Diagnosis and Evaluation of Bronchiectasis

Raya Cohen, MD, Michal Shteinberg, MD, PhD*

KEYWORDS

• Bronchiectasis • Etiology • Prognosis

KEY POINTS

- Bronchiectasis should be suspected when chronic productive cough and recurrent infections are reported.
- A diagnosis of bronchiectasis requires both compatible clinical features and radiologic features to be present, excluding traction bronchiectasis secondary to pulmonary fibrosis.
- Evaluation for etiologies should be performed and guided by clinical and laboratory features. Those with a specific treatment, in particular, should be actively sought.
- Prognostic evaluation is important and includes evaluation for chronic airway infection.
- Therapy is guided by symptoms and prognostic assessment. A partnership between the caregiver and a knowledgeable patient is key to treatment success.

INTRODUCTION

Bronchiectasis, a once-neglected disease, has gained increased recognition in the past decade. The reported prevalence of bronchiectasis is increasing, reaching 0.25% to 0.5% of the adult population,[1–3] making it the third most common chronic airways disease (after asthma and chronic obstructive pulmonary disease [COPD]). However, bronchiectasis is still under-recognized and it is frequent for a patient to have symptoms for years until a correct diagnosis is made. In this article, we will discuss the evaluation of a patient suspected to have bronchiectasis. We will focus on making the correct diagnosis, evaluating the etiology, the severity and prognosis, and the response to treatment.

MAKING THE DIAGNOSIS OF BRONCHIECTASIS

Historically, the diagnosis of bronchiectasis was an anatomic-pathologic detection of dilated and distorted bronchi as described two hundred years ago by RTH Laennec.[4] In recent years, the detection of abnormal airways increased with the introduction and widespread use of computed tomography (CT) scanning. This led to the detection of individuals with radiologic bronchiectasis with mild symptoms or no symptoms at all, and to the recognition that bronchiectasis represents a spectrum of etiologies and severities, with different prognostic consequences necessitating different approaches to management. Recent consensus statements on the definition of bronchiectasis for use in clinical trials require that both clinical features and anatomic-radiologic features exist to make the diagnosis.[5]

Clinical Features: Symptoms and Signs

The most common clinical findings reported in bronchiectasis are cough with sputum production, which occur in ~80% of patients..[6–8] Less common symptoms are dyspnea (60%) and wheezing (29%–30%). A history of hemoptysis is reported in 18% to 30% of patients.[8] Cyanosis and finger clubbing are signs that are seen late in

Pulmonology Institute and CF Center, Carmel Medical Center, Technion- Israel Institute of Technology, The B. Rappaport Faculty of Medicine, 7 Michal Street, Haifa 3436212, Israel
* Corresponding author.
E-mail address: michalsh@technion.ac.il
Twitter: @MichalShteinbe1 (M.S.)

Clin Chest Med 43 (2022) 7–22
https://doi.org/10.1016/j.ccm.2021.11.001
0272-5231/22/© 2021 Elsevier Inc. All rights reserved.
Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

the disease course and reported in 5% to 6% of patients.[6] In many patients, a history of pulmonary exacerbations (sometimes labeled as "bronchitis" or "pneumonia" and treated with antibiotics or anti-inflammatory agents) may be evident before a diagnosis is made. Typically, these events are associated with an increase of symptom severity with few laboratory and radiologic findings. However, in severe exacerbations, there may be features of severe systemic inflammation.[9] In a recent consensus definition of bronchiectasis for use in clinical trials, a requirement for the existence of 2 of the 3 following clinical manifestations was made: cough most days of the week, sputum production most days of the week, and history of infective exacerbations.[5]

Clinical Features: Demographics and Predisposing Conditions

Bronchiectasis typically is associated with increasing age, with a median age of 65 years and a female predominance: in published series and patient registries, about 55% to 60% of patients are women.[10–12] Bronchiectasis is known to frequently occur in people with other airway diseases—asthma,[13,14] COPD,[15,16] and chronic rhinosinusitis.[17,18] Clinical features of cough and pulmonary exacerbations are common to asthma, COPD, and bronchiectasis; it is therefore important to have a high index of suspicion of bronchiectasis in a patient with asthma or COPD with cough that is productive of sputum or has frequent infective exacerbations. Likewise, a patient with chronic or recurrent rhinosinusitis should be evaluated for bronchiectasis if respiratory symptoms develop.

Other conditions that may predispose to bronchiectasis are inflammatory diseases, mainly rheumatoid arthritis (RA),[19,20] Sjogren syndrome,[21] and Anti-neutrophil cytoplasmic (ANCA)-associated vasculitis,[22] as well as inflammatory bowel diseases (IBDs). It is acknowledged that in ulcerative colitis, airway symptoms may develop years after colectomy,[23] possibly reflecting airway manifestations of persistent systemic inflammation.

It is easy to overlook some conditions that are associated with bronchiectasis, especially when the clinical features are not very suggestive, or when several possible etiologies are present. It has been demonstrated that when an algorithm designed to diagnose the etiology of infection is applied, fewer patients will receive a diagnosis of "idiopathic" or "postinfective" and more will receive a specific etiology.[24] An etiology of "post-infectious" bronchiectasis likely needs to be considered only when there is clear documentation of severe infection after which persistent symptoms developed: it is the authors' view that before an etiology of "postinfectious bronchiectasis" is adopted, alternative and coincidental etiologies should be actively sought.

Table 1 summarizes key clinical features to be evaluated during an initial evaluation of a patient with bronchiectasis. **Fig. 1** shows common associations and etiologies of bronchiectasis. **Fig. 2** shows a patient with disfiguration of nails typical of the "Yellow nail syndrome."

Radiology

Bronchiectasis is defined as a combination of clinical and anatomic-radiologic features of airway abnormalities. A chapter dedicated to the radiology of bronchiectasis is found elsewhere in the series, and we will focus here on the main principles of the radiologic component of bronchiectasis.

