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Imagerie thoracique de la dyskinésie ciliaire primitive

(Thoracic imaging in primary ciliary dyskinesia)

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1 Abstract

Objectives : Few studies have been published on pulmonary imaging in PCD with high resolution computed tomography (HRCT). We retrospectively examined HRCT characteristics and correlations with clinical features in a series of patients with PCD.

Materials and methods : cases were recruited through a Swiss national registry for rare lung diseases. Clinical data were retrieved by questionnaires to the caring physicians. HRCT were centrally reviewed and scored separately by 2 expert radiologists unaware of clinical data. Discrepancies were resolved by a second consensus reading.

Results : 33 patients were included. Bronchiectasis were present in 85%. The middle lobe was the most frequently affected, followed by the lower lobes, whereas the upper lobes were relatively spared. Lobar atelectasis was found in 24% and affected only the middle lobe. No significant correlations were found between a bronchiectasis severity score and, respectively, clinical characteristics and lung function tests. Signs of bronchiolitis were common and followed the same spatial distribution as bronchiectasis.

Conclusion : the middle and lower lobes are the most frequently and severely affected by bronchiectasis in PCD patients. Signs of bronchiolitis are frequently found and co-localize with bronchiectasis.

Keywords: Primary ciliary dyskinesia; High resolution computed tomography; Bronchiectasis; Pulmonary function tests

2 Introduction

Primary ciliary dyskinesia (PCD) is a rare genetic autosomal recessive disorder with an estimated prevalence of 1/10'000 in Europe (1,2). It is characterised by abnormal structure and/or function of ciliae of the respiratory epithelium, which results in impaired muco-ciliary clearance (3), thus promoting mucus accumulation, bacterial proliferation and recurrent infections. Manifestations of PCD often start during childhood with respiratory distress, neonatal pneumonia, recurrent upper and lower respiratory tract infections, and chronic otitis media leading to hearing defects (4). The phenotypical spectrum of PCD also includes abnormal organs lateralisation during embryogenesis leading to situs inversus in half of cases (2). Recurrent bronchial infections lead to the development of bronchiectasis through destruction of elastic and muscular components of the bronchial wall (5). The prevalence of bronchiectasis in PCD increases with age, and they are almost always present in adulthood (4), but disease severity varies widely from one individual to another.

Few studies have analysed the imaging features of PCD at high resolution computed tomography (HRCT) (6–11). In some series, PCD accounted only for a small number of patients among other causes of bronchiectasis (6,7,12,13). Conflicting data have also been reported on the relationships between imaging and clinical features or lung function in PCD (6,9–19). Features of bronchiolitis have been reported in PCD at imaging and histopathology in one small case series (n=8), but this issue has not been addresses in larger studies.

The objectives of this retrospective study were to provide a detailed quantitative analysis of chest imaging abnormalities in PCD, including severity and spatial distribution of bronchiectasis, atelectasis, and features of bronchiolitis, and to examine correlations between imaging and clinical and lung function characteristics, respectively.

3 Material and methods

3.1 Case recruitment and selection

This study was undertaken by the Swiss group for interstitial and orphan lung diseases (SIOLD), a network of pulmonary physicians interested in rare pulmonary diseases, and holding a national registry aiming at recruiting cases for clinical research. A questionnaire was sent to all physicians having reported cases of PCD to the registry. Questionnaires were completed by reviewing the medical records. HRCT images were provided for central review. Patients or caregivers gave written consent for inclusion. The study protocol was approved by the local ethics committee.

The diagnostic inclusion criteria were:

1. Presence of an ultrastrucural microtubular defect at electron microscopy of nasal or bronchial ciliated epithelium or the sperm tail, or
2. Reduced ciliary beat frequency at optical microscopy,
3. Kartagener syndrome, defined as situs inversus totalis or incompletus (dextrocardia) with bronchiectasis and chronic sinusitis.

Exclusion criteria were the presence of another cause of bronchiectasis such as hypogammaglobulinemia, cystic fibrosis, connective tissue disease, human immunodeficiency virus infection, pulmonary tuberculosis, or alpha-1-antitrypsin deficiency.

3.2 Data collection

Recorded clinical data included organ lateralization, history of neonatal respiratory distress, sinusitis, sinus surgery, otitis, hypoacusis, hyposmia, cardiac abnormalities, fertility history, respiratory symptoms, number of exacerbations and number of hospitalizations related to PCD in the last 2 years, work disability in adults, quality of life measured by self-administered Saint-George Respiratory Questionnaire in patients aged >15, and treatments.

