Patterns of Disease in Patients with Middle-Lobe Predominant Bronchiectasis

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Abstract

Background: Middle-lobe predominant bronchiectasis affecting the right middle-lobe and/or lingula (RMLP) is classically described in asthenic, elderly females with skeletal abnormalities or associated nontuberculous mycobacterial (NTM) infection. **Objectives:** We aimed to evaluate the frequency and clinical characteristics of patients with an RMLP phenotype in a cohort of newly diagnosed bronchiectasis patients and determine associations with disease severity. **Methods:** A retrospective observational cross-sectional cohort study of consecutive bronchiectasis patients in our institution was performed. Data were collected on baseline variables, microbiology status, lung function, and radiology according to the modified Bhalla score. Disease severity was assessed using bronchiectasis severity index (BSI) and FACED severity scores. **Results:** Of 81 patients (mean age [SD] 62.6 [12.4], females 55 [67.9%], BMI 26.9 [5.7%]), 20 (24.7%) had RMLP disease. These patients were significantly younger, female, and with lower BMIs than patients with the classical

bronchiectasis phenotype ($p = 0.03$, 0.01 , and $p < 0.01$, respectively). Fewer symptoms of cough and daily sputum ($p = 0.01$ and < 0.01), prior exacerbation frequency ($p = 0.03$), and higher baseline forced expiratory volume ($p = 0.04$) were noted. A higher incidence of NTM at diagnosis was demonstrated ($p = 0.01$). BSI and FACED severity scores in RMLP patients were significantly lower than their counterparts (both $p < 0.001$). **Conclusions:** The RMLP phenotype is associated with younger patients than classically described in the literature. An increased rate of NTM infection in this phenotype was noted, particularly in females, but much lower than previously described. Lung function and disease severity scores in this patient group are relatively normal, suggesting a milder phenotype in patients with this form of the disease.

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Introduction

Non-cystic fibrosis bronchiectasis is a chronic suppurative lung disease with multiple aetiologies. In the majority of publications, adult bronchiectasis is described as predominantly affecting the lower lobes, with upper-lobe

involvement suggesting cystic fibrosis in younger patients, post-tubercular disease, or allergic bronchopulmonary aspergillosis [1]. For respiratory physicians, predominant involvement of the right middle-lobe and/or lingula promotes a search for *Mycobacterium avium-intracellulare*, which if present, and if the patient is elderly, female, and demure, the much coveted diagnosis of Lady Windermere syndrome can be secured [2].

There is a paucity of published literature, however, describing the frequency of right middle-lobe and lingular predominant (RMLP) bronchiectasis, demographics of those affected, and its aetiology. Since the introduction of a dedicated screening protocol in our institution in 2009, we have been struck by the frequency of RMLP bronchiectasis, the younger age of those affected, and its apparent female predominance.

We estimated the prevalence of RMLP bronchiectasis on high-resolution computed tomography (HRCT) among a well-characterised cohort of bronchiectasis patients and compared clinical indices in these patients with non-RMLP disease.

Methods

Study Population

A retrospective observational cross-sectional cohort study of consecutive patients presenting to our institution with a history of repeated episodes of bronchial suppuration and a suspected diagnosis of bronchiectasis over an 18-month period (January 3, 2011–June 29, 2012) was performed. All suspected bronchiectasis patients in our institution undergo a dedicated diagnostic clinical workup including detailed history, clinical examination, spirometry, BMI, full blood count, serum immunoglobulins, serum IgE, *Aspergillus* IgE and precipitins, HRCT scanning, bronchoscopy, and bronchoalveolar lavage (BAL) for microbiological assessment including mycobacteria, with screening for cystic fibrosis or primary ciliary dyskinesia performed in select cases as previously described [3, 4].

