LUNG TRANSPLANTATION in ILD
Special Considerations and Outcomes

Steven Hays, MD
Professor of Medicine
Medical Director, Lung Transplantation
University of California, San Francisco
San Francisco, CA USA
Disclosures

I have nothing to disclose
Adult Lung Transplants
Number of Transplants by Year and Procedure Type
ILD – the Leading Indication for Lung Transplantation

Number of Transplants

- COPD
- A1ATD
- CF
- IIP
- ILD-not IIP
- Retransplant

Transplant Year

ILD Specific Considerations

• Connective Tissue Disease
• GERD
• Pulmonary Hypertension
• Familial Fibrosis – Telomerase Mutations
• Anti-fibrotic therapy
45 yo female with SLE, complicated by PAH, nephritis, arthritis, cytopenias
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>SLT (N = 12,339)</th>
<th>BLT (N = 18,334)</th>
<th>TOTAL (N = 30,673)</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD/Emphysema</td>
<td>5,769 (46.8%)</td>
<td>4,839 (26.4%)</td>
<td>10,608 (34.6%)</td>
</tr>
<tr>
<td>Idiopathic Pulmonary Fibrosis</td>
<td>3,995 (32.4%)</td>
<td>2,938 (16.0%)</td>
<td>6,933 (22.6%)</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>214 (1.7%)</td>
<td>4,941 (26.9%)</td>
<td>5,155 (16.8%)</td>
</tr>
<tr>
<td>Alpha-1</td>
<td>728 (5.9%)</td>
<td>1,225 (6.7%)</td>
<td>1,953 (6.4%)</td>
</tr>
<tr>
<td>Idiopathic Pulmonary Arterial Hypertension</td>
<td>78 (0.6%)</td>
<td>894 (4.9%)</td>
<td>972 (3.2%)</td>
</tr>
<tr>
<td>Pulmonary Fibrosis, Other</td>
<td>424 (3.4%)</td>
<td>537 (2.9%)</td>
<td>961 (3.1%)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>50 (0.4%)</td>
<td>815 (4.4%)</td>
<td>865 (2.8%)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>236 (1.9%)</td>
<td>547 (3.0%)</td>
<td>783 (2.6%)</td>
</tr>
<tr>
<td>Re-Transplant: Obliterative Bronchiolitis</td>
<td>253 (2.1%)</td>
<td>219 (1.2%)</td>
<td>472 (1.5%)</td>
</tr>
<tr>
<td>Connective Tissue Disease</td>
<td>127 (1.0%)</td>
<td>232 (1.3%)</td>
<td>359 (1.2%)</td>
</tr>
<tr>
<td>Obliterative Bronchiolitis (Not Re-Transplant)</td>
<td>80 (0.6%)</td>
<td>237 (1.3%)</td>
<td>317 (1.0%)</td>
</tr>
<tr>
<td>LAM</td>
<td>101 (0.8%)</td>
<td>207 (1.1%)</td>
<td>308 (1.0%)</td>
</tr>
<tr>
<td>Re-Transplant: Not Obliterative Bronchiolitis</td>
<td>127 (1.0%)</td>
<td>162 (0.9%)</td>
<td>289 (0.9%)</td>
</tr>
<tr>
<td>Congenital Heart Disease</td>
<td>43 (0.3%)</td>
<td>224 (1.2%)</td>
<td>267 (0.9%)</td>
</tr>
<tr>
<td>Cancer</td>
<td>6 (0.0%)</td>
<td>26 (0.1%)</td>
<td>32 (0.1%)</td>
</tr>
<tr>
<td>Other</td>
<td>108 (0.9%)</td>
<td>291 (1.6%)</td>
<td>399 (1.3%)</td>
</tr>
</tbody>
</table>
CTD-ILD (Non Scleroderma) and Lung Transplantation

- Systemic disease
  - Risks of renal failure (SLE)
  - Liver disease (MCTD)
  - Thromboembolic disease (SLE)
  - Lymphoproliferative disease (RA)
- Higher potential for allo-sensitization
- Is there a difference in survival, allograft function or extra-pulmonary dysfunction post transplant
CTD-ILD (Non Scleroderma) and Lung Transplantation - Survival

Compared to IPF
• Younger
• Female
• No more allo-sensitized

No Difference in:
• AR / BOS
• Need for Dialysis
• Liver disease
• Lympho-Prolif. Dz
45 yo female with SLE, complicated by PAH, nephritis, arthritis, cytopenia
Scleroderma - ILD
Systemic Sclerosis

- Skin thickening
- Calcinosis
- Raynaud’s
- Telangiectasia

- Esophageal dysmotility
- GI dysmotility
- Renal disease
- Cardiac disease
Scleroderma and Aspiration Risk
Lung Transplant Survival
Scleroderma vs IPF

23 patients with SSc compared to 46 IPF at UCSF

- No difference in BOS free survival
- No difference in AR

Transplantation. 2013 Apr 15;95(7):975-80.
Scleroderma and Esophageal Dysfunction

• 35 patients with SSc underwent lung transplantation at UCLA
  • 63% had abnormal Demeester score
  • 93% had abnormal manometry
  • 57% had an air fluid level
  • 74% had patulous esophagus

• Despite the significant esophageal dysmotility and GERD…..