Bronchiectasis is best imaged on high-resolution CT scans (HRCT). According to the Fleischner society consensus statement, morphologic criteria on thin-section CT scans include bronchial dilatation with respect to the accompanying pulmonary artery (signet ring sign), lack of tapering of bronchi, and identification of bronchi within 1 cm of the pleural surface.[27] A normal ratio of a bronchus to its adjacent artery is reported to be between 0.79 and 0.86,[28] with a ratio of 1 or higher considered compatible with bronchiectasis. It is not established what is the minimal requirement for the number of dilated bronchi compatible with clinically meaningful bronchiectasis. Some clinical trials have chosen a minimal requirement of bronchiectasis in at least 2 lung lobes,[29] in keeping with the finding that the radiologic extent of bronchiectasis has been correlated with severity.[30,31]

Certain radiologic features may be associated with a certain etiology of bronchiectasis. Dextrocardia and situs inversus is the classic example and highly suggest an etiology of primary ciliary dyskinesia (PCD), but is not sensitive, as most patients with PCD do not have dextrocardia.[32] Bronchiectasis localized to a limited lung lobe or segment may suggest an endobronchial lesion—a foreign body, or a slow-growing tumor such as a carcinoid. Mucous plugging, tree-in bud infiltrates, and involvement of multiple pulmonary segments were found to be associated with infection with nontuberculous mycobacteria (NTM).[33] Several CT images of bronchiectasis are shown in **Fig. 3**.

Lung Function

Lung function may be preserved in people with bronchiectasis, especially in mild disease. In

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

Table 1
Key clinical features to seek during an initial evaluation of a person with bronchiectasis

	Clinical Feature	Typical Findings and Comments	Clinical Relevance
History: present	A description of current symptoms and their onset	Cough, sputum production (consistency[b] and quantity), shortness of breath (exertion level[c])	Bronchiectasis severity. Young age of onset should prompt seeking further clinical clues for genetic conditions, but also IBD and asthma.
	Any "chest infections" (in the preceding 12 mo)	Ask about episodes of increased cough and sputum purulence, fatigue, mild fever, hemoptysis. Look and ask for antibiotic prescriptions.	Exacerbation frequency as part of a prognostic evaluation.
History: coexisting features and past diagnoses	Smoking history		Suggests coexistence with COPD (if obstructive spirometry)
	Persistent or recurrent rhinorrhea, facial pain, loss of smell	Chronic or recurrent rhinosinusitis	Chronic rhinosinusitis is prevalent in many etiologies, but more so in CF, PCD, and asthma.
	Inflammatory conditions	Rheumatoid arthritis, Sjogren's disease, IBD	
	Infections in extrapulmonary sites	Skin infections, eczema	May suggest a primary immunodeficiency
	Hematologic and immune conditions	Typical associations are lymphoproliferative disorders	May be associated with bronchiectasis regardless of immunoglobulin levels
History: past and ongoing	Symptom onset in early life, parental consanguinity, diseased family members, a history of neonatal respiratory distress, middle ear infections, sinusitis, cardiac malformations, OTA[a] sperm defects	Neonatal respiratory distress is typical of PCD but rarely elicited in older patients	May point to an etiology of PCD
	Symptom onset in early life, parental consanguinity, diseased family members, recurrent pancreatitis, sinusitis, azoospermia in men		May point to an etiology of CF: usually pancreatic sufficient if diagnosed in adult life

(*continued on next page*)

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

Table 1
(*continued*)

	Clinical Feature	Typical Findings and Comments	Clinical Relevance
History: past and present therapies		Antibiotic use in the past year, inhalers; physical exercise and airway clearance used. What treatments did the patient find helpful?	Antibiotic use may suggest exacerbations, levels of physical activity may guide choice of AW clearance and rehabilitation therapy.
Physical examination	Body habitus	Short stature	may point to onset in early life (CF, IBD)
		Thin and tall	May suggest nodular-bronchiectatic NTM infection.
	Breath frequency		Tachypnea may point to severe bronchiectasis, or to a current severe exacerbation
	Coughing	"wet cough" may be heard	Suggestive of sputum production
	Auscultation	Rales, wheeze	Findings usually correlate with symptom severity
	Other features	Digital clubbing	Marker of severe disease
		Disfigured fingernails	Suggestive of the "yellow nail syndrome" etiology
		Dextrocardia, situs inversus	Highly suggestive of PCD

Abbreviations: CF, cystic fibrosis; NTM, nontuberculous mycobacteria; PCD, primary ciliary dyskinesia.
[a] OTA: oligo-, astheno-, terato-spermia.
[b] Sputum color and consistency may be graded according to a visual color chart.[25]
[c] Shortness of breath commonly evaluated using a modified medical research council (mMRC) scale.[26]

more advanced disease, spirometry often demonstrates a reduction in both flows (eg, FEV1) and capacities (eg, FVC) that may be proportional, typically just higher than the 70% ratio, which is the upper limit accepted as "obstructive" limitation in COPD.[7,34] In a prospective evaluation of 187 patients with bronchiectasis, Radovanovic and colleagues demonstrated that 59% of patients had a spirometry within normal limits, and that the most frequently observed functional abnormality was air trapping (70% of patients), followed by a reduction in gas diffusion (DLCO, present in 56%), airflow obstruction (in 41%), and hyperinflation (in 16%). A true restrictive ventilatory defect was present in a minority of patients (8%).[35] Owing to the wide variety in lung function, airflow abnormality is not required for making the diagnosis of bronchiectasis but does reflect bronchiectasis severity. A typical spirometry and plethysmography are shown in **Fig. 4**.

Making the Diagnosis of Bronchiectasis and Differential Diagnosis

Making the diagnosis of bronchiectasis requires that both symptoms and radiological features are present. There are cases in which radiological features are present without symptoms, or compatible symptoms without radiologic bronchiectasis. The latter case of symptoms without bronchiectasis may represent chronic airway infection and sputum production that may be termed "chronic bacterial bronchitis" or "chronic suppurative lung disease."[36] These conditions, well described in children, are thought of as predisposing to bronchiectasis and may require antimicrobial treatment and follow-up. Radiologic bronchiectasis with no symptoms does not necessitate treatment but may warrant follow-up in case symptoms develop.