Data were collected on baseline demographics including gender, age at diagnosis, BMI, smoking status, medical comorbidities (determined by the Charlson Comorbidity Index), aetiology of bronchiectasis, Medical Research Council Dyspnoea (MRC) score, number of exacerbations, and hospitalisations over the prior year, baseline microbiological status on BAL, baseline pulmonary function and baseline radiological involvement. Ethical approval was obtained from our local Research Ethics Committee. Individual patient consent was not required as this was a retrospective research study based on routine diagnostic investigations and bronchiectasis workup.

Diagnosis of Bronchiectasis

The diagnosis of bronchiectasis was defined as patients with daily mucopurulent sputum production plus dilated and thickened airways on HRCT [5]. Aetiology was defined according to

methodologies previously described; a diagnosis of idiopathic bronchiectasis was made if all aetiological screening tests were negative and no associations with other known diseases was found [3, 4].

CT images were acquired on a 64-slice multi-detector CT scanner (Somatom Sensation Cardiac 64; Siemens, Erlangen, Germany). Inspiratory spiral and expiratory sequential scans were performed at an initial collimation of 5 mm, and reconstructed at 1.0-mm thin slices at section intervals of 10 mm. Scanning parameters included a kVp of 120 (dose adjusted), 40 mAs (care dose), a rotation time of 0.5 s, and a pitch of 1.4. Intravenous contrast media was not administered, and scans were performed with patients positioned supine.

All scans were reported by radiologists with expertise in high-resolution cross-sectional imaging. Subsequent independent review for confirmation and scoring of disease severity according to the modified Bhalla score, as previously described in bronchiectasis, was performed by an expert thoracic radiologist [6]. The extent of bronchiectasis in each lobe was assessed with the lingula considered as a separate lobe. RMLP bronchiectasis was defined as localised bronchiectasis limited to the right middle and/or left lingula lobe only. Each lobe was assessed for severity of bronchial dilatation, bronchial wall thickness, the presence of mucus plugging in large and small airways, and decrease in parenchymal attenuation (online supplementary Table S1; see www.karger.com/doi/10.1159/000464252). The maximum score per lobe was 18. Total lung scores for each abnormality were defined as the mean score from all lobes. The proportion of cystic versus varicose or cylindrical bronchiectasis was also recorded along with the total number of lobes involved. A combined HRCT total score for all features across each lobe was subsequently derived from summing the individual scores.

Pulmonary Function Tests

PFTs were performed using a Sensormedics V-Max 22 device allowing calculation of forced expiratory volume (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio. Values were expressed as percentage predicted for age, sex, height, and ethnicity employing standard European Respiratory Society (ERS)/American Thoracic Society reference ranges [7]. Pulmonary function test were carried out by pulmonary physiologists trained according to the recommendations of the ERS [8].

Microbiology

BAL is routinely performed in the diagnostic workup of bronchiectasis in our institution with routine sputum culture suggested every 6 months on follow-up. Bacterial, mycobacterial, and fungal cultures via BAL were performed in 100% of our patients as part of their workup. All microbiology samples were processed in an Irish Clinical Pathology Accreditation (CPA) accredited laboratory to routine diagnostic standards using standard and select supplementary media, in accordance with British Thoracic Society guidelines on microbiological profiling in bronchiectasis [5].

Relationship between RMLP Phenotype and Disease Severity

To analyse the relationship between RMLP versus non-RMLP bronchiectasis and disease severity, statistical comparisons of known individual clinical markers of severity and 2 composite disease severity scoring systems for bronchiectasis – the Bronchiectasis Severity Index (BSI) and the FACED scoring system – were used [9, 10]. The BSI and FACED scores were modified (m-BSI

Fig. 1. Axial computed tomography images of the lower thorax in lung windows demonstrating right middle-lobe and/or lingular predominant bronchiectasis in patients with (a) idiopathic aetiology and (b) superimposed non-tuberculous mycobacterial infection, compared to more widespread bronchiectasis affecting all lung lobes in patients with (c) recurrent aspiration, and (d) chronic obstructive pulmonary disease.

and m-FACED) to exclude the number of lobes affected as the RMLP group, by definition, have limited anatomical disease. Therefore, the maximum obtainable scores for the m-BSI and m-FACED were 24 and 6, respectively, excluding 1 point in both scores for the number of lobes involved.

