The Primary Ciliary Dyskinesia Computed Tomography Score in Adults with Bronchiectasis: A Derivation und Validation Study

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Bronchiectasis · Clinical decision rule · Computed tomography · Primary ciliary dyskinesia · Kartagener syndrome

Abstract
Background: Primary ciliary dyskinesia (PCD) is a rare genetic disorder which requires a complex diagnostic workup. Thus, an easy and widely available screening method would be helpful to identify patients who need a further diagnostic workup for PCD. Objectives: The aim of the study was to develop and validate a computed tomography (CT) score for PCD to facilitate etiological diagnosis in adults with bronchiectasis. Method: Chest CTs from 121 adults with bronchiectasis were scored for bronchiectasis morphology, distribution, and associated findings. Patients with and without the etiological diagnosis of PCD (46 and 75, respectively) were compared. Significantly, different imaging findings (p < 0.05) in univariate analysis were considered for multivariate analysis. Distinct findings were used to build the score. Based on this score, receiver operating characteristic (ROC) curve analysis was performed. The score was validated with 2 independent cohorts, another cohort from the same institution with 56 patients (28 with PCD) and an external cohort from another referral center with 172 patients (86 with PCD). Results: The following parameters predicted PCD in adults with bronchiectasis and were included in the score with weighting according to their regression coefficients: 2 points were given for predominance in the middle/lower lobe, 2 points for tree-in-bud pattern, 2 points for atelectasis or prior resection of a middle/lower lobe, and 3 points for absence of em-
Primary ciliary dyskinesia (PCD) is a genetically diverse disease which causes impaired mucociliary clearance. Clinical manifestations include neonatal respiratory distress, early onset recurrent or chronic otitis media, chronic rhinosinusitis with nasal polyps, recurrent bronchitis or pneumonia, and male infertility. Pulmonary symptoms are chronic productive cough with recurrent airway infections, frequently leading to obstructive lung disease and bronchiectasis as disease progresses. PCD is associated with situs inversus, which is then referred to as Kartagener syndrome [1]. Early diagnosis and appropriate treatment may reduce long-term pulmonary morbidity and prevent the development of severe bronchiectasis [2, 3].

Among patients with bronchiectasis, 1–17% have an underlying diagnosis of PCD, and it is suspected that this etiology is not sufficiently recognized, in particular in general practice, adult respiratory medicine and otorhinolaryngology [4–6]. Outcomes of the disease in adulthood are poorly known, since most published studies focused on children [7–9]. Frija-Masson and colleagues assessed the clinical characteristics and disease progression in adults with PCD and found a heterogeneous alteration of respiratory function, which appears more severe in females and in patients with chronic *Pseudomonas aeruginosa* infection [10]. In the largest retrospective investigation of 152 adults with PCD from the UK, older age at diagnosis was significantly associated with more severe lung function impairment at diagnosis and chronic *Pseudomonas aeruginosa* infection but not with subsequent lung function decline, suggesting potential stabilization with optimal care [11]. Another recently published study characterizing an adult PCD population in Brazil revealed similar results [12]. These studies highlight the need for establishing an early diagnosis in PCD.

However, the diagnosis of PCD is complex and is based on medical history, suggestive clinical findings, nasal nitric oxide measurement, high-speed video microscopy, transmission electron microscopy, immunofluorescence microscopy, and the detection of a biallelic disease-causing mutation [13, 14]. The full diagnostic workup requires specific expertise as well as technical setup, which is available in very few centers only and which is expensive and time-consuming [15, 16]. Therefore, it needs to be better defined which bronchiectasis patients to refer to a diagnostic workup for PCD.

Today chest computed tomography (CT) is considered the gold standard for establishing the diagnosis of bronchiectasis and obligatory for inclusion in national and international bronchiectasis registries [17, 18]. CT patterns in patients with PCD differ significantly from those in patients with bronchiectasis due to other underlying etiologies [11, 19–21]. Patients with PCD typically show a higher prevalence of bronchiectasis in the middle and lower lobes and more often tree-in-bud pattern, mucus plugging, and atelectasis [11], while patients with other underlying etiologies more commonly have a predominance of bronchiectasis in the upper lobes as well as concomitant fibrotic and emphysematous changes of lung parenchyma [19].