Two conditions that are conventionally not regarded as bronchiectasis are traction bronchiectasis associated with idiopathic pulmonary

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

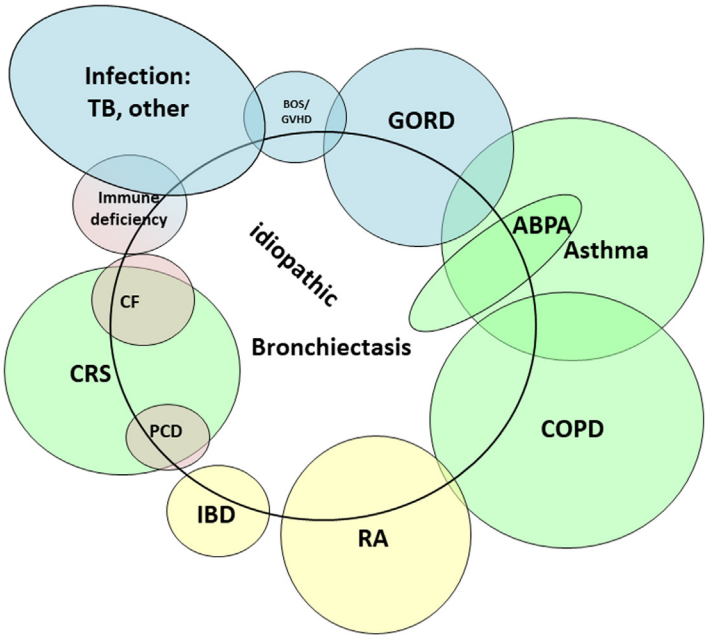

Fig. 1. Common etiologies and associations of bronchiectasis. The relative areas of overlap represent the frequency of bronchiectasis in people with each disease. Some associations exist that are not illustrated here, examples are CF and ABPA; asthma and CRS. Diseases with a clear genetic etiology are colored pink; airway diseases are colored green; and systemic inflammatory diseases are in yellow. ABPA, allergic bronchopulmonary aspergillosis; BOS, bronchiolitis obliterans; CF, cystic fibrosis; COPD, chronic obstructive pulmonary disease; CRS, chronic rhinosinusitis; CSLD, chronic suppurative lung disease; GORD, gastroesophageal reflux disorder; GVHD, graft versus host disease; IBD, inflammatory bowel disease; PBB, protracted bacterial bronchitis; RA, rheumatoid arthritis; TB, tuberculosis.

fibrosis (IPF), and cystic fibrosis (CF). In IPF, anatomic bronchiectasis is typically formed from outward mechanical traction of the bronchial walls by the surrounding fibrotic parenchyma. This entity typically is not associated with airway inflammation or infection and clinical presentation is different (dry cough and dyspnea). In CF, airway infection and inflammation are the hallmark of lung disease and are very similar to bronchiectasis, but the extrapulmonary involvement and specific treatments traditionally led to different management guidelines, and exclusion from most bronchiectasis clinical trials. However, there is not a strong reasoning why CF is excluded from "bronchiectasis" and PCD is not; CF may be viewed as one of the many etiologies of bronchiectasis and should be investigated in appropriate clinical situations.

ETIOLOGIC EVALUATION

Determining the etiology of bronchiectasis is of importance in the evaluation of patients for several reasons. First, specific etiologies such as CF, rheumatic diseases, and immune deficiencies have unique therapeutic approaches. Other genetic disorders such as PCD may have implications for screening of family members and for family planning in young patients and may in the future have specific therapies developed. Finally, many patients would like to know the cause for their illness even if there are no therapeutic implications. Recommendations for etiologic evaluation are addressed in bronchiectasis guidelines and summarized in **Table 2**. A schematic of the multidisciplinary approach to etiologic evaluation is summarized in **Fig. 5**.

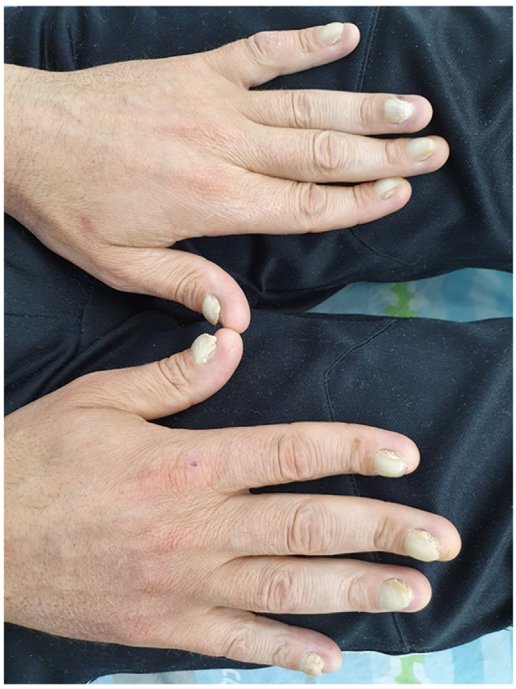

Fig. 2. Typical appearance of fingernails in a patient with the "Yellow" nail syndrome and bronchiectasis.