Statistical Analysis

Statistics were computed using SPSS® v21.0 for Windows platform and GraphPad Prism v5. Simple descriptive statistics including the mean and standard deviation were used for continuous parametric data, median and interquartile range for continuous nonparametric data, and frequencies and percentages for categorical data. Patients were divided into 2 groups defined as RMLP and non-RMLP disease. Subgroup analyses were performed using the χ^2 test or unpaired *t* test depending on data distribution. The χ^2 test was used for clinical characteristics including gender, cystic versus cylindrical disease, and microbial colonisation. Group mean spirometric values and age were normally distributed and compared using the unpaired *t* test. HRCT scores (total and by section) were

not normally distributed. Group means were compared by the Mann-Whitney U test. Stepwise binary logistic regression analysis was performed to identify the most parsimonious set of predictors associated with RMLP disease. A *p* value <0.05 was considered to be statistically significant.

The reporting of this observational study conforms to the recommendations of STROBE [11].

Results

Patient Demographics

A total of 81 patients (55 females, 68%) were found to have confirmed bronchiectasis on independent review of HRCT imaging, with a mean age (SD) of 62.6 (12.4) years, FEV₁% 85.7% (26.7) predicted, and FVC 105.7% (28.2) predicted. Of these, 20 (24.7%) were confirmed to have

Table 1. Baseline characteristics

Baseline data	Total (N = 81)	RMLP (n = 20)	Non-RMLP (n = 61)	p value
Age, years	62.6±12.4	57.4±10.5	64.3±12.4	0.03*
Females	55 (67.9)	18 (90.0)	37 (60.7)	0.01*
BMI	26.9±5.7	23.5±5.3	27.6±5.6	<0.01**
Smokers/ex-smokers	45 (55.6)	10 (50.0)	35 (77.8)	0.04*
Charlson Comorbidity Index ≥3	63 (77.7)	11 (55.0)	52 (85.2)	0.01*

Values are expressed as mean ± standard deviation or *n* (%). RMLP, right middle-lobe and lingular predominant bronchiectasis. * *p* < 0.05. ** *p* < 0.01.

Table 2. Clinical status of the patient groups

Clinical status	Total (N = 81)	RMLP (n = 20)	Non-RMLP (n = 61)	p value
Daily cough	68 (83.9)	13 (65.0)	55 (90.2)	0.01*
Daily sputum	49 (60.5)	7 (35.0)	42 (68.9)	<0.01**
Haemoptysis	4 (6.2)	0 (0)	4 (6.6)	0.567
Exacerbation in the previous year	2.36±1.16	1.85±0.62	2.42±0.73	0.03*
Exacerbation in the previous year ≥3	29 (35.8)	3 (15)	26 (32.1)	0.03*
MRC score ≥3	21 (25.9)	3 (15.0)	18 (29.5)	0.252

Values are expressed as mean ± standard deviation or *n* (%). RMLP, right middle-lobe and lingular predominant bronchiectasis; MRC, Medical Research Council Dyspnoea score. * *p* < 0.05. ** *p* < 0.01.

RMLP disease. HRCT images showing RLMP and non-RMLP bronchiectasis are shown in Figure 1. Baseline characteristics for total cohort and comparisons between RMLP and non-RMLP subgroups are shown in Table 1. Significant differences in terms of younger age, female predominance, lower BMI, fewer smokers, and lower comorbidity scores were noted in the RMLP group.

