Bronchiectasis - COPD Overlap Syndrome
BCOS - it matters

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Aims

• Highlight why BCOS occurs
• Define why the diagnosis BCOS should be sought
  – & Refute the counter argument
  – case examples
• Some suggestions on what is needed in terms of research & management of these patients
Why must COPD and Bronchiectasis overlap?

- COPD is a common neutrophilic lung disease affecting approximately 5-10% of the population. It is characterised by functional changes (airflow obstruction).
- Bronchiectasis is a rarer neutrophilic lung disease characterised by structural changes in airway calibre (dilatation) affecting 0.1-0.5% of population.
Do we have reliable tests to distinguish COPD and Bronchiectasis?

• Yes;
  – In the absence of bronchial dilatation that is permanent then bronchiectasis is excluded

• No;
  – We don’t robust scoring that is reproducible with limited observer variability on CT
  – Bronchial wall thickening / modest dilatation / definite bronchiectasis

Loebinger et al ERJ 2009
McDonnell et al Resp Med 2012
Models to explain BCOS

**Co-incidence**
Two events independent of each other happening in the same patient

**Causality**
One disease process in % of susceptible individuals leads to the second condition
Mechanistically could COPD lead to bronchiectasis?

- Pathogenesis & Aetiology of bronchiectasis without smoking:
  - Neutrophilic lung inflammation
  - Post infectious bronchiectasis
  - Reflux/ micro aspiration
  - Auto-immunity
  - Impaired immunity
  - Impaired mucociliary clearance
  - Neutrophil elastase, TNF and IL-8
  - Matrix metalloproteinases (MMP)
Mechanistically could COPD lead to bronchiectasis?

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Demonstrated as a component of COPD

-√
-√
-√
-√
-√
Can we reliably define bronchiectasis as being caused by COPD?

• NO:

• Prevalence of bronchiectasis is higher in aged populations
  – Smoking was more prevalent 40 yrs ago

• Presence of airflow obstruction, recurrent infective exacerbations and bronchial wall dilatation could be independent of the smoking history...
How common is BCOS?

COPD cohorts

• O’Brien Thorax 2000 UK 29% (n= 110- primary care pts)
• ECLIPSE cohort EU,US <5% (n=2164)
• Stewart et al COPD gene ATS 2012 20% (n=3758)
• Patel et al AJRCCM UK 50% (n=54)
• Baker et al J. COPD UK 2014 69% (n=496)
• Baker et al Abstract ATS 2011 19% (n=882)

Reported in Bronchiectasis series:

• Pasteur et al AJRCCM 2001 0%
• Anwar et al Resp Med 20%
Is there a typical CT appearance that helps us define BCOS?

• Many Bronchiectasis doctors quote “mild basal cylindrical bronchiectasis”-

• Patel et al AJRCCM 2004
  – Twenty-seven of 54 patients (50%) had bronchiectasis on HRCT, most frequently in the lower lobes (18 of 54, 33.3%).
Bronchiectasis in COPD

- S. London, UK: 406 patients (71 ± 11 years, 56% male, FEV1 52 ± 23% predicted)

- 278 (69%) patients had bronchiectasis:
  - minor, 112 (40%);
  - mild, 81 (29%);
  - moderate, 62 (22%);
  - severe 23 (8%).

Baker et al COPD: Journal of Chronic Obstructive Pulmonary Disease Dec 2014
Gatheral, Baker et al COPD: J COPD 2014,
So BCOS exists - but does it matter?

- Mortality: Belgian Cohort of BR; significant numbers with COPD
  - 5yrs f/up: Overall mortality was 20% but 50% mortality in BCOS (HR = 2.12; p = 0.038)

- Patel et al BCOS vs COPD
  - higher levels of airway inflammatory cytokines,
  - lower airway bacterial colonization,
  - higher sputum interleukin-8 levels
  - longer symptom recovery time at exacerbation

Goeminne Respir Med. 2014
Patel AJRCCM 2004
Does Bronchiectasis matter in COPD?

Prognostic Value of Bronchiectasis in Patients with Moderate-to-Severe Chronic Obstructive Pulmonary Disease

Miguel-Angel Martínez-García, María Jose Selma Ferrer, Anna Roma Dalfo, and Montserrat Bertomeu Valdecillos

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Am J Respir Crit Care Med. 2013 Apr 15;187(8):823-31
Does Bronchiectasis matter in COPD?

• B-COS independently determined
  – sputum isolation of Pseudomonas aeruginosa (Odds ratio (OR) 1.39 (95% CI 1.07 to 1.80), p = 0.013)
  – atypical mycobacteria (OR 2.44 (95% CI 1.04 to 5.69), p = 0.04),
  – annual respiratory admissions (p = 0.044) and inpatient days (p < 0.001),
  – did not predict survival (p = 0.256).
Predictors of Pseudomonas in COPD...