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

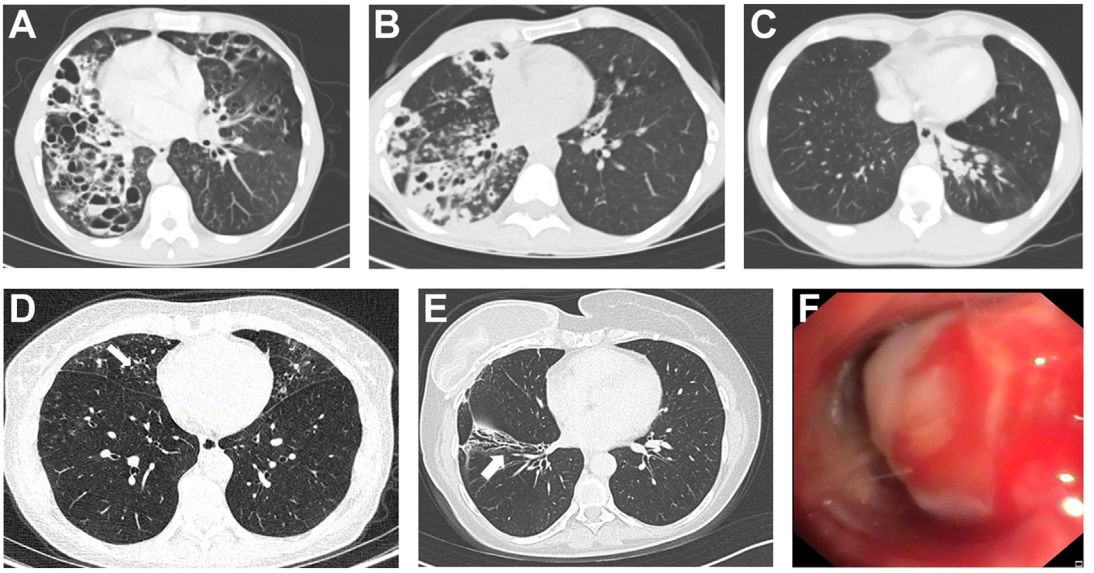

Fig. 3. Imaging of bronchiectasis. (*A*) Situs inversus and severe cystic bronchiectasis with air-fluid levels in a young man with primary ciliary dyskinesia. (*B*) Cystic bronchiectasis predominantly in the right lower lobe in a young woman with bronchiectasis and *M. simiae* infection. (*C*) Bronchiectasis filled with mucoid contents localized to the left lower lobe in a young man with hypogammaglobulinemia. (*D*) Tubular bronchiectasis in a woman with Sjogren's syndrome. The arrow points to a "signet ring" sign. (*E*) Localized varicoid bronchiectasis; bronchoscopy revealed an endobronchial tumor (*F*) with histopathologic features of a typical carcinoid. (*Courtesy of* A Abramovich, MD, Haifa, Israel.)

Genetic Disorders

CF, PCD, and primary immune deficiencies are important causes of bronchiectasis in children. CF should be sought in every child with bronchiectasis and is usually diagnosed in childhood. However, it is not unusual to diagnose PCD, atypical CF, and other less common genetic disorders in adults.[37] In patients presenting with bronchiectasis in adulthood these diseases are rare,[24,38,39] nevertheless the diagnosis of a genetic disease, if one exists, is extremely important for the treatment decisions, prognostic evaluation, and genetic counseling for the patient and family members.

The decision to screen for genetic diseases is primarily based on a compatible clinical

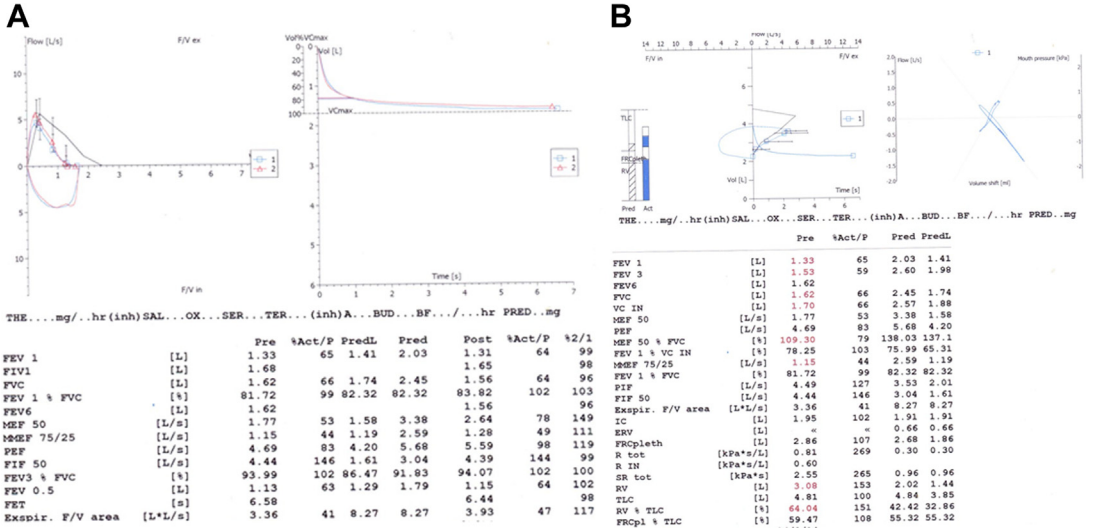

Fig. 4. Lung function in bronchiectasis. Typical spirometry (*A*) and plethysmography (*B*) of a 69-year-old woman with bronchiectasis and *M. avium* infection, demonstrating limitations in flow parameters and forced vital capacity (FVC) without reversibility (*A*), with normal total lung capacity (TLC) and increased residual volume (RV) and RV/TLC ratio. Resistance to flow is increased (*B*).

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

Table 2
Recommendations for etiologic and microbiologic evaluation—a comparison between recent management guidelines

Recommended Etiologic Evaluation:	ERS Guidelines 2017[40]	BTS 2019[42]	Spanish Guidelines 2018[41]
Recommended primary bundle of tests for all patients	Complete blood count, immunoglobulin levels, ABPA screening		
Further testing for ABPA	Specific Aspergillus IgE/skin prick test Specific Aspergillus IgG		Further testing for ABPA beyond IgE only if clinical suspicion
Further testing for Immune deficiency		Consider measuring baseline-specific antibody levels against capsular polysaccharides of *S. pneumoniae*	Serum protein electrophoresis
Recommendation for CF screening according to clinical presentation. Suggested clinical features that warrant testing:	young adults, upper lobe predominance of bronchiectasis on chest CT, sinusitis, azoospermia, pancreatitis	Infection with *S. aureus* childhood steatorrhea	family history, diabetes, ABPA
PCD screening according to diagnostic guidelines. Suggested clinical features that warrant testing:	Middle ear disease, sinusitis history of neonatal distress, symptoms from childhood, Situs anomalies Congenital cardiac defects	Male infertility	Situs anomalies
Rheumatic disease screening	Clinical evaluation for arthritis/arthralgia, morning stiffness. If present, refer to serologic testing		
Microbiologic testing:			
Sputum culture	All patients at presentation.	Repeat at least annually	
Mycobacterial culture	Not routinely, only in clinically suspected cases (based on radiology findings, symptoms, and signs)	All patients at presentation	

Recommendations for etiologic and microbiologic evaluation in all patients with bronchiectasis, and features that warrant more detailed investigations, as recommended by clinical practice care guidelines.
Abbreviations: ABPA, allergic broncho pulmonary aspergillosis; N/A, not available; SPE, serum protein electrophoresis.

presentation, therefore a thorough history taking is crucial as the first step in diagnosing these etiologies. A family history of respiratory disease in other family members or known genetic disorders in the family may also lead to screening for these causes.