Clinical Status (n = 81)

Differences in clinical symptoms between the two subgroups are demonstrated in Table 2. RMLP patients were less likely to present with symptoms of chronic cough or daily sputum compared to patients with the classical bronchiectasis phenotype (*p* = 0.01 and <0.01 respectively) and recorded fewer exacerbations over the preceding 12 months (*p* = 0.03). No differences in haemoptysis presentation or baseline MRC status were noted.

Aetiology (n = 81)

Of the 81 patients in our cohort, the commonest cause was idiopathic bronchiectasis (28.3%), closely followed

by postinfectious bronchiectasis (27.2%) secondary to childhood infections, bacterial pneumonia, pulmonary tuberculosis, and nontuberculous mycobacterial (NTM) infection. Chronic obstructive pulmonary disease and asthma accounted for the next largest groups of patients at 16.0 and 8.6%, respectively. Aspiration, confirmed on barium studies, secondary to previous cerebrovascular events, oesophageal malignancy, myasthenia gravis and postcardiac arrest, accounted for 7.4% of the cases. In the RMLP group, a significantly higher proportion of patients with NTM were identified (*p* = 0.01) (Table 3). None of the patients in the RMLP group were found to have an underlying diagnosis of chronic obstructive pulmonary disease.

Pulmonary Function (n = 77)

Spirometry was unattainable in 4 patients in total (2 from each group). On comparing the remaining patients, FEV₁% predicted was significantly higher in the RMLP group (*p* = 0.04), suggesting milder obstructive disease or normal lung function in this patient group (Table 4).

Table 3. Aetiology of bronchiectasis in the study population and according to the study groups

Aetiology	Total (N = 81)	RMLP (n = 20)	Non-RMLP (n = 61)	p value
Idiopathic	23 (28.3)	9 (45.0)	14 (22.9)	0.08
Postinfectious	22 (27.2)	7 (35.0)	15 (24.6)	0.39
Childhood infection	3 (3.7)	0 (0)	3 (4.9)	0.57
Bacterial pneumonia	7 (8.6)	0 (0)	7 (11.5)	0.18
Pulmonary tuberculosis	9 (11.1)	4 (20.0)	5 (8.2)	0.26
NTM infection	3 (3.7)	3 (0)	0 (4.9)	0.01*
Asthma	7 (8.6)	3 (15.0)	4 (6.6)	0.36
COPD	13 (16.0)	0 (0)	13 (21.3)	0.03*
ABPA	3 (3.7)	0 (0)	3 (4.9)	0.57
Alpha-1-antitripsin deficiency	1 (1.2)	0 (0)	1 (1.6)	1.00
Immune deficiency	3 (3.7)	0 (0)	3 (4.9)	0.57
Aspiration	6 (7.4)	0 (0)	6 (9.8)	0.33
Primary ciliary dyskinesia	1 (1.2)	0 (0)	1 (1.6)	1.00
Connective tissue disease	2 (2.4)	0 (0)	2 (3.3)	1.00

Values are expressed as n (%). RMLP, right middle-lobe and lingular predominant bronchiectasis; NTM, nontuberculous mycobacterial; COPD, chronic obstructive pulmonary disease; ABPA, allergic bronchopulmonary aspergillosis. * p < 0.05.

Table 4. Pulmonary function

Pulmonary function	Total (N = 81)	RMLP (n = 18)	Non-RMLP (n = 59)	p value
FEV ₁ %	85.7 ± 26.7	99.7 ± 22.2	83.9 ± 26.9	0.04*
FVC%	105.7 ± 28.2	115.2 ± 23.4	102.7 ± 28.7	0.08
Ratio%	68.9 ± 11.3	72.4 ± 6.4	67.8 ± 12.2	0.11
DLCO%	80.6 ± 22.1 (n = 57)	84.6 ± 18.9 (n = 16)	79.1 ± 23.2 (n = 41)	0.34

Values are expressed as s, mean ± standard deviation. RMLP, right middle-lobe and lingular predominant bronchiectasis; FEV, forced expiratory volume; FVC, forced vital capacity; DLCO, carbon monoxide diffusing capacity. * p < 0.05.