First and last available spirometry in stable condition as well as spirometry at time of HRCT $\pm$1 year were recorded, including forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and FEV1/FVC ratio. Correlations between lung function and clinical characteristics were made with the last available spirometry.

Sputum bacteriology data were recorded, with special interest for Gram-negative bacteria and mycobacteria. The presence of P. aeruginosa was classified as either occasional isolate, or chronic (> 2 isolates over 6 months or > 3 isolates over 2 years).

3.3 Data Analysis

HRCT scans were centrally reviewed by 2 radiologists (N.H. and P.D.) with special interest in chest imaging. The radiologists were unaware of clinical data and first read the images independently. In a second reading, both radiologists reviewed the images together and disagreements were resolved by consensus. If more than one CT scan was available, only the most recent was used.

Each lobe was analysed separately. The lingula was considered as a separate lobe. In patients with situs inversus, the lung containing the middle lobe was considered as the right lung, even if it was located on the left side due to situs inversus. Recorded variables included presence and extension of bronchiectasis, severity of bronchial dilatation, severity of bronchial wall thickening, mucus plugging in large airways, and lobar or segmental atelectasis. Four signs of bronchiolar disease were analyzed, including small centrilobular nodules, bronchiolectasis, tree-in-bud pattern and mosaic attenuation. Emphysema and ground-glass opacities were also recorded.

The presence of bronchiectasis was defined as an internal bronchial diameter larger than the diameter of the accompanying pulmonary artery, a lack of tapering of bronchi, and the presence of bronchi in the outer third of the lung parenchyma (20). Severity of bronchiectasis were assessed using the Reiff scoring system (21). Extent of bronchiectasis was determined by assigning a semi-quantitative score to each of the 6 lobes as follows: grade 0 = no bronchiectasis, grade 1 = localized bronchiectasis affecting one broncho-pulmonary segment, grade 2 = bronchiectasis in 2 or more broncho-pulmonary segments in the same lobe (21). The severity of bronchial dilatation was classified relatively to the adjacent pulmonary artery as follows: grade 0 = no dilatation, grade 1 = less than twice the diameter of adjacent pulmonary artery, grade 2 = between 2 and 3 times the diameter of

adjacent pulmonary artery, and grade 3 = more than 3 times the diameter of adjacent pulmonary artery (21). Bronchial wall thickness was quantified relative to the external diameter of the bronchi as follows: grade 0 = normal, grade 1 = internal diameter > 50% of external diameter, grade 2 = internal diameter < 50% of external diameter, grade 3 = complete obliteration (20). Other HRCT abnormalities were recorded as present or absent.

For correlations between imaging and clinical data, we used a bronchiectasis score based on the Reiff scoring system (21), which was previously used by Santamaria (6) and Frija-Masson (17). For each of the 6 lobes, the extent of involvement (0 to 2 points), the severity of bronchial dilatation (0 to 3 points), and the severity of bronchial wall thickening (0 to 3 points) were summed, giving a minimal score of 0 and a maximal score of 48. In case of lobectomy, lobar atelectasis, lung consolidation, or unclassifiable images, the case was excluded from this particular analysis.

Results were expressed in proportions for categorical variables, and as mean ± standard deviation (SD), median, and interquartile range (IQR) for numerical variables. Comparisons between dichotomous clinical characteristics and spirometric variables were made with the Mann-Whitney test. Correlations between numerical clinical characteristics and spirometric variables were assessed with the Pearson rank coefficient correlation. Comparisons between lobes were made using the Wilcoxon signed-rank test for numerical variables and with the multinomial test for proportions. Interobserver agreement for HRCT analysis was expressed as kappa coefficient.

4 Results

4.1 Study population

Filled questionnaires and imaging from 38 patients were available. 5 cases were excluded due to incomplete data. The remaining 33 patients were included. PCD was diagnosed based either on diagnostic electron microscopy (n=23), reduced ciliary beat frequency (n=1), or the presence of Kartagener syndrome (n=9).