• No difference in PG D, AR rate, BOS or Survival
Scleroderma Evaluation

- Severe pulmonary fibrosis (FVC and DLCO <40%), unresponsive to medical treatment
- Creatinine clearance above 60 mL/min
- Absence of severe skin involvement
- Absence of severe esophageal dysmotility and aspiration
- Absence of significant cardiac involvement
- Absence of severe small intestine, gastroparesis, colorectal and rectum involvement such as pseudo-obstruction, diverticulitis, and perforation

GERD is common in ILD even without symptoms

- **Higher prevalence of GERD in IPF** vs COPD in patients being evaluated for lung transplant
- **IPF patients have higher total and proximal reflux than Non-IPF** and Healthy Volunteers
- IPF patients being evaluated for transplant - **67% had reflux**
- Symptoms were only **65% sensitive and 71% specific** for diagnosis of GERD

Neurogastroenterol Motility 2015; 27: 1326-1332
Eur Respir J 2013; 42: 1322-1331
J Thorac Cardiovasc Surg 2007; 133: 1078-1084
GERD more common post transplantation

- Young: Prevalence rose from 35% pre transplant to 65% post transplant
- D’Ovidio: GERD increased from prevalence of 32% to 53% from 3 to 12 months post transplant
- Transplantation itself increases GERD
  - Vagal denervation
  - Gastroparesis
  - Loss of cough reflex
  - Impaired mucociliary clearance

Chest 2003; 124: 1689-1693
Am J Transplant 2006; 6: 1930-1938
GERD associated BOS

- BOS is a chronic inflammatory and fibrotic process of small airways: Injury, Remodeling, Repair
- D’Ovidio et al measured bile acids in BAL of 120 LTX recipients
  - 17% of recipients have high levels
  - Highest concentrations of bile acids in 70% of patients with early onset and severe BOS

J Thorac Cardiovasc Surg 2005; 129: 1144-1152
GERD Treatments

- Behavioral modifications
- Semi-recumbent sleeping posture
- PPI
- Motility agents – Macrolides
- Fundoplication – safe after lung transplantation
Pulmonary Hypertension in ILD

- Up to 32% of patients with ILD have PAH
- CTD- most commonly Systemic Sclerosis
- Sarcoidosis and PLCH
- IPF – over 60% have PAH in advanced disease
- 78 patients with IPF - 5 years survival:
  - No PAH 62%, PAH 16.7%
  - Normal DLCO 70.4%, Low DLCO 20%
  - High PAP RR 2.20, Low DLCO RR 2.7 and Group 2 RR 4.85
Elevated PAH in IPF and Risk of PGD after Lung Transplantation
PAH and IPF outcomes after Lung Transplantation
Familial Fibrosis and Lung Transplantation

• Retrospective case series of 14 lung transplant recipients with telomerase complex mutations
• All had fibrotic lung disease but only 43% had UIP pattern on CT imaging
• High incidence of cytopenias, particularly leukopenia, post transplantation (83%)
• Of these, 5 could not tolerate anti-proliferative agents - but not associated with acute rejection or CLAD
• CLAD occurred in 33% of recipients at median 3.1 years
Anti-fibrotic therapy and outcomes in Lung Transplantation

- Retrospective study of IPF patients undergoing lung transplantation at University of Munich
- Of 62 patients, 23 were on pirfenidone and 7 were on nintedanib
- Patients received anti-fibrotics were older and had higher DLCO at time of transplant
- No difference in blood product utilization, surgical complications or dehiscence
- No differences in 30 day or one year survival
Adult Lung Transplants
Kaplan-Meier Survival by Diagnosis
(Transplants: January 1990 – June 2014)

No pair-wise comparisons were significant at p < 0.05.
Adult Lung Transplants
Kaplan-Meier Survival by Diagnosis
(Transplants: January 1990 – June 2015)

Median survival (years):
A1ATD: 6.7; CF: 9.2; COPD: 5.8; IIP: 4.9;
ILD-not IIP: 6.0; Retransplant: 2.9
UCSF, National and Expected Lung Transplant Survival
Data from the Scientific Registry of Transplant Recipients January 2018
Thank you

Questions?

Steven Hays, MD
steven.hays@ucsf.edu
(415) 514-6672