Symptoms usually, but not always, start at childhood or early adulthood and the characteristics of the pulmonary disease and accompanying illness will point to the suspicious diagnosis and lead to specific screening tests.

Cystic Fibrosis

CF screening is recommended in different guidelines according to clinical presentation, with subtle differences in suggesting which individuals should undergo evaluation for CF (see **Table 2**).[40–42]

Specific imaging and clinical features should warrant referral to diagnostic testing for CF. These features include upper lobe predominance on CT with a history of recurrent respiratory infections, especially if started at an early age, chronic

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

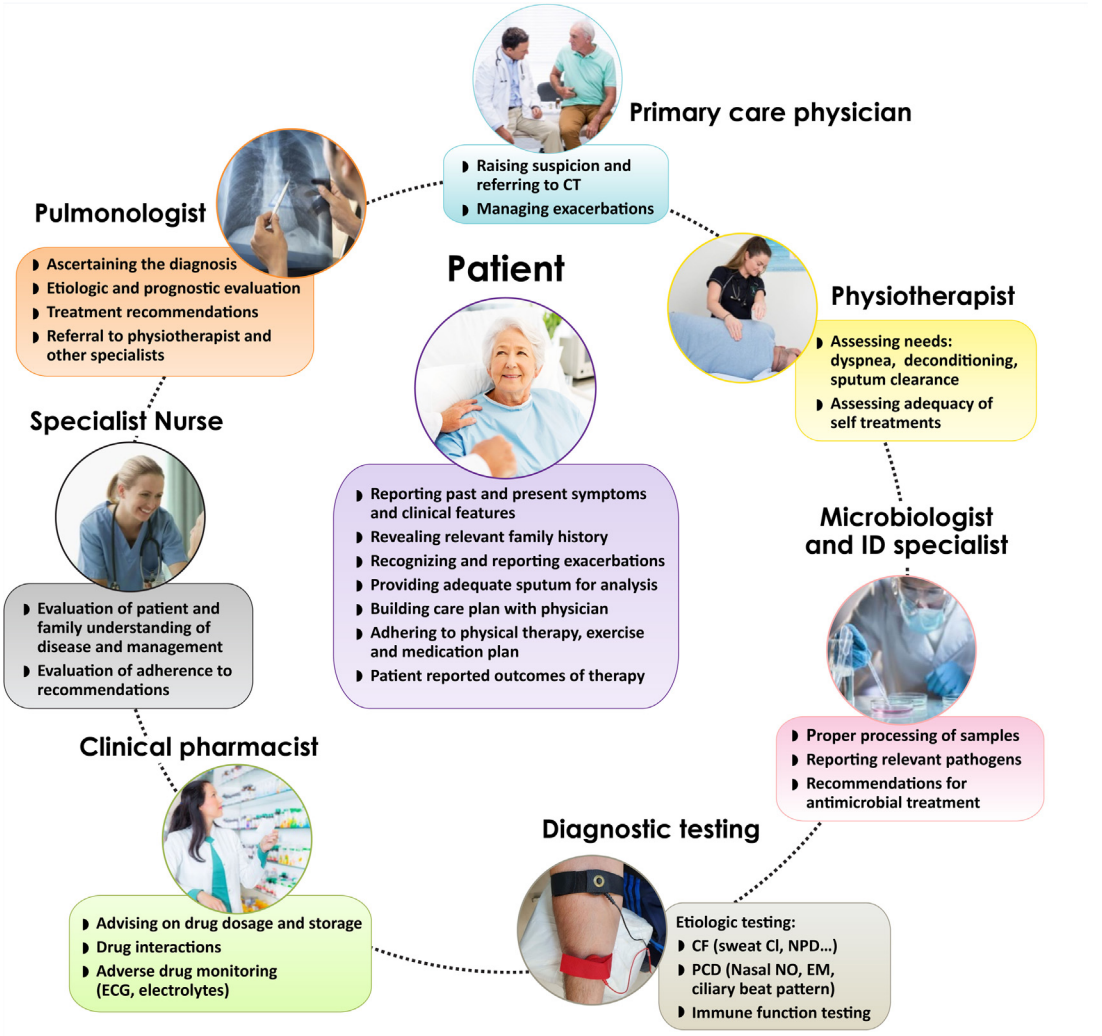

Fig. 5. Partners in bronchiectasis diagnosis and evaluation. The diagnosis of bronchiectasis requires cooperation between patient, general practitioner, and respiratory specialists. Etiologic evaluation requires close liaisons between referring clinicians and diagnostic specialists. Other partners in the evaluation of patients are listed in the schematic.

sinusitis and nasal congestion, abdominal disease—including malabsorption, intestinal obstruction, acute and/or chronic pancreatitis, and male infertility due to obstructive azoospermia. It should be kept in mind that CF presenting as an adult with bronchiectasis is very likely to be associated with pancreatic sufficiency and residual function CFTR mutations. In these cases, gastrointestinal features (except for pancreatitis) are typically absent.[43] For this reason, the Spanish guidelines recommend ruling out CF in every patient if another etiology was not found, regardless of clinical features.[41]

The first screening test suggested for CF is usually a sweat chloride test, although some diagnostic algorithms acknowledge genetic testing as a first step.[44] Over 2000 mutations in the CFTR gene have been identified to date, most of which are not CF-causing or associated with residual CFTR function (RF).[45] People with CF carrying an RF mutation typically have atypical presentation such as only respiratory system involvement, less severe disease, or a later age of presentation than expected and normal or near-normal sweat chloride and may be referred to as CFTR-related if limited to a single organ involvement. In cases where sweat or genetic testing is not diagnostic, physiologic testing such as determination of nasal potential difference and response to chloride depletion and CFTR modifying agents may aid the diagnosis.[46] Other diagnostic methods are determination of

