Identifying and Managing Respiratory Diseases and Symptoms after Transplant

Celebrating a Second Chance at Life Survivorship Symposium
April 29 – May 5, 2023

Kyle Brownback, MD, FCCP
University of Kansas Medical Center

Objectives

• Lung Basics
• Monitoring lung function
• Pulmonary conditions after transplant
• Management of those conditions
• What can you do?
Lungs

Respiratory system

Nasal Cavity
Nostril
Soft palate
Hard Palate
Oral Cavity
Larynx
Trachea
Carina of Trachea
Right Main Bronchus
Right Lung
Pharyngeal Tonsil
Nasopharynx
Oropharynx
Tongue
Epiglottis
Esophagus
Left Main Bronchus
Bronchi
Left Lung
Diaphragm
Spirometry

• Forced exhalation maneuver
• Calculates
  • Forced Vital Capacity (FVC)
  • Forced Expiratory Volume in 1 second (FEV1)
  • FEV1/FVC
Plethysmography

- Allow calculation of residual volume and total lung capacity
- Combined with assessment of diffusion capacity

Pulmonary Function Testing

<table>
<thead>
<tr>
<th>Test</th>
<th>Actual</th>
<th>Pred</th>
<th>L% Diff</th>
<th>Pred</th>
<th>L% Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>3.05</td>
<td>4.28</td>
<td>3.26</td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>2.17</td>
<td>3.01</td>
<td>2.15</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>71</td>
<td>70</td>
<td>60</td>
<td>108</td>
<td></td>
</tr>
<tr>
<td>FEV1/SVC (%)</td>
<td>66</td>
<td>70</td>
<td>0.21</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>FEF 25-75% (L/sec)</td>
<td>4.42</td>
<td>1.96</td>
<td>6.17</td>
<td>7.12</td>
<td>4.60</td>
</tr>
<tr>
<td>Gas (L/min/120s)</td>
<td>1.03</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV (ml)</td>
<td>1.45</td>
<td>0.66</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>— LUNG VOLUMES ——</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVC (L)</td>
<td>5.26</td>
<td>4.28</td>
<td>3.26</td>
<td>76</td>
<td></td>
</tr>
<tr>
<td>IC (L)</td>
<td>2.79</td>
<td>3.99</td>
<td>70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TV (L)</td>
<td>5.80</td>
<td>4.24</td>
<td>2.80</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>RV (FRC) (L)</td>
<td>3.33</td>
<td>2.05</td>
<td>2.21</td>
<td>112</td>
<td></td>
</tr>
<tr>
<td>TLC/RV (L)</td>
<td>6.60</td>
<td>7.60</td>
<td>6.10</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>RV/TLC (Pred) (%)</td>
<td>51</td>
<td>41</td>
<td>33</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>—— DIFFUSION ——</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DLCO/FVC (mL/H/mmHg)</td>
<td>24.03</td>
<td>23.72</td>
<td>11.64</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td>DLCO/VA (mL/min/mmHg)</td>
<td>23.72</td>
<td>11.64</td>
<td>3.88</td>
<td>3.27</td>
<td>1.81</td>
</tr>
<tr>
<td>VA (L)</td>
<td>6.53</td>
<td>7.40</td>
<td>6.03</td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>

Spirometry demonstrates a mild reduction in vital capacity.
Residual volume is normal.
Total lung capacity is normal.
Transport factor (diffusion capacity) not corrected for hemoglobin is normal.
RV/TLC is increased.

