Take a Breath! Managing Breathing Problems after Transplant

Celebrating a Second Chance at Life Survivorship Symposium

April 27 – May 3, 2024

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Take a Breath! Lung GVHD and Managing Breathing Problems after Transplant

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“We are all working so hard to be self-fulfilled, individually successful, and personally healthy...that we have forgotten the real purpose and path to health and healing is to make joyful connections.”
- Francis Peabody MD, 1927
Quotes from Patients with Breathing Problems after Transplant

“I need to breathe to live, but I also need to live to breathe.”

“I’m alive, but I’ve had so much loss.”

“If I had known I would get lung disease like this, I would have rather died from my AML.”

Courtesy of Guang-Shing Cheng MD
Fred Hutchinson Cancer Center
Pneumonia, Lung Disease and Transplant

- Over 50% of patients will develop pneumonia at some point after transplant. The pneumonia can occur at any time, whether in the first few months, or many years after transplant.

- Not all pneumonias are due to an infection. Many aren’t infectious at all.

- By definition, pneumonia simply means that there is “inflammation” in the lungs. For example, fluid, swelling, or irritation to lung tissue can all be present in the lungs, without having an actual infection present.

- In reality though, the lines between infectious and non-infectious pneumonia are often blurred.
Blurring of the lines

• Infectious pneumonia may often lead to a non-Infectious pneumonia.
• Patients with non-infectious pneumonia are often chronically infected.
• We can’t even tell which it is, by looking at a Chest Xray or CT scan.
• Ughh....
• We can start by defining Lung GVH. What is it? How do we test for it? How do we treat it?

If you asked transplant physicians to look at these chest Xrays and tell you which patients had an infection in their lungs, they couldn’t tell you, at least with any accuracy.
What is Lung GVHD?

• It is a form of chronic graft versus host disease (GVHD).

• An “obstructive” airway disease that occurs ~ 1-year post-transplant. **Air can get in. It can’t get back out.** The air you breathe gets trapped, then stagnant in your lungs. Chronic infections (infectious pneumonia) often occur.

• Symptoms: Shortness of breadth, chronic cough.

• Develops in 10-20% of all patients with chronic GVHD

• Medical term: Bronchiolitis Obliterans Syndrome (BOS)
Lung GVHD: Over the past decade

- New Diagnostic Techniques
- Collaborative Teams
- Predictive Biomarkers
- Novel Clinical Trials
- Your support
Primer: Pathology of Lung GVHD

Air Sac (Alveolus)

Small Airway (Bronchiole)

Normal lungs

Lung GVHD
(Bronchiolitis Obliterans Syndrome)
Risk Factors for Lung GVHD.
University of Michigan Data Base (n=1016 patients)

Patients at highest risk for developing Lung GVHD:

• Patients with a history of severe acute Graft Versus Host Disease.

• Patients who developed viral infections and/or Pneumonia within the first 100 days post-transplant.

• Patients with low lung function prior to transplant. Measured by a test called Pulmonary Function Testing (PFT).
How is Lung GVHD Diagnosed?
NIH Criteria for Diagnosing Lung GVHD\textsuperscript{1,2}

- Requires Pulmonary Function Testing (PFT).
- The main criteria is an FEV1 < 75% predicted for age and size.
- The FEV1 must have declined ≥ 10% from prior measurements.
- What does all this mean, in English?

\textsuperscript{1} Filipovich AH BBMT 2005, \textsuperscript{2} Jagasia M BBMT 2015
Pulmonary function tests are a group of tests that help healthcare providers to know the efficiency of your lungs.
PFT’s: The main parameter we (MD) look at:

FEV1: Forced Expiratory Volume in 1 second

The volume of air you can **forcibly exhale in 1 second**
Pulmonary Function Tests: Primer

- Tidal volume
- Normal Breathing
- Forced Vital Capacity (FVC)
- FEV1
Pulmonary Function Tests: Primer