The aim of this study was to develop a simple PCD prediction tool based on imaging data for use in adults with bronchiectasis, the primary ciliary dyskinesia computed tomography (PCD-CT) score. This score may assist practitioners in identifying patients for referral to further diagnostic workup at a PCD expert center and thus, to facilitate earlier recognition and appropriate management, thereby potentially preventing further progressive lung damage.

**Materials and Methods**

**Derivation Cohort**

The imaging findings were derived using data from a retrospective cohort study conducted at our Adult Bronchiectasis Clinic at the Hannover Medical School, which evaluated typical CT findings
from patients with PCD in contrast to other underlying etiologies of bronchiectasis [19]. We included all of the patients between the ages of 18 and 75 years who visited our specialized Outpatient Department between 2011 and 2017 and with a CT examination in our Radiology Department were included, in patients with PCD, also external CT scans were included. CT, computed tomography; PCD, primary ciliary dyskinesia.

CT Features and Semiquantitative Scoring
All CT examinations were evaluated by a radiologist with 7 years of experience in reading chest CTs (SD). To test interobserver variability, a radiologist with 13 years of experience in reading chest CTs (HOS) evaluated the score as a second reader. Bronchiectasis was evaluated according to Reiff et al. [25]. Extent of involvement, severity of bronchial dilatation, severity of bronchial wall thickening, and type of bronchiectasis according to Reid et al. [26] were evaluated for each lobe (with the lingula considered as a separate lobe). Moreover, the predominant site of bronchiectasis, the lobar distribution of bronchiectasis (widespread, predominantly upper lobe, predominantly middle lobe, predominantly lower lobe, middle and lower lobes equally involved, or unclassifiable), and the site of bronchiectasis (central, peripheral, or mixed) were registered [25]. In case of Kartagener syndrome, right-sided changes were assigned to the left site according to the architecture of the lobes. In addition, collateral findings like mucus plugging, tree-in-bud pattern, atelectasis, peripheral and central consolidations, peripheral and central ground glass opacities, interlobular septal thickening, and intralobular lines were scored on a scale from 0 to 2 (0 = none, 1 = 1–3 bronchopulmonary segments involved, and 2 = >3 bronchopulmonary segments involved). Mosaic attenuation, cavities, emphysema, fibrosis, and situs inversus/heterotaxy were classified as present or absent as previously described [19]. All terms were used according to the definition of the Fleischner Society [27]. At last, presence of atelectasis or prior resection of a lower or middle lobe/lingual was assessed.

Validation Cohort Hannover
The PCD-CT score was validated with a cohort of adult patients with bronchiectasis who visited our specialized Outpatient Department for adults with bronchiectasis at the Hannover Medical School between 2018 and mid of 2020. All the patients with the diagnosis of PCD (n = 28) and the same number of randomly se-
lected patients with other underlying diseases were included. CTs were evaluated according to the features of the PCD-CT score.

**Validation Cohort London**

The PCD-CT score was validated using an independent cohort of patients with bronchiectasis from another center: Royal Brompton Hospital \((n = 172)\). The validation cohort was based on PCD patients and bronchiectasis patients without PCD scored as part of previous studies and analyzed independently of the derivation study \([11, 28]\). CTs in the validation cohort were evaluated according to the features of the PCD-CT score except that fibrosis could not be evaluated since it was not part of the previous study.