4.2 Clinical characteristics and lung function

The clinical characteristics of the study population are shown in table 1. All were Caucasian. Females (n= 21, 64%) were more numerous than males (n=12, 36%) but the difference was not significant. The median age at first PCD symptoms was 0.5 years (range: 0 to 17), and the median age at PCD diagnosis was 9 years (range: 0 to 49). Situs inversus was present in 42%. As compared to those with situs solitus, patients with situs inversus tended to have a lower median age at first symptoms (0 vs 1 yr), and at diagnosis (6.5 vs 9 yr), but the differences were not significant. The mean age at HRCT was 25.9 $\pm$ 15.1 years, and 27% were <15 years.

Chronic bronchitis (91%), chronic sinusitis (82%) and otitis (81%) were the most common clinical features. A history of respiratory exacerbations was present in 79%. Twenty-seven percent had been hospitalized in the last 2 years due to PCD. Bacteriological data, available for 31 patients, are shown in table S1. H. influenzae and S. pneumoniae were the 2 most frequently isolated agents. P. aeruginosa was found in 39%, either as occasional isolate (19%) or chronic colonisation (20%). Treatments are summarized in table S2.

First and last lung function tests were available for respectively 30 and 31 patients (table 2). One patient had only one test and it was categorized as last spirometry. The first available spirometry was done at a mean age of 23 $\pm$ 14 years, and the last one at a mean age of 29 $\pm$ 14 years. No significant difference was found between first and last values of either parameter. Spirometry at HRCT time ± 1 year was available for 21 patients at a mean age was 22 ± 9.

Correlations between clinical characteristics and last pulmonary function tests are shown in table 3. There was no significant correlation between respectively, sex, age and situs inversus with any lung function measurement. Significant negative correlations were found between dyspnoea NYHA stage and respectively FEV1, FVC and FEV1/FVC. A history of respiratory exacerbations, the number of exacerbations in the last 2 years, and the number of hospitalisations in the last 2 years were significantly correlated with lower lung function. A history of work disability was significantly correlated with lower FEV1 ($p<0.01$) and lower FVC ($p<0.01$). No correlation was found between lung function parameters and SGRQ total

score. No significant association was found between presence of P. aeruginosa and any spirometric variable.

4.3 HRCT analysis

Inter-observer agreement was expressed as a kappa coefficient calculated in each lobe. The mean kappa value was 0.69 for the 3 bronchiectasis parameters, 0.63 for the small airways parameters, and 0.238 for other abnormalities.

Imaging data are summarized in figure 1. HRCT abnormalities were present in 91%. Bronchiectasis were present in 85% and were the most frequent abnormality. The middle lobe (ML) was the most frequently affected, followed by the lower lobes, which were equally affected, and significantly more than the upper lobes. There was no significant differences between the ML and the lower lobes, whereas the upper lobes were significantly less affected than the ML. The ML was significantly more affected than the lingula. The ML was the only one affected by lobar atelectasis, found in 24%. Segmental atelectasis was uncommon, without significant difference between lobes. Mucus plugging in large airways was uncommon and preferentially found in the lower lobes. Small airways abnormalities (tree in bud pattern, mosaic pattern, small centrilobular pattern and bronchiolectasis) were common, and significantly more frequent in the ML and both lower lobes. Mosaic pattern was uncommon, without differences between lobes. Ground glass opacities, and emphysema were found in a minority of patients.

A bronchiectasis severity score could be calculated for 29 patients. The mean score was 16.5 $\pm$ 11.1 (median 20, range 0 to 36). No significant correlation was found between the total score and any clinical characteristic including the age, sex, dyspnoea NYHA stage, work disability, SGRQ total score, history of exacerbations, and spirometric variables measured within one year of HRCT (n=21).

5 Discussion

The main findings of the present study are that bronchiectasis predominate in middle lobe and the lower lobes in PCD. The middle lobe was affected by complete atelectasis in one fourth of cases. Features of bronchiolar disease were common and followed a distribution similar to bronchiectasis. No significant correlation was found between imaging and clinical or spirometric variables.

5.1 Clinical features and lung function

The prevalence of situs inversus was 42%, similar to the 41 % reported by Shapiro et al. (22). Similarly to other studies (24,25), patients with situs inversus tended to be diagnosed earlier than those with situs solitus but it did not reach statistical significance in our study. A likely explanation is that the discovery of situs inversus at chest X-ray performed for neonatal respiratory distress or recurrent respiratory infections suggested PCD earlier than in situs solitus.