Impression: Normal pulmonary function studies.
CT Scan

Bronchoscopy
Pulmonary Conditions after Transplant

• Pre-existing lung conditions
• Infection
• Drug Toxicity
• GVHD

Pre-Existing Lung Conditions

• Asthma
• COPD
• Interstitial Lung Diseases (Scarring)
• Pulmonary Embolism (Blood Clot)
• Long-COVID
Infections

- Bacterial
- Viral
- Fungal
- Pneumocystis
Drug Toxicity

• Medications used to treat malignancies may cause inflammation and toxicity in the lungs

• May present with:
  • Cough (bronchitis)
  • Shortness of breath
  • Pleurisy

• May increase risk of infection

• Can cause pneumonitis, fibrosis and inflammation

<table>
<thead>
<tr>
<th>TABLE 72-2. Classification of Drug-Induced and Related Pulmonary Diseases by Type of Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEMOTHERAPEUTIC</td>
</tr>
<tr>
<td>Cytotoxic</td>
</tr>
<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>Nitrosoureas</td>
</tr>
<tr>
<td>Procarbazine</td>
</tr>
<tr>
<td>Nitrogen mustard</td>
</tr>
<tr>
<td>Bleomycin</td>
</tr>
<tr>
<td>Cisplatin</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
</tr>
<tr>
<td>Ifosfamide</td>
</tr>
<tr>
<td>Interleukin-2</td>
</tr>
<tr>
<td>Melphalan</td>
</tr>
<tr>
<td>Mitomycin C</td>
</tr>
<tr>
<td>Nitrogen mustard</td>
</tr>
<tr>
<td>PROTEASOMES</td>
</tr>
<tr>
<td>NF-kappaB</td>
</tr>
<tr>
<td>Tumor necrosis factor</td>
</tr>
<tr>
<td>Vemurafenine</td>
</tr>
<tr>
<td>Zolotin</td>
</tr>
<tr>
<td>Noncytotoxic</td>
</tr>
<tr>
<td>Mitomycin C</td>
</tr>
<tr>
<td>Doxorubicin</td>
</tr>
<tr>
<td>Gemcitabine</td>
</tr>
<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>Procarbazine</td>
</tr>
<tr>
<td>ANTIBIOTIC</td>
</tr>
<tr>
<td>Ampicillin</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
</tr>
<tr>
<td>ANALGESIC</td>
</tr>
<tr>
<td>Analgesic</td>
</tr>
<tr>
<td>Intravenous</td>
</tr>
<tr>
<td>Inhalant</td>
</tr>
<tr>
<td>MISCELLANEOUS</td>
</tr>
<tr>
<td>Acetaminophen</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
</tr>
<tr>
<td>Analgesic</td>
</tr>
<tr>
<td>Anticoagulants</td>
</tr>
<tr>
<td>Blockers</td>
</tr>
<tr>
<td>*Typically present as acute or subacute respiratory insufficiency.</td>
</tr>
</tbody>
</table>

Graft-versus-Host Disease (GVHD)

- **Idiopathic Pneumonia Syndrome**
  - Occurs first 90 days after transplant
- **Organizing Pneumonia**
  - Can occur anytime after transplant
  - Typically follows an infection
- **Bronchiolitis Obliterans Syndrome**
  - Most common manifestation
  - Typically occurs 3 months to 3 years after transplant

---

**Idiopathic Pneumonia Syndrome**

- Develops in 3-15% of post-HSCT patients
- Within 4 months of transplant

Organizing Pneumonia

• Symptoms typically include cough, shortness of breath and pleurisy
• Pattern on CT is highly suggestive
• Usually requires bronchoscopy to exclude infection
• Responds well to steroids

Bronchiolitis Obliterans Syndrome

• Inflammation in the bronchioles (middle airways)
• If not treated promptly can cause scarring
• May be asymptomatic
  • Occasionally presents with cough and shortness of breath

Bronchiolitis Obliterans – Risk Factors

- Busulfan-based regimens
- 14 months or longer duration from leukemia diagnosis to transplant
- Peripheral blood stem cell source
- Female donor to male recipient
- Grade II-IV acute GVHD
- Previous interstitial pneumonitis
- Presence of airflow obstruction prior to transplant
- Age
- History of viral respiratory tract infections

