Update in Lung Transplant

Kapil Patel, MD
Clinical Assistant Professor of Medicine
Center for Advanced Lung Disease
Stanford University Medical Center
• Introduction
• Referral and Evaluation
• Lung Allocation Score
• Infections
• Diabetes
• Gastroenterology related diseases
• Sinus Disease
• Malignancy
• Conclusion
Introduction

• 3500 lung transplants performed annually worldwide

• In 1983, UPMC performed the first lung transplant in a cystic fibrosis patient

• 3\textsuperscript{rd} most common indication for bilateral lung transplant
  • 5688 performed (Jan 1995 – July 2011)

• Highest long-term survival in lung transplant
ADULT LUNG TRANSPLANTS
Kaplan-Meier Survival by Diagnosis
(Transplants: January 1990 - June 2010)

HALF-LIFE
Alpha-1: 6.2 Years; CF: 7.5 Years; COPD: 5.3 Years; IPF: 4.4 Years; IPAH: 5.0 Years; Sarcoidosis: 5.3 Years

ISHLT
Introduction

• Advances in medical therapy have lead to a steady rise in the life expectancy in CF

• Despite therapeutic advances, respiratory failure accounts for most morbidity and mortality

• Lung transplant is the only treatment option to improve survival
Referral for Transplant

• Guideline recommendations:
  – FEV₁ < 30% of predicted

or

  – Rapidly progressive respiratory deterioration with FEV₁ > 30%
    • Increasing frequency of exacerbation requiring IV antibiotic
    • Recurrent hemoptysis
    • Refractory/recurrent pneumothorax
Evaluation

• Pulmonary
  – CXR/CT chest
  – Pulmonary Function Test
  – Six-minute walk

• Cardiac
  – Echocardiogram
  – RHC (± LHC)

• Renal
  – Cr Cl (> 50 mL/min)

• Infection
  – HIV, Hepatitis, EBV, CMV
  – Colonized Organisms

• GI
  – CT Abd/Pelvis
    • Liver
  – GERD evaluation
  – Esophagram

• Psychosocial evaluation
Transplant Listing

- Oxygen-dependent
- Hypercapnia (chronic)
- Pulmonary hypertension
- Mechanically ventilated CF patients

Bartz et al. Pre-transplant Mechanical Ventilation and Outcome in Patients With Cystic Fibrosis. J Heart Lung Transpl. 2004
Lung Allocation Score

• In 2005, the Lung Allocation Score was implemented by the Organ Procurement and Transplantation Network

• Derived from a prediction of benefit (expected 1-year post-transplant survival days and expected 1-year waiting list time survival days)
Factors used to calculate Lung Allocation Score

Factors used to predict waiting list survival...
- FVC (% predicted)
- PA systolic pressure
- Oxygen required at rest (L)
- Age
- BMI
- NYHA functional status
- Diagnosis
- Six-minute walk distance
- Continuous mechanical ventilation
- Diabetes

Factors used to predict post-transplant survival...
- FVC (% predicted)
- PCW mean pressure $\geq 20$ mmHg
- Continuous mechanical ventilation
- Age
- Serum creatinine (mg/dL)
- NYHA functional status
- Diagnosis
Lung Allocation Score

• UNOS registry identified 704 adult CF patients on waiting list from 2005-2009

• Lung transplant is associated with a 69% reduction in risk of death

Thabut et al. Survival benefit of lung transplant for cystic fibrosis since Lung Allocation Score Implementation. Am J Respir Crit Care Med. 2013
Infections

- *Pseudomonas aeruginosa*
  - Mucoid and non-mucoid organisms
  - Multi-drug resistant

- *Aspergillus species* (20%)
  - Increased risk for developing bronchiolitis obliterans syndrome and airway complications (e.g. bronchial anastomotic infection)

Hadjiliadis et al. Survival of Lung Transplant Patients With Cystic Fibrosis Harboring Panresistant Bacteria Other Than *Burkholderia cepacia*, Compared With Patients Harboring Sensitive Bacteria. J Heart Lung Transplant. 2007
Infections

- *Burkholderia cepacia complex* (3-5%)
  - *B. cenocepacia* (formly “genomovar III”)
    - Associated with increased 1 year post-transplant mortality

- Non-tuberculous mycobacterium (10-15%)
  - *Mycobacterium Avium Complex* (most common)
  - *Mycobacterium abscessus*

Diabetes

• CF related diabetes affects approximately 19% of adolescents and 40% of adults (> 40 years) with increased likelihood to develop in females

• Post-transplant: No association with mortality
GI

- Gastro-esophageal Reflux Disease
- Malnutrition
- Pancreatic Insufficiency
- Liver Disease (e.g. Cholelithiasis, biliary cirrhosis, cirrhosis)
- Distal Intestinal Obstruction Syndrome
GERD

• Prevalence of 75-90% in post-transplant CF
  – Increased risk for developing Chronic Rejection

• Nissen Fundoplication (laparoscopic antireflux surgery) superior medical therapy (PPI)

Malnutrition

• Underweight < 18.5 kg/m²

• Hypoalbuminemia

• CF and hypoalbuminemia are association with significantly reduced 1 year and overall survival

Liver Disease

• 4 - 10% of CF patients develop cirrhosis and portal hypertension resulting in synthetic dysfunction

• If significant liver disease is evident, patients may be evaluated for combined liver and lung transplant

Nash et al. Outcomes of patients with cystic fibrosis undergoing lung transplant w/ and w/out cystic fibrosis associated liver cirrhosis. (2012)
Sinus Disease

- Although, sinuses harbor organisms amongst all CF patients, it does not affect the post-transplant outcomes in CF patients

# Malignancy

<table>
<thead>
<tr>
<th>CF Non-transplanted</th>
<th>CF Transplanted</th>
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<tbody>
<tr>
<td><strong>Digestive Tract Cancers</strong></td>
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<tr>
<td>172 observed vs 153.5 expected (SIR 1.1)</td>
<td>26 observed vs 9.6 expected (SIR 2.7)</td>
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<tr>
<td>45 observed vs 12.8 expected (SIR 3.5)</td>
<td>19 observed vs 1.1 expected (SIR 17.3)</td>
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Conclusion

• Lung transplant remains to be an option for CF patients with end-stage lung disease

• Long term outcomes remains superior to those for patients with other lung diseases amenable to transplant
Conclusion

• Possible areas for future research to improve transplant outcomes include:
  
  – Surgical technique
  
  – Organ procurement and preservation
  
  – Post-operative management in the ICU