### Table 1. Patient characteristics of the derivation cohort

| Characteristic                                                                 | Non-PCD (\(n = 75\)) | PCD (\(n = 46\)) |
|-------------------------------------------------------------------------------|----------------------|-------------------|
| **Sex, \(n (%)\)**                                                           |                      |                   |
| Male                                                                          | 32 (43)              | 15 (33)           |
| Female                                                                        | 43 (57)              | 31 (67)           |
| **Age when CT performed, median (range)**                                    | 49 (18–75)           | 38 (18–72)        |
| **Etiologies, \(n (%)\)**                                                    |                      |                   |
| Idiopathic                                                                    | 25 (33)              |                   |
| Asthma/ABPA                                                                   | 11 (15)              |                   |
| Immunodeficiency                                                              | 10 (13)              |                   |
| COPD/A1AT                                                                     | 6 (8)                |                   |
| Postinfectious                                                                | 6 (8)                |                   |
| GvHD                                                                          | 6 (8)                |                   |
| NTM lung disease                                                              | 3 (4)                |                   |
| CFTR-related disorder                                                         | 3 (4)                |                   |
| Connective tissue disease                                                     | 3 (4)                |                   |
| Yellow nail-syndrome                                                          | 1 (2)                |                   |
| Eosinophilic granulomatosis with polyangiitis                                  | 1 (2)                |                   |
| **Sputum microbiology, \(n (%)\)**                                           |                      |                   |
| *Pseudomonas aeruginosa*                                                      | 15 (20)              | 18 (38)           |
| *Staphylococcus aureus*                                                       | 7 (9)                | 4 (9)             |
| *Aspergillus fumigatus*                                                       | 7 (9)                | 2 (4)             |
| *Escherichia coli*                                                            | 1 (1)                | 3 (6)             |
| *Serratia marcescens*                                                         | 3 (4)                | 2 (4)             |
| *Streptococcus pneumonia*                                                     | 3 (4)                | 0 (0)             |
| *Haemophilus influenzae*                                                      | 3 (4)                | 4 (9)             |
| No pathogen detected                                                         | 33 (43)              | 14 (30)           |
| **Lung function, mean (SD)**                                                  |                      |                   |
| FEV1\% pred                                                                  | 66 (±27)             | 70 (±23)          |
| FVC\% pred                                                                   | 80 (±26)             | 85 (±23)          |
| **Body mass index, mean (SD)**                                                |                      |                   |
| 25 (±6.2)                                                                    | 23 (±3.1)            | 21 (±2.2)         |
| **BSI score, \(n (%)\)**                                                     |                      |                   |
| 0–4                                                                           | 19 (25)              | 15 (32)           |
| 5–8                                                                           | 15 (20)              | 17 (36)           |
| >9                                                                            | 42 (55)              | 15 (32)           |
| **Exacerbations, median (IQR)**                                               | 2 (0–4)              | 2 (0–3)           |
| **Hospitalizations, median (IQR)**                                            | 0 (0–1)              | 0 (0–1)           |

SD, standard deviation; IQR, interquartile range; PCD, primary ciliary dyskinesia; CT, computed tomography.

**Statistical Methods**

The IBM SPSS Statistics (version 25.0, IBM Corp., Armonk, NY, USA) statistical software program was used for statistical analysis. Inter-rater agreement between the 2 independent readers was measured with Cohen’s kappa coefficient. Unweighted kappa coefficients were calculated for binary items, while the weighted version was used for the ordinally scaled sum score. Weighting was chosen according to the squared distance from the diagonal in the contingency table of ratings. Imaging features were compared between patients with and without PCD. Group comparisons were performed using the Mann-Whitney U test for ordinal variables and the chi-square test for categorical variables. All reported \(p\) val-
ues are two-sided unless indicated otherwise. \( p \) values <0.05 were considered statistically significant. The best model from logistic regression allowed for the calculation of the PCD-CT score to estimate the probability of a positive PCD diagnosis. The score for each predictor corresponds to the respective regression coefficient, which was rounded to the nearest integer [29]. A receiver operating characteristic (ROC) analysis was performed to assess the predictive performance of PCD-CT score. The predictive threshold was determined using the highest Youden index [29].

**Results**

**Derivation Group**

The derivation cohort from Hannover Medical School included 121 patients, 46 with the diagnosis of PCD. Of those, 41 patients had a definite diagnosis of PCD, and in 5 patients, the diagnosis was highly likely. Genetic testing had been done in 36 patients. Characteristics including the etiologies of the non-PCD patients are shown in Table 1.

