Interstitial Lung Disease: An Overview

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Disclosures

• Grants to study Genomic Predictors of IPF Outcomes
  • National Institutes of Health (NHLBI)
  • American Thoracic Society
  • American Lung Association

• Grant to study early ILD detection
  • UC-Davis Gordon Wong endowment

• IPF Consulting
  • Genentech
  • Boehringer Ingelheim
Objectives

• Understand the classification framework for common interstitial lung diseases (ILD)

• Appreciate the wide spectrum of ILD presentation

• Pursue a standardized ILD diagnostic work-up
What the textbook says

Interstitial Lung Disease Classification

Interstitial lung disease

- Etiology known
  - Inorganic exposure
    - Asbestos
    - Silica
    - Hard metals
    - Coal dust
  - Organic exposure
    - Birds
    - Hay
    - Mold
    - Mycobacteria
  - Smoking
    - DIP
    - RB-ILD
    - LCH
  - Drugs
    - Nitrofurantoin
    - Amiodarone
    - Methotrexate
    - Chemotherapy
  - Connective tissue disease
    - Rheumatoid arthritis
    - Polymyositis/dermatomyositis
    - Scleroderma
    - Sjögren syndrome
  - Granulomatous
    - Sarcoidosis

- Etiology unknown
  - Idiopathic interstitial pneumonias
    - IPF
    - Non-IPF
      - NSIP
      - COP
      - LIP
      - AIP

What we actually see on a regular basis

Interstitial Lung Disease

**Etiology Known**

- Connective tissue disease
  - RA, SSc, Sjogrens, IIM

- Environmental ILD
  - Hypersensitivity pneumonitis

- Occupational ILD
  - Asbestosis/Silicosis

- Drug-induced ILD
  - Amio/MTX/Chemo

**Idiopathic Interstitial Pneumonia**

- Smoking-related
  - Desquamative interstitial pneumonia
  - Respiratory bronchiolitis-ILD

- Chronic Fibrosing
  - Idiopathic pulmonary fibrosis
  - Idiopathic NSIP

- Inflammatory +/- fibrosing
  - Cryptogenic organizing pneumonia

**Unclassifiable**

- None of the above

**Other**

- Sarcoidosis
Interstitial Lung Disease

Inflammatory Predominant ILDs
- CTD-ILD (most)
- Hypersensitivity Pneumonitis (early)
- Cryptogenic Organizing Pneumonia
- Cellular idiopathic NSIP
- Drug-induced ILD

Fibrotic Predominant ILDs
- Systemic sclerosis-ILD
- Hypersensitivity pneumonitis (late)
- Idiopathic pulmonary fibrosis
- Fibrotic idiopathic NSIP
- Asbestosis
Inflamatory ILD can manifestations as:

- Non-specific Interstitial Pneumonia
- Organizing Pneumonia

Kligerman et al. Radiographics 2009
Travis et al. AJRCCM 2013
Fibrotic ILD can manifest as:

- Peripheral predominant fibrosis
- Airway-centric fibrosis
Inflammatory ILD can manifestations as:

- Cellular non-specific Interstitial Pneumonia
- Organizing Pneumonia
Fibrotic ILD can manifest as:

- Usual Interstitial Pneumonia
- Airway-centric fibrosis
The ILD Evaluation

Goals

• Standardized work-up to improve diagnostic accuracy
• Avoid unnecessary lung biopsy
• Diagnose early in the disease course
• Treat the disease early
The ILD Evaluation

History

Environmental history (Birds, mold)? - HP
Joint pain/swelling, rash, muscle weakness, skin tightening, dysphagia? - CTD-ILD
New medication? - Chemo/Amio/MTX
Job exposures? - asbestosis, silicosis
Family history of ILD? – familial IPF
Smoking history? – smoking-ILDs
Early graying, bone marrow abnormality, liver disease? – short telomere-related ILD

Laboratory work-up
- Autoimmune serologies

Physical Exam
- Autoimmune features?
- Crackles? Location?

High-resolution CT Scan
The ILD Evaluation

- History unrevealing
- Physical exam non-specific
- Laboratory work-up negative
- High-resolution CT non-diagnostic

Unclassifiable ILD

Surgical Lung Biopsy
- Must have sufficient lung function
- Largely safe, but small and finite risk of death and exacerbation
The ILD Evaluation - PFT

• Helps characterize physiology
  – Forced vital capacity (FVC)
  – Diffusion capacity (DLCO)

• Can assist with prognostication
  – Baseline values
  – Longitudinal change over time

The ILD Evaluation - Bronchoscopy

• Generally of limited use with a few notable exceptions
  - Hypersensitivity pneumonitis – cellular analysis
  - Sarcoidosis – lymph node bx/Tbbx
  - Asbestosis – cellular analysis, histology
  - Amiodarone toxicity – cellular analysis, histology