---

Table 2—Suggested Diagnostic Criteria for BO

<table>
<thead>
<tr>
<th>Suggested Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Allogeneic HSCT</td>
</tr>
<tr>
<td>2. Chronic GVHD</td>
</tr>
<tr>
<td>3. Evidence of airflow obstruction with FEV₁/FVC &lt; 0.7 and FEV₁ &lt; 75% predicted</td>
</tr>
<tr>
<td>4. Air trapping or small airway thickening or bronchiectasis on HRCT of the chest</td>
</tr>
<tr>
<td>with inspiratory and expiratory cuts, residual volume of PFT &gt; 120% predicted</td>
</tr>
<tr>
<td>5. Absence of infection based on clinical symptoms, radiographs, microbiologic</td>
</tr>
<tr>
<td>cultures, sputum culture, or BAL</td>
</tr>
<tr>
<td>6. Pathologic confirmation of constrictive bronchiolitis (biopsy not required for</td>
</tr>
<tr>
<td>clinical diagnosis if all above criteria met)</td>
</tr>
</tbody>
</table>

BO = bronchiolitis obliterans; GVHD = graft-vs-host disease; HRCT = high-resolution CT scan; PFT = pulmonary function test. See Table 1 legend for expansion of other abbreviations. (Adapted with permission from Soubani and Pandya.⁵⁷)
How Do We Treat?

- Management of systemic GVHD
  - Corticosteroids
  - Ruxolitinib (Jakafi)
  - Belumosudil (Rezurock)
  - Ibrutinib (Imbruvica)
  - Extracorporeal photopheresis
  - Rituximab

How Do We Treat?

- Pulmonary GVHD
  - Inhaled steroids
    - Reduce inflammation at site of medication deposition
    - Both fluticasone (Flovent) and budesonide/formoterol (Symbicort) have been studied
  - Montelukast (Singulair)
    - Blocks allergic pathway signaling
  - Short-acting bronchodilators (albuterol)
    - Immediately improve bronchial relaxation
How Do We Treat?

- Assess for need of supplemental oxygen
- Pulmonary rehabilitation
- Assess for other conditions
  - Sleep apnea
  - Pulmonary hypertension
  - Asthma
  - Chronic infections

What Can I Do?

- Optimize Medications
  - Treat underlying asthma and COPD
  - Assessed prior to transplant with PFT
- Smoking/vaping cessation
- Environmental stimuli
  - Air pollution
  - Air purifiers?
What Can I Do?

• Infection avoidance
  • Many/Most respiratory conditions after transplant follow a viral illness
  • Best way to prevent these conditions is by avoiding illness
    • Masks
    • Hand hygiene
    • Sick contact avoidance
    • Vaccination

What Can I Do?

• Physical activity
  • Improves/maintains functional status
  • Prevents complications of debilitation
  • Earlier recognition of symptoms
  • Innumerable positive benefits
What Can I Do?

• Symptom detection
  • Notify transplant teams with new symptoms
  • Cough +/- sputum production
  • Chest pain
  • Shortness of breath
  • Abnormal breathing sounds/patterns (wheezing)
• Leads to earlier evaluation
  • PFT/CT chest
• Earlier detection of new conditions often leads to more effective treatments

• Home spirometry?

Conclusion

• Lungs are susceptible to a myriad of conditions after transplant
• Regular PFT monitoring after transplant is standard of care
• New respiratory symptoms after transplant require further investigation
  • Typically with PFT and CT chest
• Promote lung health in yourself
  • Exercise
  • Infection avoidance
  • Avoiding noxious Stimuli
Thank You

• Dr. Sunil Abhyankar, MD
• Dr. Joseph McGuirk, MD
• Dr. Leyla Shune, MD
• Dr. Anuraj Singh, MD
• Lung GVHD Consortium Group

QUESTIONS?

Kyle Brownback, MD, FCCP
University of Kansas Medical Center
LET US KNOW HOW WE CAN HELP YOU

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

Give us call: 888-597-7674 or 847-433-3313