Comparisons across the spectrum of lung function severity showed that patients with minimal airflow limitation were more likely to be in the RMLP group than those with severe airflow limitation ($p < 0.001$).

Radiological Disease (n = 81)

A higher proportion of patients in the non-RMLP group were noted to have cystic bronchiectasis on HRCT (RMLP 5.0%, non-RMLP 23.0%; $p = 0.10$), but this did not reach statistical significance. A breakdown of the modified Bhalla score per individual HRCT feature is demonstrated in Table 5. The extent of bronchiectasis and degree of bronchial wall thickening and dilatation were significantly different between the 2 groups (all $p <$

0.01), denoting less severe disease in the RMLP group. No differences in extent of parenchymal dilatation or mucus plugging of the small or large airways were noted.

Microbiology (n = 81)

BAL samples were culture positive in 41 (50.6%) patients (RMLP 45.0%, non-RMLP 52.4%), with multiple pathogens cultured in 7 (8.6%) of the total cohort. Three (15%) patients in the RMLP group cultured NTM (all females) with none in the non-RMLP group ($p = 0.01$) (Table 6). The most commonly identified organisms from BAL of the total cohort were *Haemophilus influenzae* 23.4%, methicillin-sensitive *Staphylococcus aureus* 12.3%, *Streptococcus pneumoniae* 8.2%, coliforms 6.2%, *Pseudo-*

Table 5. Radiological features

	Total (N = 81)	RMLP (n = 20)	Non-RMLP (n = 61)	p value
<i>HRCT parameters</i>				
Cystic, n (%)	15 (18.5)	1 (5.0)	14 (23.0)	0.10
Number of lobes involved	2.33±1.47	0.80±0.41	2.62±1.56	<0.001***
Total HRCT score	14.1±11.3	7.6±4.8	16.2±12.0	0.002**
<i>Modified Bhalla HRCT scores according to HRCT features (score out of 18 for all lobes)</i>				
Extent of bronchiectasis	5.1±3.8	2.7±1.7	5.9±4.0	<0.01**
Bronchial wall dilatation	4.3±3.4	2.5±1.8	4.8±3.7	<0.01**
Bronchial wall thickening	3.5±2.8	1.9±1.0	4.0±3.0	<0.01**
Extent of mucus plugging in small airways	0.3±0.7	0.2±0.4	0.3±0.7	0.36
Extent of mucus plugging in large airways	0.6±1.0	0.2±0.4	0.7±1.1	0.81
Extent of decreased attenuation	0.5±1.2	0.2±0.7	0.6±1.4	0.87

Values are expressed as mean ± standard deviation, unless otherwise indicated. HRCT, high-resolution computed tomography; RMLP, right middle-lobe and lingular predominant bronchiectasis. ** p < 0.01. *** p < 0.001.

Table 6. Microbiology on diagnostic bronchoalveolar lavage

Microbiology	Total (N = 81)	RMLP (n = 20)	Non-RMLP (n = 61)	p value
<i>Haemophilus influenzae</i>	19 (23.4)	6 (30.0)	13 (21.3)	0.54
MSSA	10 (12.3)	3 (15.0)	7 (11.5)	0.70
<i>Streptococcus pneumoniae</i>	7 (8.2)	0 (0)	7 (11.5)	0.19
<i>Escherichia coli</i>	5 (6.2)	0 (0)	5 (8.2)	0.33
<i>Pseudomonas aeruginosa</i>	4 (4.9)	0 (0)	4 (6.6)	0.57
MRSA	2 (2.5)	1 (5.0)	1 (1.6)	0.44
<i>Mycobacterium avium intracellulare</i>	3 (3.7)	3 (15.0)	0 (0)	0.01*
<i>Aspergillus fumigatus</i>	1 (1.2)	0 (0)	1 (1.6)	1.00
<i>Candida albicans</i>	1 (1.2)	0 (0)	1 (1.6)	1.00
<i>Acinobacter</i>	1 (1.2)	0 (0)	1 (1.6)	1.00
<i>Moraxella catarrhalis</i>	1 (1.2)	0 (0)	1 (1.6)	1.00
>1 pathogen cultured in BAL	7 (8.2)	0 (0)	7 (11.5)	0.19

