Disclosure

I have no relevant financial relationships with any companies related to the content of this course.
Outline

- Transplanting ILD in the US
- Evaluating transplant candidacy in ILD patients
- Optimizing ILD patients for transplant
- Outcomes of lung transplant for ILD patients

Transplanting ILD in the United States

- Restrictive lung disease is the most common indication for lung transplant
  1331 (57.1%) patients transplanted in 2016

- Lung Allocation Score (range 0-100)

  \[ \text{LAS} = \frac{\text{Probability of living 1 year post-transplant}}{\text{Benefit}} - 2 \times \frac{\text{Probability of living 1 year in the waitlist}}{\text{Urgency}} \]

A = Obstructive Lung Disease
B = Pulmonary Vascular Disease (PH)
C = Cystic Fibrosis
D = Restrictive Lung Disease (ILD)
Transplanting ILD in the United States

Candidates with restrictive lung disease have the highest waitlist mortality
25.5 deaths per 100 waitlist years

There is a shortage of suitable donor lungs.

In 2016, there were 2692 candidates and only 2345 lung transplants were performed in the US.

The goal is to select candidates likely to have survival benefit from transplant.


Evaluating Lung Transplant Candidacy

Sick enough to need transplant?  
Well enough to have a successful transplant?

>50% risk of dying in 2 years from lung disease  
> 80% likelihood of surviving 
≥ 90 days post-transplant & 
≥ 5 years if adequate graft function

Determining Lung Transplant Candidacy

At the time of diagnosis
- FVC < 80% of predicted
- DLCO < 40% of predicted
- Requirement for supplemental oxygen
- Failing medical therapy

FVC decline ≥ 10% in 6 months
DLCO decline ≥ 15% in 6 months
Desaturation < 88%
6 MWT < 250 m
> 50 m decline in 6 MWT in 6 months
Pulmonary hypertension
Hospitalization

Patients with Interstitial Lung Disease

Evaluation and Selection for Lung Transplant

**Physiology**
- Prognosis
- Bilateral / single lung transplant
- Timing of transplant
- Organ function
- Comorbidities
- Malignancy

**Body Composition**
- Frailty
- Deconditioning
- Malnutrition
- Obesity

**Psychosocial Readiness**
- Motivation
- Mental readiness
- Medical compliance
- Substance abuse
- Caregiver support
- Financial resources

The decision to add patients to the wait list is discussed in multidisciplinary meeting.

### Absolute Contraindications

1. Recent malignancy
2. Untreatable organ dysfunction
3. Coronary artery disease not amenable to revascularization
4. Acute medical instability
5. Poorly controlled infection with resistant microbes
6. BMI $\geq 35$ kg/m²
7. Severely limited functional status with poor rehabilitation potential
8. Medical non-adherence
9. Substance abuse or dependence

Relative Contraindications

1. Age > 65 years + other relative contraindications
2. Age > 75 years
3. Mechanical ventilation or extracorporeal life support
4. Prior chest surgery *
5. Infection with *Burkholderia cenocepacia* or *gladioli*, *Mycobacterium abscessus*
6. Infection with HIV, hepatitis B, hepatitis C
7. BMI 30-34.9 with central obesity
8. Severe malnutrition


Short Telomere Syndromes

14 patients with telomerase mutations

• 10 developed leukopenia (<6 months post-transplant)
  5 did not tolerate anti-proliferative agents
• 5 developed thrombocytopenia
• 6 had recurrent respiratory infections
  Pseudomonas, Staphylococcus, Aspergillus
• 4 developed CLAD (median 3.1 years)
• 10 developed chronic renal insufficiency
• 3 had malignancy

Systemic Considerations in ILD Patients

**Bone marrow failure**
- Risk for cytopenias (specially induced by Mycophenolate, Valgancyclovir, Sirolimus)
  - Bone marrow biopsy
  - Trial of Mycophenolate


**Esophageal dysmotility & GERD**
- Risk for aspiration
  - 24h pH monitoring/impedance, esophageal manometry
  - Lifestyle changes


**Myositis**
- Should be in remission.
- May consider tacrolimus trial if uncontrolled despite steroids / mycophenolate.


Medication Considerations in ILD

**Steroids**
- Prednisone dose < 40 mg → no difference in mortality or complications


**Pirfenidone and Nintedanib**
- No increase in complications: bleeding, anastomotic/wound healing, mortality. (N= 7P, 2N, 6 Controls)


- No anastomotic complications. No difference in bleeding, wound healing, need for revision, mortality. (N=23P, 7N, 32 Controls)

Optimize Your ILD Patient for Lung Transplant

1. Recognize trajectory & refer early
2. Improve frailty
3. Improve body composition
4. Provide enough oxygen
5. Age-appropriate cancer screening

Frailty is a State of Risk

Frailty is associated with
- Disability
- Delisting
- Death

Frailty is modifiable with
- Pulmonary rehabilitation
- Nutrition

Singer JP, et al. AJRCCM. 2015
Underweight and Obesity are associated with Death after Lung Transplant

Singer JP, et al. AJRCCM. 2014

My Diet and Exercise Are More Important than Ever

Improve Body Composition

- **Goal Body Mass Index** 18.5 – 30 kg/m²
  (Adiposity is associated with post-transplant mortality.)

- Refer to nutritionist
  Supplements, tube feedings
  Weight loss

- Wean off prednisone as much as possible (≤ 20 mg daily)

- Control hyperglycemia

Clausen ES, et al. J Heart Lung Transplant. 2018

Prevent Pulmonary Hypertension (PH)
It’s associated with waitlist mortality!

Provide Enough Oxygen

- Reassess oxygen requirements.
- Treat sleep apnea.
- Obtain echocardiogram if diffusion capacity declines.
- Consider referral to PH specialist.