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchiectasis score (&gt;5)</td>
<td>9.8</td>
<td>1.7 - 54.8</td>
<td>0.009</td>
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<tr>
<td>Antibiotic prescriptions/year</td>
<td>1.7</td>
<td>1.1 – 2.5</td>
<td>0.008</td>
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<tr>
<td>Days of hospital stay</td>
<td>1</td>
<td>0.9 - 1</td>
<td>0.3</td>
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<tr>
<td>Corticosteroid courses/year</td>
<td>0.7</td>
<td>0.5 – 1.2</td>
<td>0.2</td>
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</tbody>
</table>

Do BCOS patients harbour the same Ps aer isolates?
Standards of care... should we look for BCOS in COPD?

• In bronchiectasis
  – Physiotherapy training (ACBT) is recommended
  – Nebulised antibiotics eg gentamicin
  – ?Lower threshold for long term macrolide therapy than COPD

• BCOS diagnosis may also prompt;
  – Aetiological testing as per BTS guidelines
  – Screening for Non Tuberculous mycobacteria (NTM)
COPD Treatments not to be used in BCOS

- Inhaled steroids (?)
- Endobronchial valves and Endobronchial coils
- Single lung transplant (but bilateral lung transplant can be used)
Case 1 B-COS?

- 68 yr old smoker
- 6th admission in 12 months
- Sputum volume 30 mls / day or more
Case 1 B-COS?
Case 1

- Careful history as child recurrent LRTI
- Mounier Kuhn syndrome PLUS emphysema
- Bronchiectasis and then COPD..?
Case 2: COPD 2012

Male

COPD 35 Pk yr history

Recurrent exacerbations

HRCT by me?

Bronchiectasis..

2012 “no bronchiectasis seen”..
Case 2: 3 yrs later- BCOS 2015

Male
COPD 35 Pk yr history
Further exacerbations
HRCT by me?
Bronchiectasis..
Symptoms worse than 2102
“Bilateral multilobar bronchiectasis”..
Case 3: ? COPD associated bronchiectasis

Female
40 pack years
Usually culture negative
FEV1
Case 4: “COPD” - ? BCOS

Prev LVRS surgery for advanced Emphysema

Hx of recurrent AE-COPD
Baseline tests as per BTS broncheuictasis guidance

• Hypogammaglobulinaemia; Immunology review Late diagnosis of CVID

• Now on long term Ivlg

• Likely CVID and COPD mixed
Case 5: BCOS

- 2011
- 8 Exacerbations per year-
  - Referred to COPD clinic
  - FEV1 25% pred
  - Gentamicin nebulised therapy and physio started after BCOS diagnosed

- 2015 4
- exacerbations per yr and no hospitalisations
  - FEV1 30% predicted....
What we don’t know...

• What predicts BCOS in COPD (Pseudomonas in sputum)
• Does treating BCOS aggressively reduce admissions or mortality?
  – Is there a genetic locus predicting BCOS (eg MMP1, etc etc)
• Do anti-inflammatory therapies for COPD help or worsen BCOS?
  – ICS, PDE4 inhibitors roles all unclear
Suggested references

## GOLD II  

<table>
<thead>
<tr>
<th>Females (n = 380)</th>
<th>Males (n = 574)</th>
<th>p value</th>
<th>Females (n = 293)</th>
<th>Males (n = 618)</th>
<th>p value</th>
<th>Females (n = 77)</th>
<th>Males (n = 219)</th>
<th>p value</th>
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<tbody>
<tr>
<td><strong>Comparing</strong></td>
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<td><strong>Clinical Data</strong></td>
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<tr>
<td>Age (years)</td>
<td>63.0 ± 7.1</td>
<td>63.8 ± 7.3</td>
<td>0.043</td>
<td>62.6 ± 6.8</td>
<td>64.2 ± 7.0</td>
<td>&lt; 0.001</td>
<td>60.7 ± 6.8</td>
<td>63.0 ± 7.0</td>
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<tr>
<td>Number of exacerbations&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.8 ± 1.2</td>
<td>0.5 ± 0.9</td>
<td>&lt; 0.001</td>
<td>1.2 ± 1.4</td>
<td>0.9 ± 1.3</td>
<td>0.005</td>
<td>1.5 ± 1.6</td>
<td>1.1 ± 1.4</td>
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<td><strong>Imaging</strong></td>
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<td>Emphysema (%)</td>
<td>11.2 ± 9.5</td>
<td>12.7 ± 9.5</td>
<td>0.002</td>
<td>20.1 ± 11.7</td>
<td>20.0 ± 11.5</td>
<td>0.876</td>
<td>27.1 ± 13.7</td>
<td>28.6 ± 12.1</td>
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<tr>
<td>Bronchiectasis (%)</td>
<td>&lt; 1</td>
<td>2</td>
<td>0.057</td>
<td>3</td>
<td>6</td>
<td>0.044</td>
<td>9</td>
<td>7</td>
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