Recognising primary ciliary dyskinesia in adult bronchiectasis – insights from the PROGNOSIS study

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Primary ciliary dyskinesia (PCD) is a rare, complex disorder arising from genetic defects in ciliary structure and function. In adults, PCD remains an often-overlooked contributor to bronchiectasis, a heterogeneous condition with a globally increasing prevalence, typically characterised by chronic cough, sputum production, and recurrent infections. The recently published Prospective German Non-CF-Bronchiectasis Registry (PROGNOSIS) study offers critical insights into the prevalence and clinical markers of PCD among adults with bronchiectasis, potentially highlighting pathways for earlier diagnosis and better management.[1]

PCD diagnosis in adults presents unique challenges. Symptoms can vary widely, and many healthcare providers lack familiarity with PCD-specific presentations, leading to significant underdiagnosis. The PROGNOSIS study aimed to identify the prevalence and clinical characteristics of PCD in a large cohort of adults with bronchiectasis by analysing data from 1 000 patients across 38 centres.

Among 1 000 adults with bronchiectasis, 87 (9%) were found to have PCD, positioning it as the fifth most common cause of bronchiectasis in this cohort. The study highlighted five key clinical markers that clinicians can use to identify potential PCD cases among adults with bronchiectasis:

- **Upper airway disease.** Chronic rhinosinusitis and/or nasal polyps emerged as a strong indicator, observed in 78% of PCD patients compared with only 28% in non-PCD cases. This feature increased the likelihood of PCD approximately six-fold.
- **Younger age at presentation.** Patients aged <53 years were five times more likely to have PCD than older patients, underlining the importance of considering PCD in younger adults presenting with bronchiectasis.
- **Radiological involvement of middle and lower lobes.** Radiological findings showed a distinct pattern of bronchiectasis in the middle and lower lung lobes in PCD patients, suggesting a 3.7-fold increased likelihood of PCD for individuals with this radiological distribution.
- **Prolonged disease duration.** Bronchiectasis duration >15 years was strongly associated with PCD, with a four-fold increased likelihood, highlighting the progressive nature of PCD.
- **Isolation of *Pseudomonas aeruginosa*.** Positive respiratory cultures for *P. aeruginosa* were more common in PCD patients (66%) than in non-PCD patients (32%), and associated with a 2.4-fold increased PCD risk.

These findings seem to emphasise a distinct phenotype for PCD patients: generally younger, non-smokers, with more extensive lung disease, recurrent exacerbations, and higher rates of hospitalisation. Interestingly, despite these features, PCD patients reported fewer symptoms of breathlessness compared with those with other bronchiectasis aetiologies, while facing greater treatment burdens such as reliance on inhaled antibiotics, physiotherapy, and other long-term therapies.

Owing to the absence of a single definitive diagnostic test for PCD, the PROGNOSIS study employed a combination of several techniques to assist with diagnosis:

- **Nasal nitric oxide (nNO) measurement.** Low nNO levels, a hallmark of PCD, were measured in 71% of patients. While not definitive, low nNO levels can serve as an initial screening tool.
- **High-speed video microscopy (HSVM).** Used in 59% of cases, HSVM evaluated ciliary function in respiratory epithelial samples, identifying abnormal beating patterns specific to PCD.
- **Genetic testing.** Performed in 55% of cases, genetic testing (e.g. for mutations in *DNAH5* and *DNAI1*) provides definitive evidence of PCD, particularly for cases without classic clinical markers such as situs inversus.
- **Transmission electron microscopy (TEM).** This test allowed direct visualisation of ciliary structural defects in 41% of patients. TEM is highly specific for PCD, but remains limited to specialised centres owing to its technical demands.
- **Saccharin test.** Historically, this has been used as a test of nasal mucociliary clearance. Although once common, this test has been phased out owing to low specificity, and was used in only a few cases in the PROGNOSIS study.

The PROGNOSIS study presents important actionable clinical insights for providers. Early diagnosis of PCD allows for tailored management strategies, including targeted antibiotic therapy and intensive physiotherapy to manage frequent exacerbations and chronic infections. Furthermore, confirming a PCD diagnosis is essential for genetic counselling, given the heritable nature of the disease. Access to family planning resources and genetic counselling can be transformative for patients and families. PCD patients also often face unique challenges in terms of their quality of life owing to their high treatment burdens and social limitations, emphasising the importance of specialised rehabilitation and psychosocial support.

The PROGNOSIS study contributes valuable data on the prevalence and presentation of PCD among adults with bronchiectasis. Given the observed prevalence of PCD and its distinctive markers, clinicians managing bronchiectasis should consider PCD in younger patients who present with chronic rhinosinusitis, longstanding disease, recurrent Pseudomonas infections, or lower lobe bronchiectasis.

There may be some limitations in terms of translating the phenotypic characteristics of the study to developing nations. In the latter, lower lobe bronchiectasis is characteristic of idiopathic (presumed post-infective) bronchiectasis. Middle-lobe bronchiectasis is also a feature of Brock's syndrome secondary to tuberculosis.

1. Ewen R, Pink I, Sutharsan S, Rademacher J, Ringshausen FC; PROGNOSIS Study Group. Primary ciliary dyskinesia in adult bronchiectasis: Data from the German Bronchiectasis Registry PROGNOSIS. Chest 2024;166(5):938-950. https://doi.org/10.1016/j.chest.2024.05.023