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

intestinal current, or organelle swelling.[47] CF was reported to be the etiologic factor in between 0.6% and 2.7% of adult bronchiectasis in previously published series.[42,48]

Primary Ciliary Dyskinesia

PCD is determined as the etiology of bronchiectasis in 1% to 6.3% of adults.[11,24,38] A history of affected family members or parental consanguinity, newborn respiratory distress, onset of symptoms before 6 months of age, productive cough, upper airway disease, middle ear involvement, and sperm motility defects should suggest PCD and prompt referral to diagnostic testing. Diagnostic approaches differ between guidelines. There is no gold standard to the diagnosis, and the different diagnostic approaches require expertise and may not be widely available.[49,50] The clinical presentation and diagnostic evaluation of people with PCD is detailed in a dedicated article in this issue.

Other Genetic Diseases

Other less common genetic diseases can cause bronchiectasis but are usually not part of screening and are tested for in specific circumstances. It is recommended to screen all patients for genetic and acquired immunodeficiency at presentation with a blood count and immunoglobulin level, with or without subclasses and response to vaccine antigens. In the EMBARC bronchiectasis registry, 3.6% of patients were found to have an immunodeficiency, the most common being common variable immunodeficiency. Interestingly, these patients did not have a higher rate of exacerbations and had less severe respiratory symptoms compared with patients suffering from bronchiectasis due to other etiologies.[51] Some immunodeficiencies will be suspected due to pathologic aforementioned screening tests, but as there are hundreds of gene mutations causing immunodeficiencies in various mechanisms, patients with recurrent infections, without a clear etiology after initial evaluation, should be considered for a more thorough immunologic evaluation in the search for rare congenital (or acquired) immunodeficiencies.

α1-Antitrypsin deficiency is another rare genetic disorder associated with bronchiectasis. Its prevalence varies between different regions.[52] Patients with early-onset emphysema, especially in the lower lobes should be considered for α1AT deficiency testing. Some, such as the US Alpha-1 Foundation and Spanish bronchiectasis guidelines, recommend screening in every patient with unexplained bronchiectasis.[41,53]

Rheumatic Diseases

Several inflammatory diseases are found with increasing frequency in people with bronchiectasis, mainly RA and IBD. Diagnostic testing for these conditions is suggested according to a clinical presentation that might point to such diseases. The most common rheumatic disease associated with bronchiectasis is RA: in an EMBARC registry analysis, 7.5% of individuals with bronchiectasis had RA.[54] Patients with combined RA and bronchiectasis have increased severity[20,54] and elevated mortality.[19] A thorough inquiry regarding related symptoms such as arthritis or arthralgia of the hand joints, morning stiffness, and so forth, is strongly suggested.[54,55] Other rheumatic diseases found to be associated with bronchiectasis are Sjogren's syndrome, Marfan's syndrome, systemic sclerosis, systemic lupus erythematosus, and ankylosing spondylitis.[56]

In the presence of suggestive symptoms and/or signs, a basic serologic screening, including rheumatoid factor, anti-cyclic citrullinated peptide, and antinuclear antibody can be the first step, followed by specific serologic testing if necessary. Consideration should be given to further evaluation by a rheumatologist, as subtle clinical clues might only be apparent to experts in the field. Detecting a previously undiagnosed rheumatic disorder may alter treatment and disease management. It was demonstrated that autoantibodies associated with RA are prevalent in people with bronchiectasis without RA, and some of them later developed clinical RA.[57,58] However, recommendations for screening and treatment for early RA among people with bronchiectasis are absent.

CLINICS CARE POINT

- Determining the etiology of bronchiectasis may have important implications. Clinical care guidelines advocate initial screening for all patients, with more detailed testing when certain clinical features are present.

PROGNOSTIC EVALUATION

It is well recognized that certain features of bronchiectasis are associated with more frequent symptoms, pulmonary exacerbations and hospitalizations, and increased mortality. Some well-described markers of adverse outcomes are increased symptom burden,[59] especially dyspnea[31] and malnutrition,[31] chronic infection, particularly with *Pseudomonas aeruginosa* (PA),[59–61] previous exacerbations,[60,62] impaired lung function,[59,60,62] and concomitant COPD[63]

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

and RA.[19,64] Several international cohorts have defined clinical scoring systems that have been found to be associated with mortality and exacerbations and are summarized in **Table 3**. These parameters should be evaluated, as treatment decisions and intensity of treatment are dictated by severity.

Severity scoring systems in bronchiectasis mainly rely on objective parameters, such as radiology, lung function, and microbiology. However, increased symptom burden as assessed by quality of life (QOL) questionnaires is similarly associated with adverse outcomes.[59,62] In a recent prospective cohort of 333 patients with bronchiectasis, Gao and colleagues have demonstrated that symptom score at stable state using the St. George's respiratory questionnaire was significantly correlated with the time to a pulmonary exacerbation.[67] The authors have performed a post hoc analysis of a prospective randomized trial of inhaled mannitol, which originally did not demonstrate an overall exacerbation reduction,[68] and found an effect of the intervention in a subpopulation of patients with a high symptom score. Assessing symptoms as well as severity scores may therefore be useful to guide treatment decisions.

Several tools exist to aid evaluation of symptom severity, including dyspnea scale and QOL

Table 3
Prognostic scores for bronchiectasis[a]

Parameter	FACED[30]	E-FACED[65]	BSI[66]
FEV_1	≥50% 0	≥50% 0	>80 0 50–80 1
	<50% 2	<50% 2	30–49 2 <30 3
Body mass index			≥18.5 0 <18.5 2
Chronic PA infection	No 0 Yes 1	No 0 Yes 1	No 0 Yes 3
Chronic infection with organisms other than PA			No 0 Yes 1
Dyspnea mMRC score	0-II 0 III-IV 1	0-II 0 III-IV 1	1–3 0 4 2 5 3
Age (y)	<70 0	<70 0	<50 0 50–69 2
	≥70 2	≥70 2	70–79 4 80+ 6
Number of lobes affected [b]	1–2 0 ≥3 1	1–2 0 ≥3 1	1–2 0 ≥3 [c] 1
Hospitalization for pulmonary exacerbations [d]		0 0 ≥1 2	No 0 Yes 5
Pulmonary exacerbations without hospitalizations [d]			0–2 0 3 or more 2
Total score range	0–7	0–9	0–26
Mild severity score range	0–2 points	0–3	0–4
Moderate severity score range	3–4 points	4–6	5–8
Severe-high severity score range	5–7 points	7–9	9+

Validated prognostic scores that have been demonstrated to predict mortality and exacerbations in bronchiectasis. For each parameter, points are given according to the specified result, and a total score is comprised by summing the individual points.