Values are expressed as n (%). RMLP, right middle-lobe and lingular predominant bronchiectasis; MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; BAL, bronchoalveolar lavage. * p < 0.05.

monas aeruginosa 4.9%, methicillin-resistant *S. aureus* 2.5%, and 1 patient each with *Aspergillus fumigatus*, *Candida*, *Acinetobacter*, and *Moraxella catarrhalis*. There were no significant differences between the 2 groups in relation to any other microbiological organisms.

Disease Severity Scores

Increased disease severity scores were observed in the non-RMLP group compared with RMLP patients with

both the m-BSI (5.93 [1.65] vs. 3.85 [2.12], $p < 0.001$) and the m-FACED bronchiectasis severity scores (2.21 [1.52] vs. 1.64 [1.48], $p < 0.001$) (Fig. 2b). Subgroup analysis of RLMP patients with and without NTM was not possible due to small patient numbers.

Regression Analysis

Stepwise binary logistic regression analysis identified low BSI (OR 0.70, 95% CI 0.54–0.94; $p = 0.004$) to be sig-

Fig. 2. Non-cystic fibrosis bronchiectasis cohort with and without right middle-lobe and lingular predominant (RMLP) bronchiectasis as determined by an independent, blinded expert thoracic radiologist on high-resolution computed tomography (HRCT). **a** Individual markers of disease severity measured include: (i) forced expiratory volume in 1 s (FEV₁) percent predicted and (ii) radiological extent of bronchiectasis throughout all lobes according to the modified Bhalla scoring system. **b** Bronchiectasis severity scores include: (i) modified bronchiectasis severity index and (ii) modified FACED score. Box plots indicate the median and 25th–75th percentiles; whiskers indicate 5th–95th percentiles.

nificantly associated with RMLP disease. A trend towards a lower total HRCT score in the RMLP group was also noted but did not reach statistical significance (OR 0.92, 95% CI 0.83–1.01; $p = 0.073$).

Discussion

RMLP bronchiectasis has traditionally been associated with elderly, asthenic, female patients with NTM infection. To our knowledge, this is the first study to specifically explore the frequency, microbiological and severity characteristics of RMLP disease in a cohort of bronchiectasis patients. We found RMLP disease to be a relatively common anatomical pattern, affecting a quarter of our patients (25%). We also observed significant statistical associations between RMLP bronchiectasis and younger age, females, low BMI, reduced symptom profiles, superior baseline lung function, reduced extent and severity of radiological disease, NTM on microbiology, and reduced modified composite bronchiectasis severity scores. Identification of these patients may therefore aid treatment approaches in terms of ascertaining which patients have less severe disease and could potentially be followed up in a primary care or nurse-led setting.

The right middle lobe and lingula are relatively isolated anatomically with poor collateral ventilation, de-

creasing the possibility of reinflation once atelectasis occurs, and with a more angular relationship to the main bronchi potentially creating less effective conditions for drainage. These airways may therefore be more prone to injury [12]. It is interesting to note that the most commonly damaged lobes in patients with primary ciliary dyskinesia are also the right middle lobe and lingula [13]. The less severe clinical and radiological characteristics of RMLP bronchiectasis probably relates to the fact that whilst these airways are more easily damaged, the mechanism of disease is largely a structural phenomenon not shared by other airways, and the disease is therefore more likely to remain localised.