Mean PAP ≥25 mmHg

Optimization works!

63 yo M respiratory therapist with OSA & familial IPF

• 2009: lung biopsy. Mean PA 17 mmHg
• 2010: too early for transplant → pulmonary rehabilitation & loose weight

• September 2015: Listed. O₂ at rest 5 LPM, exertion 8 LPM. Mean PA 29 mmHg
• May 2016: admitted from clinic. O₂ at rest 13 LPM, exertion 20 LPM

• 1 month wait in the hospital: O₂ at rest 15 LPM HFNC, ambulation 15 LPM NRB
  • Walking 2-3 times daily

• Bilateral lung transplant on ECMO. Mean PA 41 mmHg
• Discharged 9 days post-transplant

Case 2: Struggling to transplant

• 58 yo M gardener with diabetes who developed SOB
• 6 months later → hospitalized for hypoxic respiratory failure
  • Oxygen 80%, 30 LPM by HFNC
  • Transferred to our ICU for transplant evaluation

• BMI 34, deconditioned
• No significant other, no children/relatives
• Not had colonoscopy
Case 2: Struggling to transplant

Day 12 \(\rightarrow\) intubation and **mechanical ventilation**
Day 14 \(\rightarrow\) Tracheostomy, heart catheterization (PA mean 51 mmHg)
Day 17 \(\rightarrow\) CT colonography
Day 20 \(\rightarrow\) listed for transplant
Day 22 \(\rightarrow\) VA-ECMO
Day 24 \(\rightarrow\) Bilateral lung transplant
  - 90 min lysis of adhesions
  - Poor cardiac contractility \(\rightarrow\) VA ECMO post-op
Day 25 \(\rightarrow\) re-exploration for left hemothorax, chest open
Day 26 \(\rightarrow\) re-exploration, chest closure, ECMO decannulation
Day 35 \(\rightarrow\) re-exploration for left chest wall hematoma

Case 2: Struggling to transplant

- **Complications:**
  - Profound weakness
  - Oropharyngeal dysphagia
  - Required tube feedings

- Discharged 56 days post-transplant to skilled nursing facility
- Required physical therapy
- Caregiver friends
Lung Transplant Survival for ILD

Conditional 1-year survival 7 years

Telomere Length of Pulmonary Fibrosis Patients is Associated with Survival

26 patients with telomere length < 10th percentile

- 10 had macrocytosis
- 54% died within 5 years (vs 18%)
- Lower adjusted 5-year survival (HR 10.9)
- 28% had Grade 3 Primary Graft Dysfunction (vs 7%)
- 50% had CLAD (vs 23%)
- Shorter adjusted time to CLAD (HR 6.3)
Survival Benefit of Lung Transplant for ILD

Table 4. Percentage of patients with expected survival benefit conferred by transplantation, by strata of recipient/donor characteristics

<table>
<thead>
<tr>
<th>Recipient/Donor Characteristic</th>
<th>1 Year*</th>
<th>2 Years*</th>
<th>3 Years*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>64.4</td>
<td>73.8</td>
<td>81.9</td>
</tr>
<tr>
<td>Native disease grouping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obstructive</td>
<td>22.1</td>
<td>39.2</td>
<td>56.3</td>
</tr>
<tr>
<td>Pulmonary vascular</td>
<td>52.9</td>
<td>64.6</td>
<td>73.0</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>95.3</td>
<td>98.9</td>
<td>99.7</td>
</tr>
<tr>
<td>Restrictive</td>
<td>50.0</td>
<td>94.8</td>
<td>97.7</td>
</tr>
<tr>
<td>LAS at transplantation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0–32.4</td>
<td>0.3</td>
<td>6.8</td>
<td>26.8</td>
</tr>
<tr>
<td>32.5–34.9</td>
<td>13.9</td>
<td>36.7</td>
<td>55.2</td>
</tr>
<tr>
<td>35.0–39.9</td>
<td>68.1</td>
<td>84.9</td>
<td>94.2</td>
</tr>
<tr>
<td>40.0–44.9</td>
<td>99.9</td>
<td>99.9</td>
<td>100.0</td>
</tr>
<tr>
<td>45.0–49.9</td>
<td>99.9</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>50.0–100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Median LAS 43.9

Life after lung transplant

Quality of life

Paul

Double lung transplant for scleroderma in 2010

Life after lung transplant

Back to work!

Russell

Double lung transplant for Idiopathic Pulmonary Fibrosis (IPF) in 2012

Medications after Transplant

▶ **Immunosuppression**
  - Prednisone
  - Tacrolimus
  - Mycophenolate Mofetil

▶ **Infection Prophylaxis**
  - Pneumocystis jirovecii
  - Aspergillus
  - Pseudomonas
  - Cytomegalovirus

▶ **Treatment of Metabolic Complications**
  - Hyperglycemia
  - Hyperkalemia
  - Hypomagnesemia
  - Hypertension
  - Osteoporosis prophylaxis
  - Peptic ulcer prophylaxis

▶ **Treatment of pre-transplant conditions**
  - Benign Prostate Hypertrophy
  - Latent tuberculosis
  - Raynaud’s phenomenon
  - Epilepsy
Staying Healthy after Transplant requires Diligence

1. Prevent infections
2. Daily exercise
3. Adequate nutrition
4. Strict adherence to medications
5. Follow up with transplant team
6. Follow up with primary care provider

Avery RK, Michaels MG; and the AST Infectious Diseases Community of Practice. Am J Transplant. 2013;13(s4):304-310


Learn more
http://lungtransplanteducation.ucsf.edu
Thank you

Aida.Venado@ucsf.edu