Abbreviations: BSI, bronchiectasis severity index; E-FACED, *E*xacerbations, *F*EV1, *A*ge, *C*hronic infection, *E*xtent, *D*yspnea; FACED, *F*EV1, *A*ge, *C*hronic infection, *E*xtent, *D*yspnea; mMRC, modified medical research council; PA, *Pseudomonas aeruginosa*.

[a] Chronic infection: FACED scores account only PA infection; BSI takes other chronic infections as well.
[b] The number of lobes where bronchiectasis airways exist, with the lingula counted as a separate lobe.
[c] In the BSI, cystic bronchiectasis gets 3 points, similar to 3 or more lobes affected.
[d] Pulmonary exacerbations in the previous year. mMRC dyspnea score (scale of 4 for FACED, 5 for BSI).

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

questionnaires, as summarized in **Table 4**. Some questionnaires are exhaustive and are mainly used for research purposes. St. George's Respiratory Questionnaire (SGRQ)[69] and Quality of life-Bronchiectasis (QOL-B), among others, are well-known and studied questionnaires that show correlation to subjective and objective variables, such as anxiety and depression, sputum volume, and exacerbations.[70] Recently, the simple and short COPD Assessment Test (CAT) score, developed for evaluating COPD symptoms, was validated in bronchiectasis in a prospective cohort study comparing it to SGRQ, QOL-B, and also the Leicester Cough Questionnaire (LCQ), with good correlation.[71] The advantages of the CAT score are its simplicity, and familiarity to many physicians and patients from COPD practice.

MICROBIOLOGIC EVALUATION

Testing the airway microbiology is important for both chronic and exacerbation management as well as part of the prognostic importance. Management guidelines recommend that all bronchiectasis patients should have sputum samples sent for microbiology at presentation, at follow-up visits (at least annually) and also during exacerbations to guide antimicrobial therapy.[40–42] The most important culture result is the presence or absence of *Pseudomonas aeruginosa,* which has a strong influence on prognosis, including mortality and exacerbation rate,[61] and as a result requires specific treatment considerations.

Fungal cultures are not indicated routinely by guidelines. However, the detection of fungi is frequent in bronchiectasis patients, especially *Aspergillus* species. In microbiome studies, detection of *Aspergillus* in sputum was found to be associated with more frequent exacerbations, daily purulent sputum, and chronic antibiotic use.[72,73] Isolation of *Aspergillus* from a sputum sample should be followed by further investigation to the possibility of ABPA or chronic or invasive pulmonary aspergillosis, as these conditions require specific treatment.[74]

NTM pulmonary disease can cause bronchiectasis or be a complication of bronchiectasis. Most guidelines suggest testing sputum for mycobacteria at presentation and some also advocate testing at regular intervals. Mycobacterial testing is also advised in patients with deteriorating or very symptomatic disease and in those with frequent exacerbations.[40,41] Testing for mycobacteria is also important before initiating long-term antibiotic

Table 4
Comparison between commonly used symptom assessment tools in bronchiectasis

	St George's Respiratory Questionnaire	Quality of Life—Bronchiectasis	CAT
No. of questions	50 (3 domains)	37 (8 domains)	8
Score range	0–100 (0 = no symptoms, higher-worse symptoms)	0–100 (higher score = better HRQOL)	0–40 (0 = no symptoms)
Need for processing	Manual or online scoring required	Manual or online scoring required	Not required
Internal consistency (Cronbach α coefficient, >0.7 considered acceptable)	0.59–0.92	0.65–0.91	0.84–0.88
MCID	Not reported for bronchiectasis. 4–5.8 units for COPD	7–10 units	4 units
Correlation with other outcome measures	• Exacerbations • Extent of bronchiectasis on CT • *Pseudomonas aeruginosa* • Sputum volume	• Extent of bronchiectasis on CT • Sputum volume	• FEV1 • 6-min-walk distance • BSI

Different QOL questionnaires reviewed in a meta-analysis by Spinou et al., Thorax 2016.[70] CAT from Finch et al., Chest 2020.[71]

Abbreviations: BSI, bronchiectasis severity index; CAT, COPD assessment test; HRQOL, health-related quality of life; MCID, minimal clinically important difference.

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

treatment with a macrolide because monotherapy can cause the emergence of macrolide-resistant mycobacteria, which can be extremely difficult to treat.

Sputum Sampling and Processing

Obtaining and processing an adequate sputum sample should meet acceptable quality criteria, such as recommended by the Infectious Disease and Microbiology specialist consensus guidelines.[75,76] Sputum should be expectorated into a sterile container, the first morning sputum being the most diagnostic. Sputum volume should be at least 2 ml and the sputum should not be kept for more than 2 hours at room temperature, or 18 hours if refrigerated before processing. Laboratories should test sputum samples for acceptability, to exclude samples most likely originating from the upper airways. This is achieved by analyzing the predominant type of cells seen in the culture, with squamous epithelial cells pointing to secretions originating in the oropharyngeal area and inflammatory cells originations from the site of inflammation, presumably the lower respiratory tract. Good quality sputum samples have a higher yield for diagnosing the correct pathogen. Nonacceptable samples should be rejected. For patients unable to produce a good sputum sample, obtaining a bronchoalveolar lavage sample should be considered.