The female predominance in our patients suggests that women may have additional risk factors for RMLP disease, both anatomical and innate [14, 15]. The localised pulmonary restriction from breast tissue or pregnancy, just as patients with pectus excavatum, may be enough in some individuals to compromise the distal airway further and ignite the cycle of airway injury. Pericardial fat pads may also play an aetiological role in women more than men by compressing the medial aspects of the right middle lobe and lingula. Women may also have different cough characteristics to men and deliberately, as the fictional Lady Windermere, suppress cough and sputum expectoration [16]. In cystic fibrosis it has been shown that females acquire earlier microbial infections and often have a worse prognosis than their male counterparts, and

that oestrogen may have a causal role in the development of colonisation by mucoid *Pseudomonas aeruginosa* [17, 18].

NTM infection has long been associated with middle-lobe and lingular bronchiectasis [12]. Whilst NTM infection was more common in our RMLP patients, we cannot determine if NTM was causative or a super-added infection. However, since only 15% of the RMLP patients were BAL positive for NTM, this perhaps suggests that NTM infection may not be the cause of the majority of RMLP disease but, rather, may be a secondary event in already damaged airways. The overall frequency of NTM in our bronchiectasis population was only 4%, despite the routine use of bronchial washings, which are reported to be twice as sensitive as sputum for isolation of NTM [19], and is therefore far lower than that described with reported rates of 10 and 30% in the UK and US, respectively [20, 21]. In the UK study, no significant differences were found between NTM-positive and NTM-negative groups in terms of age, sex, spirometry, co-existent sputum bacteriology, or use of long-term antibiotics [21]. In the US study, the probability of NTM isolation was significantly higher in elderly female patients with bronchiectasis and those with a low BMI [20]. In this cohort, patients with RMLP were significantly younger than their counterparts; the mean age of RMLP NTM-positive patients was 52 years, which is much lower than that reported in the literature elsewhere.

Potential explanations for differences between populations may relate to geographical variations in both the prevalence and causative organisms of NTM infection or genetic predisposition [22]. NTM are also notoriously difficult to culture, especially in the presence of other colonising organisms, possibly accounting for a degree of variability [23]. There is mounting evidence to suggest that patients with NTM-related bronchiectasis have a distinct immunologic phenotype that results in an imbalance of cytokines leading to inability of the host to resist mycobacterial infection [24, 25]. Use of macrolides for acute exacerbations and long-term prophylaxis in bronchiectasis has been heavily associated with the development of NTM infection, particularly in the USA [26]. In the CF community, conflicting data have been reported in terms of NTM and macrolides with in vitro models suggesting an increased risk of NTM with prolonged macrolide treatment and epidemiological studies suggesting that prior macrolide use may be protective for preventing NTM infection [27, 28]. In the present study, sampling was conducted at the time of new diagnosis hence all patients were prophylactically mac-

rolide naïve and therefore this should not confound our results.

Positive attributes of our study include a rigorous standardised approach to the investigation and diagnosis of bronchiectasis with functional testing, lower airway microbiological sampling with bronchial washing, and detailed immunophenotyping at baseline. For study purposes, patients were only accepted as having bronchiectasis after a secondary specialist review of imaging. Criticism could be made of our cross-sectional, retrospective design and the absence of longitudinal data on clinical parameters and airway microbiology. Large prospective observational studies are required to determine cause and association of NTM and bronchiectasis and to provide further information to assist diagnosis and management in this difficult area.

Conclusion

In conclusion, we have demonstrated that 25% of the patients in our cohort had RMLP bronchiectasis, the presence of which was associated with younger age, female sex, low BMI, reduced symptoms, increased NTM infection, preserved lung function, and reduced disease severity. This may represent a clinically important phenotype in bronchiectasis, identification of which should support investigation for NTM infection. Further investigation into the impact and longitudinal follow-up of RMLP bronchiectasis patients is needed.

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Disclosure Statement

All authors declare that they have no conflicts of interest to disclose.

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