The most common clinical features were pulmonary (91%), sinus (82%) and otologic disease (81%), similar to a recent meta-analysis of up to 29 studies, which found a weighted mean frequency of 88% for lower respiratory symptoms, 69% for sinusitis and 74% for otitis media (26). Congenital heart abnormalities were found in 9% of our study population, slightly higher than the 5% reported in another large study (27).

Treatments used in our study population were similar to previous reports (28). Most patients (87%) performed daily physical therapy, and half of them were supervised by a professional at least once a week. Eighty-two percent regularly used bronchodilators and 52% were under long-term inhaled steroids. Although there is no evidence of the effectiveness of inhaled steroids in PCD, part of their use may be explained by concurrent asthma, which seems more prevalent in PCD than in the general population (28). As recommended (27), annual influenza vaccination and pneumococcal vaccination were done by the majority. Only a minority of patients were receiving continuous antibiotic therapy.

Our PCD population had mean lung function parameters well under the normal range already at the first available measurement, but no significant loss of lung function was

subsequently observed during a mean follow-up of 6 years. These data are similar to those of a retrospective study in 24 PCD patients by Ellerman et al. (29). These authors hypothesized that loss of lung function occurred while the disease was undiagnosed and undertreated, whereas onset of regular physical therapy and antibiotics after diagnosis prevented further loss of lung function. Another longitudinal study found that spirometry worsened with increasing age in a third of patients and remained stable or improved in two-thirds (30). As previously suggested, it is possible that longitudinal lung function follow-up is not a sensitive marker of disease progression in PCD (16). Using cross-sectional data, we found significant correlations between lung function and clinical features of disease severity such as dyspnea stage, history of exacerbations, number of exacerbations, number of hospitalizations, and work disability. This shows that lung function is nevertheless related to disease severity. SGRQ total score was not correlated to lung function. Pifferi et al. did a similar analysis using the SGRQ total score and found that worse score was significantly correlated with older age. They did not however correlate it to lung function (31).

Our bacteriological data were consistent with previous series with a predominance of H. influenza (58%) and S. pneumoniae (55%). The prevalence of P. aeruginosa chronic infection in our series (20%) was in the range of previous reports (5 to 39%) (27). Non tuberculous mycobacteria were found in only 6%, similarly to the 3% reported in a recent series (17), whereas a frequency of 20% was found in one study (23). S. maltophilia was rarely found (6%) and there were no isolates of B. cepacia. This suggests that, in contrast to cystic fibrosis, S. maltophilia and B. cepacia are not typical of PCD. As previously suggested, their presence in a patient with bronchiectasis of unclear cause might decrease the likelihood of a PCD diagnosis (17). Conflicting data have been reported on the association between P. aeruginosa infection and worse lung function. Frija-Masson et al. (17) and Boon et al. (29) found significantly lower FEV1 when a chronic P. aeruginosa infection was present ($p<0.05$), whereas Pifferi et al. found no relationship (11). Similarly to the latter study, we didn't find any significant correlation between any spirometric parameter and P. aeruginosa infection.

5.2 Imaging

To our knowledge, a precise description of bronchiectasis in PCD using a well-defined scoring system was not reported previously. Using this tool, we found that the spatial distribution of bronchiectasis severity was similar for each of the 3 variables studied (extent of involvement, bronchial wall dilatation, and bronchial wall thickeness), suggesting that these parameters evolve in parallel with disease progression.

Bronchiectasis were preferentially localized in the lower lobes, whereas upper lobes were less often affected. These observations were true for all 3 bronchiectasis characteristics analysed. This finding is consistent with previous observations, in which bronchiectasis prevalence ranged from 20% to 72% in the upper lobes, and from 35% to 94% in the lower lobes (9,11,14,17). This distribution contrasts with the early stage of cystic fibrosis, where abnormalities are mainly seen in the upper lobes, before affecting all lobes with disease progression (33). The ML was frequently affected by bronchiectasis, as previously reported (8,9). The ML was significantly more affected than the lingula in our study which has not been reported previously. On the contrary, Santamaria et al. found that the lingula (70%) was more frequently affected than the ML (30%) (14). Interestingly, the ML was the only one affected by complete atelectasis in our series. One can hypothesize that the anatomically location and shape of ML bronchus could make it more prone to mucus accumulation, bronchial inflammation and damage, and lobar collapse. However, our data do not support this hypothesis, as only one case had mucus plugging in the ML, whereas plugging was more common in the lower lobes. Mucus plugging in large airways was only detected in our study in about 20% of patients while it was reported in 31 to 93% in previous studies (8–10,13,14). However, it is not clear if other studies recorded this parameter in both large and peripheral airways, or in large airways only.

