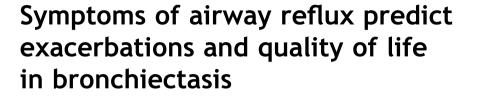


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KEYWORDS	Summary
Bronchiectasis;	Aim: We have explored the association of the upper airway symptoms related to cough with
Cough; Reflux;	exacerbation frequency, sputum microbiology and inflammatory markers in patients with non cystic fibrosis bronchiectasis.
Severity;	Methods: Patients with bronchiectasis completed the Hull Airway Reflux Questionnaire
Exacerbations	(HARQ). A score of >13 was taken to indicate the presence of reflux. Patients were followed-up with longitudinal spirometry, sputum culture and Leicester cough questionnaire (LCQ). Myeloperoxidase (MPO), free neutrophil elastase (NE) activity, Interleukin (IL)-8 and Tumour Necrosis Factor (TNF)- α was measured from spontaneous sputum samples. <i>Results:</i> 163 completed the study. 59.5% were female. Mean age was 65.7 years. 73.6% reported airway reflux using HARQ.
	Patients with airway reflux had more severe cough symptoms as assessed by the LCQ [15.2 (3.5) vs. 19.4 (1.9)], $p < 0.001$. Sputum levels of MPO, NE, IL-8 and TNF- α were all significantly higher in the reflux positive group ($p < 0.05$ for all comparisons).
	In a multivariable logistic regression, airway reflux was independently associated with cough severity (-3.27, standard error 0.81, $p = 0.0002$). Airway reflux, age, FEV ₁ % predicted and colonization with <i>Pseudomonas aeruginosa</i> were independently associated with an increased risk of \geq 3 bronchiectasis exacerbations in one year.
	<i>Conclusion:</i> The symptoms of airway reflux independently predict severity and exacerbation frequency in non cystic fibrosis bronchiectasis.
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Introduction

First described by Laennec in 1819, bronchiectasis is a disease of both children and adults characterized by inflamed and dilated airways. Bronchiectasis remains a chronic debilitating condition with most patients suffering daily symptoms of cough and sputum and a progressive course punctuated with exacerbations. It has been suggested that recurrent aspiration of gastric contents triggering tracheobronchial inflammation is a potential aetiological factor in bronchiectasis.^{1,2} In a study in 1999, with 100 bronchiectasis patients and 94 controls, it was concluded that in bronchiectasis, patients who tested positive for the Helicobacter pylori (HP) and suffered from acid reflux had lower percent predicted FEV₁ and FVC compared to healthy controls, suggesting that HP may have a role in the pathogenesis of bronchiectasis.³ A high seroprevalence (76%) of HP in patients with bronchiectasis has been detected⁴ and it has been proposed that aspiration of HP exotoxins may contribute to airway inflammation.⁴

Chronic cough is arbitrarily defined as a cough lasting for more than 8 weeks. Although conventionally regarded as being caused by three main aetiologies, gastroesophageal reflux, asthma and postnasal drip, chronic cough is increasingly considered a single entity, the Cough Hypersensitivity Syndrome.⁵ It has been demonstrated that in patients with chronic cough and peptic gastroesophageal reflux aspiration of both acid and weakly acidic refluxate is associated with symptoms.^{6–8} Similarly other respiratory disease symptom association studies have shown a correlation between events and episodes of non acid or mildly acid reflux.⁹ The extra oesophageal symptoms of reflux into the airways (chronic cough, hoarseness, globus and chronic laryngitis) are thought to be due to damage of the respiratory epithelium and appear unrelated to pH of the refluxate.⁷ Indeed cough due to reflux frequently presents without heartburn and has been given the misnomer of silent reflux. Here the term airway reflux is used to describe this extra oesophageal reflux of diverse composition.¹⁰

That classic gastroesophageal reflux disease is a comorbidity in patients with bronchiectasis is suggested by the reported high prevalence compared to the general population (range of 10-20% in the general population).¹¹ Gastroesophageal reflux is associated with a decreased health-related quality of life (HRQoL) in individuals without lung disease who have symptoms of heartburn and acid regurgitation,¹² but the degree of compromise to healthrelated quality of life in patients with bronchiectasis has not been studied.

The aim of our study was to assess the contribution of symptoms of airways reflux to cough severity and exacerbation frequency in patients with non cystic fibrosis bronchiectasis.

Methods

Study design

Patients were recruited from the South East of Scotland Bronchiectasis Clinic, over 1 year from March 2010 to March 2011, into a prospective study. Patients gave informed consent and the Local Research Ethics committee approved the study (approved by Scotland REC A; approval No. 10/S1103/3).

Patient selection

Patients with clinically significant bronchiectasis confirmed by high resolution CT (HRCT) scan who were clinically stable with no exacerbation or antibiotic therapy in the previous four weeks were eligible for entry in to the study. Patients taking proton pump inhibitors or H_2 receptor antagonists at the time of the study were excluded.

Hull airways reflux questionnaire

Patients were asked to complete the Hull Airways Reflux Questionnaire (HARQ), a self administered, validated instrument, which sensitively and reproducibility assesses the symptom complex of airway reflux.¹³ There are 14 questions each rated between 0 and 5, where 0 equals no problem and 5 equals frequent/severe problem. A score of 13/70 has been shown to be the upper limit in a normal population and a score of >13 was taken to indicate the presence of airways reflux. (See Appendix 1 in online supplement).

Cough severity

Cough severity was assessed using the Leicester Cough Questionnaire (LCQ).¹⁴ The LCQ has 19 items divided into 3 domains: physical (8 items), psychological (7 items) and social (4 items). The total severity score ranges from 3 to 21, where a lower score indicates a greater impairment of health status due to cough. We have previously validated the Leicester Cough Questionnaire for use in non cystic fibrosis bronchiectasis.¹⁵

Exacerbations

The current BTS guidelines for non cystic fibrosis bronchiectasis define an exacerbation as presentation with an acute deterioration (usually over several days) with worsening local symptoms (cough, increased sputum volume or change of viscosity, increased sputum purulence with or without increasing wheeze, breathlessness, haemoptysis) and/or systemic upset.¹⁶ The frequency of outpatient antibiotic courses in the 1 year following study entry was determined by patient interview and confirmed by examination of hospital prescription and general practitioner records.

Sputum microbiology

Sputum was collected into a sterile container over a four hour period from wakening. 1 ml of the sample was processed for routine qualitative microbiology. The remaining sample was ultracentrifuged at 23 200 rpm for 90 min at 4 °C. The sol phase was removed and immediately frozen at -70 °C. Download English Version:

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