated at 30-40%
• Normal sized RV with mildly reduced function
• Enable to estimate RVSP

ABG: pH 7.30, pCO2 121, pO2 216 (Apr 7 on ICU arrival)

• TLC (P): 5.5 (L)

LAB DATA:
• Cr: 57  AST: 15  ALT: 18  ALP: 144  BILT: 3
• INR: 1.05  ALB: 24  HbA1C: 0.091
• Hb: 93  WBC: 24.0  Plt: 272

Listed on Apr 8, 2016  Status 2,  Bilateral only
VV-ECMO for bridge to recovery/ bridge to lung transplant

After admission to ICU

Resp. condition deteriorated acutely  
\[ \text{pH 7.16, pCO2 >140, pO2 87} \]

VV-ECMO was placed via 22 Fr RIJ and 25 Fr RF

Tracheostomy

After ECMO insertion

Apr 7

Apr 8

Apr 15

ABG: pH 7.27 pCO2 61 pO2 67

Gradually Deteriorated, Needed increased ECLS Flow
Developed septic shock
Bacteremia with gram-negative *Pseudomonas*

3 vasopressors at maximum dose VASOPRESSIN, LEVOPHED, and ADRENALIN

Despite VV ECMO (flow of 7 L/min), Significant hypoxemia (without pump recirculation)
ABG: pH 7.14 pCO2 52, pO2 60
Refractory vasodilation - sepsis

April 17, 2016
Remove the Septic Source: Bilateral Pneumonectomy

- Switch to Central VA-ECMO (22Fr aortic cannula, 34/46 two-stage IVC venous cannula)
- Right-sided pneumonectomy first, then left pneumonectomy
- Insertion of Right lung PA-LA Novalung
  - Outflow: Pulmonary arterial (34 Fr single-stage venous cannula)
  - Inflow: right superior pulmonary vein (28 Fr Pacifico)

April 17, 2016
Remove Septic Source: Bilateral Pneumonectomies
Immediate Postop BLT

Bilateral Lung Transplant

April 22, 2016 (5 days after pneumonectomy)

- On central VA-ECMO
- Left side implantation first (CIT: 3h 15 min, WIT: 49 m)
- Removed the PA cannula from right PA (for the PA-LA Novalung)
- Removed the LA cannula from right superior pulmonary vein
- Right lung implantation (CIT: 4h 45 min, WIT: 50 min)
- 6 U pRBC and 2 U platelets

Immediate Postop BLT
M Cypel, T Waddell, L Singer, L DelSorbo, E Fan, M Binnie, N Ferguson, S Keshavjee