Small airways abnormalities have not been analysed in detail in previous studies. Similarly to the large airway findings, bronchiolectasies, small centrilobular nodules, and tree in bud pattern were preferentially found in the lower lobes, whereas the upper lobes were relatively spared. Thus, the spatial distribution of bronchiolar disease followed the same pattern as bronchiectasis. The middle lobe and lingula had an intermediate prevalence of

small airway abnormalities between lower and upper lobes. Interestingly, small airways abnormalities were absent where no bronchiectasis were found. Although an indirect sign of bronchiolitis, mosaic pattern was uncommon with no zonal predominance.

Ground glass opacities were also uncommon in our study (15%) as compared to other reports (62%-65%), while emphysema (21%) was in the range of previous reports (7%-14%) (9,15). These two abnormalities are not specific to PCD and not related to the pathophysiology of bronchial or bronchiolar disease.

With a bronchiectasis score previously used in 2 PCD studies (6)(17), we did not find any significant correlation between bronchiectasis severity and FVC, FEV1 and FEV1/FVC, respectively. Using other scores, especially the Brody score, some studies found significant correlations between bronchiectasis severity and worse FEV1 and FVC (9,11,12,14–16), whereas others failed to find such correlations (6,10,34). One hypothesis to explain these conflicting data might be the lack of sensitivity of spirometric parameters to describe disease severity. Surprisingly, age did not correlate significantly with bronchiectasis score in our study, in contrast to other studies (9,11,14,16,18). We were not able to explore correlations between bronchiectasis severity and the presence of P. aeruginosa due to lack of data.

The limitations of our study are mainly due to its retrospective nature, the small size of the study population, and the fact that only bronchiectasis were analysed in a semi-quantitative manner, whereas small airway abnormalities were not precisely quantified. This prevented a more detailed analysis of the role of small airways in disease severity and progression, and should be addressed in another study. One strength of our study is the standardized reading of HRCT by 2 radiologists, with good consistency between readers as reflected by the kappa coefficient.

6 Appendix

6.1.1 Table 1. Clinical characteristics of 33 patients with PCD

	n=	%	mean	± SD	median	IQR
Caucasian	33	100				
Female, %	33	64				
Situs inversus, %	33	42				
Age at first symptoms, yr	33		2.7	± 4.4	0.5	4
-with situs inversus	14		3.9	± 6	0	8.5
-without situs inversus	19		1.9	± 2.5	1	3.5
Age at diagnosis, yr	33		13.8	± 13.1	9	15
-with situs inversus	14		10.7	± 13.6	6.5	16.7
-without situs inversus	19		16.1	± 12.6	9	19
Age at HRCT, yr	33		25.9	± 15.1	22.3	16.7
Active smoker, %	32	6				
Dyspnea NYHA stage at last visit	32		1.3	± 1.2	1.5	2
SGRQ total score at last visit	22		39.1	± 20.9	37	41.8
Chronic bronchitis, %	33	91				
Chronic sinusitis, %	33	82				
Otitis, %	31	81				
Hypoacusis, %	27	67				
Hyposmia, %	20	30				
Frontal sinus aplasia, %	26	58				
History of acute exacerbations, %	33	79				
Number of exacerbations/year in the last 2 years	33		2.3	± 2.5	2	2
Number of hospitalizations related to PCD in the last 2 years	33		0.6	± 1.3	0	1
Congenital cardiac abnormalities, %	33	9				
Had had children, %	30	17				
History of infertility, %	25	24				

