Bronchiectasis and Nontuberculous Mycobacteria: It Is Not Over till It Is Over

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The incidence of nontuberculous mycobacterium pulmonary disease (NTM-PD) is increasing worldwide [1, 2]. It is especially common among patients with chronic lung diseases such as bronchiectasis [3]. According to recent British Thoracic Society guidelines and European Respiratory Society guidelines [4, 5], patients diagnosed with bronchiectasis should be candidates for nontuberculous mycobacterial (NTM) screening. Such an evaluation is important because macrolides play important roles in treating both NTM-PD and bronchiectasis [5, 6]. Prescribing macrolides to prevent exacerbation in patients with bronchiectasis could cause macrolide resistance in those with undetected NTM colonization [6, 7]. Data are needed on NTM-PD prevalence in patients with bronchiectasis because NTM-PD can affect the level of emphasis placed on NTM screening in these patients [5]. Thus, the European Multicentre Bronchiectasis Audit and Research Collaboration of the European Respiratory Society emphasizes evaluating the microbial colonization in patients with bronchiectasis as the third highest research priority [8].

Zhu et al. [9] attempted to resolve this issue by analyzing the prevalence of NTM isolation and NTM-PD by conducting a meta-analysis that included 21 studies. The pooled isolation rate for NTM in patients with bronchiectasis was 7.7% (95% confidence interval 5.0–11.7%, $I^2 =$

97.7%, $p < 0.001$). Interestingly, these rates showed regional diversity: the rates in descending order were 50.0% in North America, 9.5% in Asia, 7.5% in Africa, 5.6% in Oceania, and 5.4% in Europe.

This meta-analysis is advantageous because it provides an updated systematic review that includes recent studies and an analysis of the regional prevalence of NTM infections among patients with bronchiectasis. Interestingly, the authors found that non-purulent sputum, weight loss, and fatigue were more common among those with isolated NTM than among those without isolated NTM. The authors also reported that *Mycobacterium avium* complex and *M. abscessus* complex were the most common species identified in patients with bronchiectasis.

However, the study included some of the common problems of meta-analyses. First, the included studies were heterogeneous. Although the authors conducted various subgroup analyses, considerable heterogeneity remained, thus making a solid conclusion unattainable [10]. Such heterogeneity resides in many patient characteristics and, more importantly, in each center's discordant principles for NTM screening. The methods of specimen analysis also differed: sputum culturing was performed in 15 studies, bronchoalveolar lavage fluid culturing was performed in one study, and sputum or

bronchial aspirates were performed in 4 studies. The authors of one study considered sputum polymerase chain reaction a valid method for NTM isolation; this method is not recommended for microbiologically diagnosing NTM-PD [8]. With this diversity among the studies, the pooled prevalence of the NTM identification should be accepted cautiously.

Furthermore, NTM isolation does not guarantee an NTM-PD diagnosis [11, 12]. NTM is ubiquitous and prone to respiratory tract colonization and specimen contamination. Only three of the 21 studies included in this meta-analysis provided the NTM-PD prevalence, which is also problematic for drawing a conclusion.

Patients with bronchiectasis should be screened for NTM on initial evaluation, but these patients can also subsequently develop NTM-PD. Our analysis of the prospective cohort of 221 patients with bronchiectasis without NTM isolation at their initial evaluation provided some insight [13]. During the median follow-up duration of 55 months, NTM was isolated from 35 patients (15.8%). Of those patients, 31 (14.0%) were ultimately diagnosed with NTM-PD within a median 37-month observation. NTM-PD development was combined with worsening radiographic lesions.

The meta-analysis by Zhu et al. [9] provided a valuable summary of NTM prevalence among patients with bron-

chiectasis. Nonetheless, it should be cautiously interpreted because of the significant heterogeneity across studies and the insufficient data on NTM-PD development. Until more homogenous studies are published, clinicians should take an individualized approach to patients with bronchiectasis considering regional NTM prevalence. Most importantly, clinicians should consider that NTM-PD can develop later in patients with bronchiectasis but without NTM at their initial evaluation. It is not over till it is over.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

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