- **Tidal Volume**
- **Forced Vital Capacity (FVC)**
- **Normal Breathing**
- **FEV1**
- **PFT**
Early Diagnosis of Lung GVHD is Critical.
Survival by FEV1 at “Time of Initial Diagnosis” of Lung GVHD

Median FEV1 = 57% at diagnosis of Lung GVHD

$\text{p}=0.0023$
The problem is that we start treating here

Normal lungs  →  Lung GVHD
(Bronchiolitis Obliterans Syndrome)
We need to be treating here

Normal lungs → Lung GVHD
We need to recognize who’s at risk here

Normal lungs

Lung GVHD
(Bronchiolitis Obliterans Syndrome)
The patient perspective on early detection

- 54 patient surveys administered via email at 3 sites (FHCC, Stanford, Geneva)
- 30 respondents (55% response rate)

5. What aspects of BOS and lung complications after stem cell transplant should researchers focus on? rank in order of importance (1 to 6; 1 being of highest priority)

1. Early diagnosis and prevention
2. Treatment
3. Biological mechanisms
4. Patient and clinician education
5. Quality of life
6. Other - write in next question

Courtesy of Guang-Shing Cheng
Recommendation for monitoring PFT

“85% of success is just showing up”
- Woody Allen, 1987

Just get PFT’s done
How often should PFT be performed?

2020 NIH Consensus Development Project (Kitko TCT 2021)

- Obtain PFT every 3 months for 1\textsuperscript{st} year after BMT.

- Once chronic GVHD is diagnosed: Obtain PFT every 3 months.
Issue: Are there alternatives to PFT’s?
PFT testing in your hands

- NIH funded study. Guang-Shing Cheng MD (Seattle)
- Patients perform PFT’s weekly, at home.
- Wireless Bluetooth-enabled device.
- Readings sync with patient’s smart phone. Patient’s can see their FEV1.
- Readings transmitted electronically to MD
- Large, four center study now in progress.
New CT scan technology: Called PRM
Color codes the lungs to see areas of lung damage

1 year post-BMT
Mild lung symptoms. PFT and CT both normal

2 years post-BMT
Lung GVH is diagnosed

5 years post-BMT
Severe symptoms
Therapy for Lung GVHD

• Few Randomized Clinical Trials
• Two trials that have impacted care:
  a. Inhaled Steroids (Bergeron A, Am J Respir Crit Care Med. 2015)
  b. FAM Therapy, n=36 patients (Williams KM, BBMT 2016)

  F = Inhaled Fluticasone (inhaled steroid)
  A = Azithromycin (oral antibiotic and anti-inflammatory agent)
  M = Montelukast (Singular) (oral anti-inflammatory agent)
Trials for Lung GVHD (BOS) on ClinicalTrials.gov

- Belumosudil
- Avelestat (NCT02669251)
- Ruxolitinib (NCT03315741, NCT04908375)
- Nintedanib (NCT03805477)
- Liposomal CSA (NCT04107675)
- Itacitinib (NCT02669251)
- Pirfenidone (NCT03315741)
- Pirfenidone (NCT03315741)
Therapy: The power of exercise

PFT report: 50-year-old male with chronic GVHD

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<th>LUNG MECHANICS</th>
<th>Baseline Actual</th>
<th>Pred</th>
<th>%Pred</th>
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<tr>
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FEV1 = 52%
DLCO 107%

DLCO measures your ability to transport air into the blood stream.

Lung function:
Pre-bike riding stage:
FEV1 = 58%, DLCO = 77%

After years of bike riding
FEV1 = 52%, DLCO = 107%
What is the bravest thing you’ve ever said?” asked the boy.

“Help,” said the horse

Excerpt from “The Boy, the Mole, the Fox and the Horse.” - C.Mackesy
Thank you everyone.

• To BMT InfoNet.
• To the patients we serve.
• To the medical teams we work with.
• To all of you.

“Happy are those who dream dreams, and have paid the price to make them come true.” - L.J. Suenens
Questions?

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