Diffuse Interstitial Lung Diseases: Is There Really Anything New?

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**Background**

- Re-classification of idiopathic interstitial pneumonias (2002); change in concept of a *single* diagnostic gold-standard
- Classification update (2013) - likely to fine-tune...
- Advances in understanding of ILDs in many (apparently disparate) fields

**Diffuse Interstitial Lung Disease**

*So What *Is* New...?*

- Classification update
- Changes in diagnostic criteria/certainty
  - “New” guidelines for diagnosis of UIP / IPF
  - Atypical features & clinical predictors of IPF
  - UIP vs NSIP
  - UIP vs NSIP vs HP
- Natural history / acute exacerbation in IPF
- Genetic linkages, short telomeres & ageing lung
- New entities...

**Idiopathic Interstitial Pneumonias Classification Update (2013)**


**Diffuse Interstitial Lung Disease**

*The State of Play...*

DILD of known cause
- Drugs, collagen vascular disease

Idiopathic Interstitial Pneumonias
- DIP / RB-ILD
- NSIP
- LIP

Granulomatous DILD
- Sarcoidosis

“Others”
- Langerhans’ cell histiocytosis, LAM
Idiopathic Interstitial Pneumonias

Classification Update (2013)

- Cryptogenic fibrosing alveolitis = IPF
- Idiopathic NSIP (no longer ‘provisional’)
- Distinction between
  - Major, Rare and Unclassifiable IIPs
  - Chronic vs SR-ILDs vs acute/subacute
- Clinical (biological) behaviour patterns

Multidisciplinary evaluation


Idiopathic Interstitial Pneumonias

Categorisation of IIPs

MAJOR IIPs
- IPF
- Idiopathic NSIP
- RB-ILD
- DIP
- Cryptogenic organizing pneumonia
- AIP

Chronic
Smoking-related
Acute/subacute


Idiopathic Interstitial Pneumonias

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Idiopathic Interstitial Pneumonias

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Idiopathic Interstitial Pneumonias

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- Idiopathic NSIP
- RB-ILD
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Chronic
Smoking-related
Acute/subacute

Idiopathic Interstitial Pneumonias
Categorisation of IIPs

RARE IIPs
Idiopathic LIP
Idiopathic Pleuroparenchymal Fibroelastosis

UNCLASSIFIABLE
Inadequate C-R-P data OR Major C-R-P discordance OR
Inadequate ATS / ERS recognition, characterisation OR
Complex HRCT/pathology patterns


Usual Interstitial Pneumonia/IPF
Typical HRCT Features

Possible UIP Pattern
- Subpleural, basal
- Reticular pattern
- Absence of features inconsistent with UIP pattern

Inconsistent with UIP
- Upper/mid-zone
- Peribronchovascular
- GGO > reticular
- Micronodules ++
- Multiple cysts
- Diffuse mosaicism/air-trapping (>3 lobes)
- Consolidation

Usual Interstitial Pneumonia/IPF
Typical HRCT Features

Usual Interstitial Pneumonia
Atypical HRCT Features

98 patients with biopsy-proven UIP (n=73) and NSIP (n=23)
HRCT evaluation:
Definite/Probable UIP; Definite/Probable NSIP; Indeterminate

<table>
<thead>
<tr>
<th>Histological Diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite UIP</td>
<td>16</td>
</tr>
<tr>
<td>Probable UIP</td>
<td>11</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>25</td>
</tr>
<tr>
<td>Probable NSIP</td>
<td>17</td>
</tr>
<tr>
<td>Definite NSIP</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
</tr>
</tbody>
</table>


Usual Interstitial Pneumonia/IPF
Clinical – Radiological (HRCT) Predictors

- Retrospective study
- 135 patients (UIP/IPF=97; other IIPs=38)
- HRCT, PFTs, 6MWT (within 6/12 of biopsy)
- Clinical-radiological predictors of IPF

Idiopathic Pulmonary Fibrosis
Non-diagnostic HRCT Findings

- 55 biopsy-proven IPF (“Core Group”)
- Two other cohorts
  Clinical/HRCT IPF (n=20)
  "Mixed" (n=48: NSIP, sarcoid, chronic HP, DIP, Hx, OP...)
- 3 thoracic radiologists

- List of differential diagnoses (no limits)
- Likelihood:
  0: condition not included in DDx; 1: 5-25% (unlikely); 2: 30-65% (intermediate); 3: 70-95% (high) and 4: 100% (definite)