Regarding the variable selection, we used the significant variables (Table 2) from the Reiff score and in addition collateral findings (mucus plugging, tree-in-bud pattern, atelectasis, consolidations, ground glass, interlobular thickening, and intralobular lines) and took through an univariate analysis. In our previous study, the detailed results were published [19]. A brief overview of the results is shown in Table 2. Univariate analysis showed that the following imaging findings were found to be significantly different in patients with and without PCD and were entered into the multivariate regression model: atelectasis or previous resection of a middle or lower lobe \( (p \leq 0.001) \), mucus plugging \( (p = 0.031) \), predominance of bronchiectasis in the middle and lower lobe \( (p = 0.001) \), tree-in-bud pattern \( (p < 0.001) \), and absence of fibrotic or emphysematous changes \( (p < 0.001) \) (Table 3). All these variables with a \( p \) value \( \leq 0.05 \) in the univariate analysis (Table 3) were included in the multivariate analysis. Interobserver agreement was very good for the binary features of the score with an unweighted \( \kappa \) ranging between \( \kappa = 0.69 \) for

| Table 2. Results of the collateral findings in CT for patients with and without PCD for (a) ordinary scale (group comparisons were performed using the Mann-Whitney U test) and (b) binary scale (group comparisons were performed using the Mann-Whitney U test) |
|---------------------------------|---------------------------------|---------------------------------|
| **a**                           | **PCD (n = 46)**                 | **Non-PCD (n = 75)**            |
|                                 | mean | median | mean | median | Group   | \( p \) value |
| Mucus plugging                  | 1.46 | 2.00   | 0.99 | 1.00   | 0.001   |              |
| Tree in bud                     | 1.48 | 2.00   | 0.69 | 1.00   | <0.001  |              |
| Consolidations peripheral       | 0.26 | 0.00   | 0.59 | 0.00   | 0.019   |              |
| Consolidations central          | 0.00 | 0.00   | 0.08 | 0.00   | 0.050   |              |
| Ground glass peripheral         | 0.57 | 1.00   | 0.89 | 1.00   | 0.013   |              |
| Ground glass central            | 0.07 | 0.00   | 0.28 | 0.00   | 0.026   |              |
| Interlobular thickening         | 0.35 | 0.00   | 0.80 | 1.00   | <0.001  |              |
| Intralobular lines              | 0.20 | 0.00   | 0.81 | 1.00   | <0.001  |              |

| **b**                           | **PCD (n = 46)**                 | **Non-PCD (n = 75)**            |
|                                 | \( N \) (%) | \( N \) (%) | Group | \( p \) value |
| Situs inversus                  | 8 (17%)      | 0 (0%)      | <0.001 |              |
| Emphysema                       | 2 (4%)       | 19 (25%)    | 0.003  |              |
| Mosaic attenuation              | 14 (30%)     | 26 (35%)    | 0.631  |              |
| Atelectasis                     | 38 (83%)     | 45 (60%)    | 0.009  |              |
| Cavity                          | 1 (2%)       | 7 (9%)      | 0.124  |              |
| Atelectasis of a middle or lower lobe | 9 (20%) | 5 (7%) | 0.031 |              |
| Volume loss in a middle or lower lobe | 24 (52%) | 18 (24%) | 0.002 |              |
| History of resection of a middle/lower lobe | 12 (26%) | 9 (12%) | 0.047 |              |
| Prevalence in middle/lower lobe | 41 (89%)     | 47 (63%)    | 0.002  |              |

PCD, primary ciliary dyskinesia; CT, computed tomography.
interstitial (fibrotic and emphysematous) changes and \( \kappa = 1.00 \) for situs inversus [19]. Figure 2 shows typical findings in 2 patients with PCD.