• Cryobiopsy – larger biopsy performed
  - May establish diagnosis in patients unable to undergo surgical lung biopsy
  - Increased risk of bleeding and pneumothorax
  - Highly operator dependent
The ILD Evaluation – Multi-disciplinary Discussion

Multidisciplinary Approach
The process of achieving a multidisciplinary diagnosis in a patient with ILD is dynamic, requiring close communication between clinician, radiologist, and when appropriate, pathologist (1). Clinical data (presentation, exposures, smoking status, associated diseases, lung function, laboratory findings) and radiologic findings are essential for multidisciplinary diagnosis.

MDD
Pulmonologist
Chest Radiologist
Pulmonary pathologist
# How important is a MDD?

**Idiopathic Interstitial Pneumonia**

**What Is the Effect of a MDD?**

<table>
<thead>
<tr>
<th>Step</th>
<th>Information Provided</th>
<th>Participants</th>
<th>Output</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - Individual</td>
<td>HRCT</td>
<td>Clinicians, Radiologists</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>2 - Individual</td>
<td>HRCT + Standardized clinical data</td>
<td>Clinicians, Radiologists</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>3 - Group Discussion</td>
<td>HRCT + Standardized clinical data</td>
<td>Clinicians, Radiologists</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>4 - Group Discussion</td>
<td>HRCT + Standardized clinical data + SLB</td>
<td>Clinicians, Radiologists, Pathologists</td>
<td>Diagnosis</td>
</tr>
<tr>
<td>5 - Group Discussion</td>
<td>HRCT + Standardized clinical data + SLB</td>
<td>Clinicians, Radiologists, Pathologists</td>
<td>Consensus Diagnosis</td>
</tr>
</tbody>
</table>

Flaherty et al. AJRCCM 2004.
How important is a MDE?

**Idiopathic Interstitial Pneumonia**
What Is the Effect of a Multidisciplinary Approach to Diagnosis?


Division of Pulmonary and Critical Care Medicine and Department of Radiology, University of Michigan Health System, and Department of Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan; University of California, San Francisco, San Francisco, California; University of Washington, Seattle, Washington; Mayo Clinic, Scottsdale, Arizona; and Armed Forces Institute of Pathology, Washington, DC

**TABLE 3. INTEROBSERVER AGREEMENT AT EACH DIAGNOSTIC STEP**

<table>
<thead>
<tr>
<th>Step</th>
<th>Clinicians [κ (95% CI)]</th>
<th>Radiologists [κ (95% CI)]</th>
<th>Clinicians–Radiologists [κ (95% CI)]</th>
<th>All Observers [κ (95% CI)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.41 (0.29, 0.52)</td>
<td>0.72 (0.57, 0.86)</td>
<td>0.39 (0.29, 0.49)</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>0.51 (0.37, 0.64)</td>
<td>0.80 (0.67, 0.93)</td>
<td>0.44 (0.34, 0.54)</td>
<td>NA</td>
</tr>
<tr>
<td>3</td>
<td>0.67 (0.54, 0.79)</td>
<td>0.78 (0.65, 0.91)</td>
<td>0.55 (0.44, 0.66)</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>0.75 (0.64, 0.86)</td>
<td>0.84 (0.72, 0.96)</td>
<td>0.78 (0.70, 0.86)</td>
<td>0.79 (0.71, 0.86)</td>
</tr>
<tr>
<td>5</td>
<td><strong>0.86 (0.76, 0.95)</strong></td>
<td><strong>0.90 (0.80, 0.99)</strong></td>
<td><strong>0.88 (0.81, 0.96)</strong></td>
<td><strong>0.88 (0.81, 0.94)</strong></td>
</tr>
</tbody>
</table>

**Kappa Score**
- 0.8-1.0 – Excellent
- 0.6-0.8 – Good
- 0.4-0.6 – Moderate
- 0.2-0.4 – Fair
- 0-0.2 - Poor

*Definition of abbreviations: CI = confidence interval for corresponding statistic; NA = not applicable.*
ILD General Management Considerations

• Standardized Evaluation
• Multi-disciplinary discussion
• Co-morbidity assessment and treatment
• Pulmonary Rehab referral
• Assessment for supplemental oxygen needs
• Therapeutics
• Clinical Trials

Consider ILD center referral for all patients with ILD
Delayed Access and Survival in Idiopathic Pulmonary Fibrosis
A Cohort Study

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Figure 2. Survival from the time of evaluation at a tertiary care center adjusted for age and FVC across quartiles of delay. Entry time into the cohort began at study enrollment.
References