Usual Interstitial Pneumonia/IPF
Clinical – Radiological Predictors

<table>
<thead>
<tr>
<th>Score</th>
<th>Alveolar (lobar)</th>
<th>Interstitial (lobar)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>GGO &lt;5%</td>
<td>Septal thick, no HC</td>
</tr>
<tr>
<td>2</td>
<td>GGO &lt;25%</td>
<td>HC &lt;25%</td>
</tr>
<tr>
<td>3</td>
<td>GGO 25-49%</td>
<td>HC 25-49%</td>
</tr>
<tr>
<td>4</td>
<td>GGO 50-75%</td>
<td>HC 50-75%</td>
</tr>
<tr>
<td>5</td>
<td>GGO &gt;75%</td>
<td>HC &gt;75%</td>
</tr>
</tbody>
</table>

Fell CD et al. Clinical predictors of a diagnosis of idiopathic pulmonary fibrosis Am J Respir Crit Care Med 2010;181:832-837

Usual Interstitial Pneumonia/IPF
Clinical – Radiological Predictors

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>PPV</th>
<th>Specificity</th>
<th>Sensitivity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>95</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>80</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

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Usual Interstitial Pneumonia/IPF
Clinical – Radiological Predictors

IPF – NSIP
Linkages


UIP & NSIP
Linkages

(UIP & NSIP)

Linkages


HRCT

Diagnostic Confidence

Diffuse Interstitial Lung Diseases
Changes in Diagnostic Confidence

• 118 consecutive patients with biopsy-proven DILD
• Three thoracic radiologists
• Up to 3 diagnoses (in order of likelihood); level of confidence for 1st choice

<table>
<thead>
<tr>
<th>Diagnostic Modality</th>
<th>High Confidence (%)</th>
<th>Correct (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHEST RADIOGRAPHY</td>
<td>23</td>
<td>77</td>
</tr>
<tr>
<td>COMPUTED TOMOGRAPHY</td>
<td>49</td>
<td>93</td>
</tr>
</tbody>
</table>


Copmtes: OPOLE CFMCE OPE

CT was of limited value in the diagnosis of extrinsic allergic alveolitis. This is at least in part due to the paucity of data in the literature. The CT appearance has been described in only a few patients (9), and the CT findings have not been correlated with pathologic specimens or with the clinical stage of disease. Whereas

Usual interstitial pneumonia 89%
• Silicosis 93%
• Lymphangitis carcinomatosis 85%
• Sarcoidosis 77%


Lynch DA. Can CT distinguish hypersensitivity pneumonitis from idiopathic pulmonary fibrosis. AJR 1995;165:807-811

Can CT Distinguish
### Diffuse Interstitial Lung Diseases

**Changes in Diagnostic Confidence**

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Match (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic HP</td>
<td>78 (90/120)</td>
<td>70 (80/120)</td>
<td>79 (95/120)</td>
<td>85 (110/120)</td>
</tr>
<tr>
<td>Confirmed diagnosis</td>
<td>63 (65/100)</td>
<td>55 (55/100)</td>
<td>46 (45/100)</td>
<td>85 (115/120)</td>
</tr>
<tr>
<td>Probable diagnosis</td>
<td>17 (10/60)</td>
<td>11 (10/60)</td>
<td>84 (64/100)</td>
<td>30 (95/120)</td>
</tr>
<tr>
<td>IPF</td>
<td>57 (36/80)</td>
<td>90 (50/50)</td>
<td>90 (36/100)</td>
<td>70 (60/120)</td>
</tr>
</tbody>
</table>


### Idiopathic Pulmonary Fibrosis

**Natural History / Acute Exacerbations**

August 2007

December 2010


**PROPOSED DIAGNOSTIC CRITERIA**

- Established/concurrent diagnosis of IPF
- Worsening breathlessness (<30 days)
- HRCT: New GGO and/or consolidation
- No infection (endotracheal aspirate/BAL)
- Exclusion of alternative causes
Pulmonary Fibrosis
Genetics and the Ageing Lung...

- Genetic predisposition to lung fibrosis?
- Family history in up to 20% of IPF patients
- Mutations in genes coding for telomerase (hTERT and hTR) of increasing interest

Genetics and the Ageing Lung...

Telomere Shortening in Familial and Sporadic Pulmonary Fibrosis


Copley SJ et al. Lung morphology in the elderly: comparative CT study of subjects over 75 years old versus those under 55 years old. Radiology 2009;251:566-573


Diffuse Interstitial Lung Diseases
What's Happened in the Last 5 Years?

- Diagnosis / Follow-up
  - More precise definitions - IPF/UIP
  - Greater experience - UIP vs NSIP vs chronic HP
  - Recognition of overlapping and evolving forms - NSIP → UIP
  - Variable prognosis of IPF - rapid vs slow progress or acute deterioration

- Importance of age and ageing
  - Predictive value of age in UIP
  - “Normal” ageing
  - Links with genetics – short telomeres

- New entities
  - IPFFE