**Development of the PCD-CT Score**

Of the 5 binary variables considered for selection, the best logistic regression model included 4 significant imaging features. In the order of importance (based on their corresponding odds ratio), these features were absence of fibrosis and emphysema, predominance of bronchiectasis in the middle/lower lobe and atelectasis, tree-in-bud pattern, and atelectasis or history of resection of a middle/lower lobe (Table 3). The presence of each imaging feature contributed to the total score following adjustment of its regression coefficient values to points between 2 and 3 (Table 3). The points for the score were based on the regression coefficient rounded to whole numbers. Situs inversus was observed only in patients with PCD, and thus, group comparisons could not be performed. The score was significantly higher in patients with PCD (mean 7.83 [SD ± 1.50], median 9 [IQR 7–9]) than in patients without PCD (mean 4.25 [SD ± 2.25], median 4 [IQR 3–6]; \( p \leq 0.001 \)) (Table 4). The discriminant ability (area under the curve, AUC) of this model was 0.90 (95% CI 0.85–0.96; \( p < 0.001 \)) (Fig. 3a). The highest combined sensitivity and specificity (83 and 83%, respectively) was at the cutoff value of >6 points (Table 5). Regarding only those patients without situs inversus, the AUC was 0.90 with a sensitivity of 84% and a specificity of 83%.

**Validation Cohort Hannover**

Validation of the PCD-CT score with 28 PCD-positive patients and 28 non-PCD bronchiectasis patients from our specialized Outpatient Department for adults with bronchiectasis at the Hannover Medical School. The score was significantly higher in patients with PCD (mean

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**Table 3. Imaging findings for the prediction of PCD by chest CT, selected by stepwise logistic regression**

| Imagen Finding                                      | Descriptive Data | Univariate analysis | Multivariate analysis | Regression coefficient | Odds ratio (95% CI) | PCD-CT score |
|-----------------------------------------------------|------------------|---------------------|-----------------------|------------------------|---------------------|--------------|
|                                                     | All (n = 121)    | PCD (n = 46)        | Non-PCD (n = 75)      |                        |                     |              |
| Atelectasis or previous resection of a middle or lower lobe |                  |                     |                       |                        |                     |              |
| Mucus plugging                                      |                  |                     |                       |                        |                     |              |
| Tree-in-bud pattern                                 |                  |                     |                       |                        |                     |              |
| Situs inversus                                      |                  |                     |                       |                        |                     |              |
| Predominance of bronchiectasis in middle and/or lower lobes |                |                     |                       |                        |                     |              |
| Absence of fibrosis and emphysema                   |                  |                     |                       |                        |                     |              |

\( \text{SD, standard deviation; IQR, interquartile range; PCD-CT, primary ciliary dyskinesia computed tomography; CT, computed tomography; PCD, primary ciliary dyskinesia.} \)

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**Table 4. Descriptive data and results for group comparisons for the PCD-CT score**

| PCD-CT score | All | PCD | Non-PCD |
|--------------|-----|-----|---------|
|              | mean (SD) | median (IQR) | mean (SD) | median (IQR) | mean (SD) | median (IQR) | p value |
| Derivation cohort (n = 121) | 5.61 (±2.65) | 6 (4–7) | 7.83 (±1.50) | 9 (7–9) | 4.25 (±2.25) | 4 (3–6) | <0.001 |
| Internal validation cohort (n = 56) | 6.00 (±2.62) | 6.50 (5–9) | 7.43 (±2.12) | 9 (6.25–9) | 4.73 (±2.28) | 5 (3–6.50) | <0.001 |
| External validation cohort (n = 272) | 5.41 (±2.09) | 7 (5–7) | 6.53 (±1.05) | 7 (5–7) | 4.28 (±2.26) | 5 (2–7) | <0.001 |

**SD, standard deviation; IQR, interquartile range; PCD-CT, primary ciliary dyskinesia computed tomography; CT, computed tomography; PCD, primary ciliary dyskinesia.**
7.43 [SD ± 2.12], median 9 [IQR 6.25–9]) than in patients without PCD (mean 4.73 [SD ± 2.28], and median 5 [IQR 3–6.50]; p ≤ 0.001). ROC curve analysis confirmed the performance of the score with AUC 0.83 (95% CI 0.72–0.94) (Fig. 3b). With the cutoff value of >6 points, the sensitivity was 75% and the specificity was 75% (Table 5).