SGRQ: Saint George respiratory questionnaire

6.1.2 Table 2. Pulmonary function tests

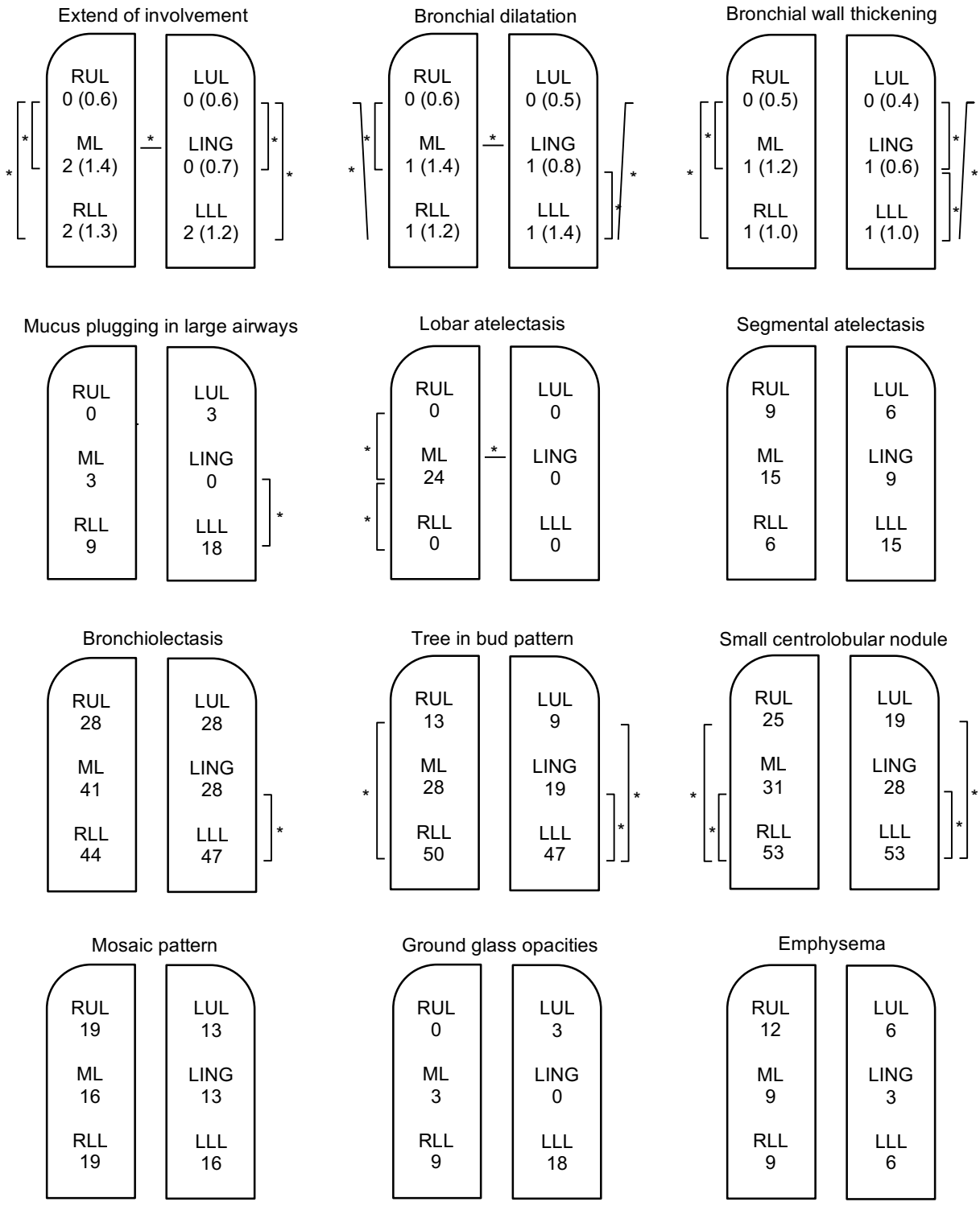
	First PFT (n=30)	Last PFT (n=31)	HRCT PFT ± 1 year (n=21)
	mean ± SD	mean ± SD	mean ± SD
Age at PFT	23 ± 14	29 ± 14	22 ± 9
FEV1, % pred	64 ± 23	63 ± 25	67 ± 22
FVC, % pred	76 ± 18	75 ± 23	78 ± 18
FEV1/FVC	71 ± 15	70 ± 15	72 ± 12

