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Imaging to Advance Bronchiectasis Phenotyping

Bronchiectasis is a heterogeneous disease with a wide range of clinical presentations, and its prevalence is on the rise globally, contributing significantly to morbidity and mortality (1). Over the past decade, there has been an increase in understanding of its pathophysiology, which is largely due to multinational patient registries (2, 3). Registry studies have shed light on clinical phenotypes and patient risk factors, shaping treatment priorities and facilitating the development of targeted therapies. Despite these advancements, there remains a gap in our understanding of the radiographic abnormalities found in these patients.

Chest computed tomography (CT) remains the benchmark for diagnosing bronchiectasis, offering an invaluable tool to identify patients at risk of poor outcomes. In this issue of the *Journal*, Pieters and colleagues (pp. 87–96) report a quantitative analysis of CT findings from a subset of the European Multi-center Bronchiectasis Audit and Research Collaboration (or, EMBARC) Registry (4). Drawing from patients across six European countries and eight study sites, the authors rigorously evaluated CT images from 524 participants. Using an annotated grid-scoring method, the authors determined the presence and extent of atelectasis, consolidation, bronchiectasis with and without mucus plugs, airway wall thickening, and parenchymal abnormalities. Composite scores encompassing total bronchiectasis, total mucus plugging, and total CT inflammation characteristics were created. A final score integrating all three categories was used to encapsulate the spectrum of radiographic abnormalities.

As expected, Pieters and colleagues found that patients in their study presented extensive radiographic abnormalities and a broad range of features, including abnormal airway dilation and mucus plugs, highlighting the disease's heterogeneity. Older individuals and those with longer disease duration exhibited more severe scores. The presence of nontuberculous mycobacteria (NTM) and *Pseudomonas* were significantly associated with higher overall disease burden scores. All composite radiographic scores negatively correlated with lung function and were associated with clinical severity scores. Last, both CT inflammation and total disease scores were associated with hospital admissions.

In clinical practice, clinicians frequently encounter patients with bronchiectasis who have considerable abnormalities on CT but relatively low symptom burdens, whereas in other cases, the reverse scenario occurs. The challenge lies in determining the clinical relevance of radiographically apparent abnormalities. Findings from this study suggest that a thorough evaluation of CT images can help identify risk profiles and pinpoint which abnormalities may carry greater clinical significance. Despite this, only a few studies have systematically evaluated radiographic abnormalities.

For instance, Park and colleagues evaluated bronchiectasis severity using the Bhalla score, which was initially developed to evaluate cystic fibrosis in 155 patients with non–cystic fibrosis bronchiectasis (5). Patients with higher radiographic scores were associated with worse lung function and increased frequency of hospitalizations, but not with NTM isolation (5). In contrast, Eisenberg and colleagues applied the Bhalla score in 242 patients with bronchiectasis, demonstrating that radiographic scores, along with advanced age and female gender, could predict the presence of NTM-associated pulmonary disease (6). Similarly, using the Reiff radiographic score, another study showed that higher scores could distinguish between patients with bronchiectasis who had NTM-associated pulmonary disease and patients with bronchiectasis who did not (7). These observations were supported by research on 84 patients with a history of NTM airway isolation, revealing a correlation between radiographic severity and NTM active disease but not colonization (8). The study by Pieters and colleagues echoes these observations, further highlighting that a comprehensive radiographic score could serve as a biomarker for phenotyping patients with bronchiectasis.

Mucus plugging as evidenced on CT scans may indicate active infection or persistent inflammation. Beyond bronchiectasis, mucus

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plugging has been associated with poor outcomes across various conditions such as asthma, chronic obstructive pulmonary disease, bronchiolitis obliterans syndrome, and primary ciliary dyskinesia, among others, and it has even become an endpoint in therapy evaluations (9–13). In the study by Pieters and colleagues, the extent of bronchiectasis and the presence of mucus plugging (found in up to 89% of patients) and parenchymal abnormalities were associated with important clinical outcomes. These findings support the importance of airway clearance therapies in this patient population.

This study boasts several strengths, notably its inclusion of one of the largest cohorts of patients with bronchiectasis, which allows for a thorough examination of the relationships between radiographic abnormalities and clinically relevant outcomes. The European Multicenter Bronchiectasis Audit and Research Collaboration cohort, well characterized and multicentric, provided a robust foundation for the study, which utilized a meticulously validated visual radiographic scoring system. However, there are noteworthy limitations to consider. First, the radiographic abnormalities identified represent only a snapshot lacking information on their stability or progression, particularly given that radiographic scores may change over time (5). The scoring system requires expert training, takes a long time, and is subject to interobserver variability, which hinders its large-scale application. Although some studies have addressed this limitation using artificial intelligence–based algorithms, these technologies are still in the nascent stages of development and have not yet been incorporated into routine clinical practice (14, 15). Last, it is worth noting that the median time between scanning and enrollment was 7 months. This challenges the interpretation of certain associations, such as the link between radiographic scores and hospital admission in the year before study entry. This association was found when the time elapsed was under the median value only, indicating that patients who underwent clinical assessment before imaging were primarily affected.

In conclusion, we congratulate Pieters and colleagues on this important work. Their study's findings move us toward more accurate phenotyping of bronchiectasis, supporting the hypothesis that radiographic abnormalities may provide valuable clinical insights. As our knowledge of bronchiectasis expands and with advancements in imaging technologies and scoring systems, precise phenotyping will help clinicians advance diagnosis and tailor treatments more effectively for these patients. We eagerly look forward to longitudinal studies that aim to bridge the gap between imaging technologies and clinical application and, thereby, deepen our understanding of bronchiectasis biology. ■

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