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Non cystic fibrosis bronchiectasis: A longitudinal retrospective observational cohort study of Pseudomonas persistence and resistance

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Bronchiectasis;
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Summary
Background: The hallmark of non-cystic fibrosis bronchiectasis is recurrent bronchial infection, yet there are significant gaps in our understanding of pathogen persistence, resistance and exacerbation frequencies. *Pseudomonas aeruginosa* is a key pathogen thought to be a marker of disease severity and progression, yet little is known if the infection risk is seen in those with milder disease or if there is any potential for eradication. These data are important in determining risk stratification and follow up.
Methods and patient cohort: A retrospective review of consecutive adult patients attending a specialist UK bronchiectasis clinic over a two-year recruitment period between July 2007 and June 2009 was performed. Analysis of our primary outcome, longitudinal microbiological status, was recorded based on routine clinical follow-up through to data capture point or date of death. Patients were stratified by lung function and infecting organism.
Results: 155 patients (mean (SD) age 62.2 (12.4) years; 60.1% female) were identified from clinic records with microbiological data for a median (IQR) follow up duration of 46 (35–62) months. Baseline mean FEV_1% predicted was 60.6% (24.8) with mean exacerbation frequency

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of 4.42/year; 73.6% reported 3 or more exacerbations/year. *Haemophilus influenzae* was isolated in 90 (58.1%) patients and *P. aeruginosa* in 78 (50.3%) patients with persistent infection in 51 (56.7%) *H. influenzae* and 47 (60.3%) *P. aeruginosa*, respectively. Of the *P. aeruginosa* colonised patients, 16 (34%) became culture negative on follow-up with a mean of 5.2 negative sputum cultures/patient. *P. aeruginosa* was isolated from 5 out of 39 patients (12.8%) with minimal airflow limitation as compared to 18 out of 38 patients (47.4%) with severe airflow limitation. Although hospital admissions were significantly higher in the *P. aeruginosa* infected group (1.3 vs. 0.7 admissions per annum, $p = 0.035$), overall exacerbation rates were the same (4.6 vs. 4.3, $p = 0.58$). Independent predictors of *P. aeruginosa* colonisation were low FEV_1% predicted (OR 2.46; 95% CI 1.27—4.77) and polymicrobial colonisation (OR 4.07; 95% CI 1.56—10.58). 17 (11%) patients were infected with multi-resistant strains; however, none were pan-resistant.

Conclusions: P. aeruginosa is associated with greater persistent infection rates and more hospital admissions than *H. influenzae*. Exacerbation rates, however, were similar; therefore *H. influenzae* causes significant out-patient morbidity. *P. aeruginosa* infection occurs across all strata of lung function impairment but is infrequently multi-resistant in bronchiectasis. Careful microbiology follow up is required even in those with well-preserved lung function.

Introduction

Non-cystic fibrosis (CF) bronchiectasis is characterised by irreversibly damaged and dilated bronchi with impaired mucociliary clearance that leads to recurrent bacterial infections. Frequent exacerbations are a significant cause of morbidity and mortality and may contribute to substantial socioeconomic costs manifest by increased hospitalisations and healthcare utilisation [1,2]. Recent European evidence suggests a steady increase in bronchiectasis-associated hospitalisations and subsequent mortality, particularly in older patients, females and those with associated chronic obstructive pulmonary disease (COPD) [3]. UK studies have demonstrated a 29% death rate in bronchiectasis patients over 13 years, twice that predicted in age matched patients [4].

The British Thoracic Society (BTS) bronchiectasis guidelines emphasise microbiology assessment to guide antimicrobial therapy [5]. Prior studies demonstrate a predominance of non-typeable *Haemophilus influenzae* and *Pseudomonas aeruginosa*, as two significant pathogens in adult bronchiectasis [6]. *P. aeruginosa* persistence has been shown to be associated with poorer lung function, more extensive disease and poorer quality of life [7,8]. It has traditionally been suggested that only patients with severely impaired lung function are considered at risk for *P. aeruginosa* infections [9]. Few studies have assessed the association between persistently isolated pathogens and exacerbations or the potential impact of *P. aeruginosa* on lung function impairment [7]. This is important as there is an increasing need to define which patients with bronchiectasis need specialist follow up and which can be discharged from specialist clinics for primary care follow up only.

We therefore assessed the longitudinal microbiological profile in adult patients with non-cystic fibrosis bronchiectasis in a UK population and investigated associations between markers of functional impairment, exacerbation frequency and microbiological status.

Methods

Study design

A retrospective observational cohort analysis of consecutive adult patients attending a specialist UK bronchiectasis clinic between July 2007 and June 2009 in the North East of England was performed. Rigorous aetiological screening investigations were undertaken to establish disease phenotype according to a standardised protocol [10]. The diagnosis of bronchiectasis was established in all cases by high-resolution computed tomography (HRCT). Retrospective data collection and analysis of our primary outcome, longitudinal microbiological status, was recorded based on routine clinical follow-up from initial recruitment visit through to data capture point (October 2013) or date of death. Data pertaining to secondary outcomes, exacerbation frequency and hospital admission rates, was collected over a pre-defined one year follow-up period (July 2010—June 2011) by means of telephone or outpatient interview assessment. Patients had their individual case notes reviewed for collection of demographic details, aetiological investigations, smoking history, Medical Research Council (MRC) dyspnoea score, baseline and follow up lung function, nebulised antibiotic treatment and chronic macrolide treatment.

Patients and setting

The inclusion criterion was a clinico-radiological diagnosis of non-CF bronchiectasis on HRCT. Consecutive patients attending clinic during the recruitment period were included to ensure a fully representative cohort

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