6.1.3 Table 3. Correlation between clinical characteristics and last pulmonary function tests.

	Last pulmonary function (n=31)		
	FEV1, % pred	FVC, % pred	FEV1/ FVC, %
Sex	NS	NS	NS
Age	NS	NS	NS
Situs inversus	NS	NS	NS
Dyspnea NYHA stage[a]	-0.66 (-0.82 ;-0.39)	-0.65 (-0.82 ;-0.37)	-0.6 (-0.79 ;-0.3)
History of respiratory exacerbations	present 59±26 absent 80±11 p=0.01	present 72±24 absent 87±8 p=0.02	present 68±16 absent 76±3 p=0.04
number of exacerbations/yr in the last 2 yr	-0.55 (-0.75 ;-0.24)	-0.53 (-0.75 ;-0.22)	-0.40 (-0.66 ;-0.06)
number of hospitalisations in the last 2 yr	-0.59 (-0.78 ;-0.3)	-0.54 (-0.75 ;-0.24)	-0.53 (-0.74 ;-0.22)
P. aeruginosa isolates in sputum	NS	NS	NS
work disability[b]	present 42±25 absent 75±14 p<0.01	present 54±20 absent 88±12 p<0.01	NS
SGRQ total score[c]	NS	NS	NS

Comparison between groups were made with the Mann Whitney test for dichotomic variables, and Pearson correlation coefficient for numerical variables. [a]n=30, [b]n=29, [c]n= 21.

6.1.4 Figure 1



Results are expressed as a median (mean) score for extent of involvement, bronchial wall thickening and bronchial dilatation, and as % of positive findings for other lung abnormalities. *p<0.05. Wilcoxon signed rank test was used for extent of involvement, bronchial wall dilatation and bronchial wall thickening. Multinomial test was used for all other parameters. For clarity, only significant differences between lobes of the same lung, and between the same lobes of both lungs (i.e. upper lobes, lower lobes, or ML and LING respectively) are shown.

6.1.5 Table S1. Sputum bacteriology in 31 patients with PCD.

	%
H. influenzae	58
S. pneumoniae	55
M. catarrhalis	3
P. aeruginosa	39
occasional finding	19
chronic colonisation	20
S. aureus	16
Klebsiella species	13
N. meningitidis	10
S. maltophilia	6
B. cepacia	0
M. tuberculosis	3
non tuberculous mycobacteria	6
C. albicans	16
A. fumigatus	10

Data represent the percentage of patients in whom the strain was isolated at least once. For P. aeruginosa, the presence of isolates was further subdivided as either occasional finding or chronic colonization, defined as > 2 isolates over 6 months or > 3 isolates over 2 years.

6.1.6 Table S2. Treatments

	n=	% yes
Pneumococcal vaccination	26	85
Yearly influenza vaccination	26	88
Macrolides	33	9
Antibiotics long term prophylaxis	33	6
Inhaled antibiotics	33	12
Inhaled rhDNAse	33	6
Inhaled long-term corticosteroids	33	42
Systemic long-term corticosteroids	33	3
Bronchodilators	33	82
Physical therapy	31	87
Long-term oxygen therapy	33	12
Home mechanical ventilation	33	6
Permanent tracheotomy	33	3
Lung transplantation	33	6

6.1.7 Table S3. Detailed distribution of bronchiectasis scores

			Lobar distribution of lung abnormalities						
Parameters	n=	value	RUL	LUL	ML	LING	RLL	LLL	Score > 0 in any lobe, %
Extent of involvement, %	31	0	58	61	23	52	36	36	84
		1	23	23	16	26	3	10	
		2	19	16	61	23	61	55	
Severity of bronchial dilatation, %	30	0	60	63	27	47	33	37	83
		1	27	30	27	30	27	20	
		2	10	0	27	17	27	13	
		3	3	7	20	7	13	30	
Bronchial wall thickening, %	30	0	57	60	27	47	30	37	83
		1	37	40	43	43	50	37	
		2	3	0	10	10	10	13	
		3	3	0	20	0	10	13	
Any sign of bronchiectasis, %	33	1, 2 or 3	48	42	76	55	64	67	85

RUL: right upper lobe, LUL: left upper lobe, ML: middle lobe, LING: lingula, RLL: right lower lobe, LLL: left lower lobe.

6.1.8 Table S4. HRCT abnormalities proportions

	n=	Proportion of patients with abnormality present in any lobe
Mucus plugging in the large airways, %	33	21
Lobar atelectasis, %	33	24
Segmental atelectasis, %	33	45
Bronchiolectasis, %	32	69
Tree in bud pattern, %	32	63
Small centrilobular nodules, %	32	72
Mosaic pattern, %	32	28
Ground glass opacities, %	33	15
Emphysema, %	33	21

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