Validation Cohort London
External validation of the PCD-CT score used data from an independent set of 86 PCD-positive patients and 86 non-PCD bronchiectasis patients from Royal Brompton Hospital as previously described [11, 28]. The score was significantly higher in patients with PCD (mean 6.53 [SD ± 1.05], median 7 [IQR 5–7]) than in patients without PCD (mean 4.28 [SD ± 2.26], median 5 [IQR 2–7]; p ≤ 0.001). ROC curve analysis confirmed the performance of the score with AUC 0.79 (95% CI 0.73–0.86) (Fig. 3c). With the cutoff value of >6 points, the sensitivity was 74% and the specificity was 73% (Table 5). Regarding only those patients without situs inversus, the AUC was 0.81 with a sensitivity of 79% and a specificity of 73%.

Estimating the Probability of a PCD
Regarding the total cohort of 349 patients, the AUC was 0.84 with a sensitivity of 77% and a specificity of 77%. The subgroup analysis in patients without situs inversus (n = 301) revealed an AUC of 0.84 with a sensitivity of 79% and a specificity of 77%.

The distribution of the PCD-CT score is visualized in Figure 4. Based on the results of the derivation and validation cohort, the probability of a PCD can be estimated for each result of the PCD-CT score. Based on these results, a calculator is provided (calculator will be published with citation of the paper on www.mdcalc.com after ac-
ceptance) and risk stratification is estimated in low risk (0–4 points, risk 0–7%), intermediate risk (5–6 points, risk 31–39%), and high risk (>6 points, risk >50%) for having PCD.

Proposal for the Diagnostic Workup

As mentioned above, all patients with situs inversus had Kartagener syndrome. Thus, situs inversus could not be included in the derivation of the PCD-CT score. Nevertheless, the presence of situs inversus in a symptomatic patient with bronchiectasis should always raise suspicion for PCD/Kartagener syndrome and should therefore trigger further diagnostic workup for PCD. Thus, we propose a two-step approach based on the CT findings for the diagnostic workup of adult patients with bronchiectasis (Fig. 5). In patients without situs inversus, the PCD-CT score should be calculated, and patients with a score >6 should be referred to further diagnostic workup for PCD (Fig. 5).

Table 5. Test performance in the derivation and validation group

| PCD-CT score     | Hannover derivation | Hannover validation | London validation | Overall       |
|------------------|---------------------|---------------------|-------------------|--------------|
| Number           | 121 (46 PCD)        | 56 (28 PCD)         | 172 (86 PCD)      | 349 (160 PCD) |
| ROC AUC          | 0.90                | 0.83                | 0.79              | 0.84         |
| Sensitivity      | 0.83                | 0.75                | 0.74              | 0.77         |
| Specificity      | 0.83                | 0.75                | 0.73              | 0.77         |
| Positive predictive | 0.75                | 0.75                | 0.74              | 0.74         |
| Negative predictive | 0.89                | 0.75                | 0.74              | 0.80         |

ROC, receiver operating characteristic; AUC, area under the curve; PCD-CT, primary ciliary dyskinesia computed tomography.

Fig. 3. ROC curve analysis for PCD-CT score for the derivation cohort Hannover (a), the validation cohort Hannover (b), and the validation cohort London (c). Analysis revealed an AUC of 0.90 for the derivation cohort, 0.83 for the validation cohort Hannover and 0.79 for the validation cohort London. ROC, receiver operating characteristic; PCD-CT, primary ciliary dyskinesia computed tomography; AUC, area under the curve.
Discussion

The present derivation and validation of the PCD-CT score is the first study to describe an imaging tool for screening of PCD as the underlying etiology of bronchiectasis in adults. We have developed a simple score based on CT findings for determining the likelihood of an individual having a diagnosis of PCD. The PCD-CT score was developed and validated in 2 expert bronchiectasis and PCD centers in Germany and the UK.

The score includes tree-in-bud pattern, predominance in the middle/lower lobe, absence of emphysema or fibrosis, and atelectasis or history of resection of middle/lower lobe (Table 3). Situs inversus was only observed in patients with Kartagener syndrome. For this reason, univariate and multivariate analyses could not be performed, and situs inversus was not included in our score. Nevertheless, situs inversus should always trigger further diagnostic workup for PCD and is included in our flowchart (Fig. 5). Accordingly, our score only includes radiological abnormalities of lung parenchyma and demonstrates the diagnostic value without clinical features and situs inversus. This enhances the value of the chest CT findings for screening of PCD.

Genetic testing is increasingly considered an early step in the PCD diagnostic workflow. However, this test is expensive, and it should only be used when PCD is likely. Physicians can use the PCD-CT score in conjunction with other clinical features in patients with bronchiectasis to identify patients who require further diagnostic workup in a specialized PCD center and to increase the pretest probability of genome analysis. Knowledge of PCD as the underlying etiology of bronchiectasis is of particular importance due to the possibility of upcoming targeted therapies such as azithromycin [30], nebulized hypertonic saline and inhibitors of the epithelial sodium channel [31], the emphasis of physiotherapy, rehabilitation, consequent treatment of upper airway complications, and fertility counseling [32].

Bronchiectasis is the final common pathway of a variety of diseases, which explains the heterogeneity of the disease. One of the most important steps in the management of patients with bronchiectasis is the identification of the underlying etiology [22, 33]. A careful evaluation of those with treatable traits or which may change patients’ management is recommended by international experts and guidelines [22, 34, 35]. In the European Respiratory Society bronchiectasis guidelines, a minimum bundle of etiological tests is recommended including differential blood count, serum immunoglobulin, and testing for allergic bronchopulmonary aspergillosis [22]. The possibility of in-depth analysis of bronchiectasis etiology might be limited by high costs and might be run only in tertiary centers. In primary care and resource limited settings, cheap and easy-to-use tests are needed to determine a likelihood of an underlying etiology. PICADAR represents a simple diagnostic tool to aid appropriate referral of patients for diagnostic testing [36]. It can be used in any patient with chronic respiratory...
The strengths of our study are the implementation in 2 independent cohorts from different healthcare systems, with robust performance in the validation cohort. Furthermore, the score includes quite simple radiological items with a high interobserver variability that can be easily evaluated by nonspecialized radiologists and chest physicians.

In conclusion, the PCD-CT score provides the first externally validated score to help practitioners in identifying adults with bronchiectasis who require further diagnostic workup for PCD, but it needs prospective validation before it can be recommended for broad use in clinical practice. The score may improve recognition of this rare and underdiagnosed disease and allow identifying patients to be referred for PCD testing.

**Statement of Ethics**

The study was approved by the Internal Review Board (No. 2675-2015) of our institution.

**Conflict of Interest Statement**

Dr. Dettmer received grants and/or advisory/lecture/clinical trial fees from Bayer and Boehringer Ingelheim. Prof. Loebinger received grants and/or advisory/lecture/clinical trial fees and/or nonfinancial support from Bayer, Grifols, Polyphor, and Astra Zeneca. Dr. Ringshausen and/or his institution received grants and/or advisory/lecture/clinical trial fees and/or nonfinancial support from Aposan, AstraZeneca, Bayer, Boehringer Ingelheim, Celtaxis, Chiesi, Corbus, Grifols, Infectopharm, Insmed, MSD, Novartis, PARI, Parion, Polyphor, Vertex, and Zambon. Dr. Ringshausen serves as member and co-chair of the scientific advisory board of the German PCD and Kartagener syndrome patient support group. Prof. Vogel-Clausen received grants and/or advisory/lecture/clinical trial fees from Siemens Healthineers, AstraZeneca, GSK, Novartis, and Boehringer Ingelheim. Prof. Wacker received grants and/or advisory/lecture/clinical trial fees from Siemens, Visage, and Delcath. All other authors declare that they have no conflict of interest in relation with this study.

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**Author Contributions**

J.R., S.D., and F.R. conceived of the presented idea. S.D. and H.S. evaluated the CT scans in Hannover. J.R., F.R., and S.D. collected the data for the derivation cohort and A.S., P.I.P.P., R.W., and M.L. for the validation cohort in London. J.F. was responsible for the statistical evaluation. J.V.C., T.W., and F.W. contributed to the interpretation of the results. All authors discussed the results and contributed to the final manuscript.
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