FOLLOW-UP AND EVALUATION OF TREATMENT OUTCOMES

The goal of treatment is an improvement in daily symptoms as well as reduced rate of exacerbations. Assessing these outcomes in patients' needs to be done periodically, to detect suboptimal response, or a deteriorating condition that may warrant a change in treatment. After presentation, a common approach is to evaluate the patient after 3 to 6 months depending on the severity of symptoms at presentation. Thereafter, the patient should be evaluated at least once a year, with more frequent follow-up in cases of uncontrolled symptoms or recurrent exacerbations.[42]

Evaluation of the patient with bronchiectasis should include an evaluation of symptom burden and frequency of exacerbations. It is also important to appreciate the rate of pulmonary function decline as compared to expected per age. Some bronchiectasis patients will show a rapid decline and should be treated and followed more intensively. Although not suggested by practice guidelines, it is reasonable to repeat spirometry once a year for follow-up of pulmonary function.[77] More frequent testing is advised in case of worsening symptoms or severe disease.[42]

Most patients will have a baseline CT scan as part of their initial diagnosis and prognostic assessment. Repeating the CT scan periodically, however, has implications such as in radiation exposure, cost, and utilization of health resources, and is probably not necessary for many patients. Repeating a CT scan should be considered in rapidly deteriorating patients or when related conditions such as mycobacterial disease or ABPA are suspected.

Evaluation of Adherence to Treatment

Evaluation and treatment of bronchiectasis involve many aspects of care, including specialized tests, airway clearance and physical activity, inhaled and oral medications, immunizations, and early recognition of exacerbations.[40,41] These many aspects require dedication of time and emotional resources by the patient and may impose a burden on the daily life of patients. In a prospective study of 75 individuals with bronchiectasis prescribed inhaled antibiotics, adherence to treatment was assessed by structured questionnaires and evaluation of the "medication possession ratio" (MPR, the ratio between actual filling of prescriptions and recommended dosing). It was found that adherence to medications is overestimated by patients, as results of self-reports were higher than MPR. Adherence rates were generally poor, with 41% for airway clearance (by self-reporting), 53% for inhaled antibiotics, and 54% for other respiratory medications. It was found that adherence to treatment over the study period was significantly associated with older age, less prescribed medications, and lower treatment burden (per Quality of Life—Bronchiectasis questionnaire—Treatment Burden domain), and with beliefs of necessity and safety of treatments.[78]

These findings highlight the importance of regularly assessing adherence to treatment recommendations, especially in patients who continue to experience symptoms and exacerbations despite treatment. They also emphasize the importance of patient education and engagement of patients as partners in the treatment (see **Fig. 5**). Treatment burden should be assessed, and treatment regime regularly reviewed to ensure compatibility with the patient's lifestyle and needs. Ways to achieve this may be through individual education of the patient and caregivers by health care staff, through participation in education programs including rehabilitation programs, and through referral to Internet resources (**Box 1**). However, data on the efficacy of programs to enhance patients' adherence to treatments are sparse,[79] and studies are needed on these strategies.

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

Box 1
Internet resources with information on bronchiectasis for patients and health care providers

- ELF—European lung foundation—for patients. Covers general overview of bronchiectasis, physiotherapy, patient checklist, information regarding infections, available treatments, and drugs in development. Contains videos demonstrating airway clearance techniques. https://www.europeanlung.org/en/lung-disease-and-information/lung-diseases/bronchiectasis; https://www.europeanlungino.org/bronchiectasis
- EMBARC—European registry site, contains information for health care professionals and patients. https://www.bronchiectasis.eu/
- Bronchiectasis toolbox—by the Australian thoracic society—for patients. Covers general overview of bronchiectasis, physiotherapy, patient checklist, information regarding infections, available treatments, and drugs in development. Contains videos of AW clearance techniques. https://bronchiectasis.com.au/
- Bronchiectasis severity (BSI) online calculator: http://www.bronchiectasisseverity.com

CLINICS CARE POINTS

- A diagnosis of bronchiectasis requires that both symptoms and radiological features are present.
- Bronchiectasis may coexist with other airway diseases. Sputum production and frequent infectious exacerbations should prompt a referral to HRCT to look for bronchiectasis.
- Bronchiectasis may complicate rheumatic disorders and inflammatory bowel disease. Respiratory symptoms in such patients should raise a suspicion of bronchiectasis.
- Features associated with severity of bronchiectasis include older age, lower lung function, dyspnea, chronic infection with *Pseudomonas aeruginosa*, frequent hospitalizations and exacerbations, and radiologic severity.
- Prognostic scores and symptom scores are useful to predict outcomes.
- Adherence to treatment recommendations is frequently suboptimal and related to treatment burden and beliefs toward treatments.
- Adherence is highly associated with treatment outcomes and should be regularly assessed.
- Educating patients is likely to improve adherence and outcomes. Several programs and educational materials are available.

SUMMARY

Evaluation of the patient with bronchiectasis is an ongoing effort, starting with determination of the diagnosis, and continuing with etiologic and prognostic evaluation, including assessment of airway infection. As clinical clues may appear after the initial evaluation, and clinical severity may change over time, repeating etiologic and prognostic evaluation needs to be assessed periodically. Evaluation response to treatment is important to optimize outcomes and reduce treatment burden. A partnership between patients, health care providers frequently necessitating multidisciplinary collaboration, is key to treatment success.

DISCLOSURE

Dr M. Shteinberg has received research grants from Novartis, Israel; Trudell pharma, Canada; GSK- Israel; travel grants from Novartis, Actelion, Boeringer Ingelheim, GSK, Rafa; speaker's fees from Boeringer Ingelheim, GSK, Astra Zeneca, Teva, Novartis, Kamada; and advisory fees from GSK, Boeringer Ingelheim, Zambon, Vertex pharmaceuticals. Dr M. Shteinberg is a member of the EMBARC group management. Dr R. Cohen has nothing to disclose.

REFERENCES

1. Quint JK, Millett ERC, Joshi M, et al. Changes in the incidence, prevalence and mortality of bronchiectasis in the UK from 2004 to 2013: a population-based cohort study. Eur Respir J 2016;47(1):186–93.
2. Ringshausen FC, de Roux A, Diel R, et al. Bronchiectasis in Germany: a population-based estimation of disease prevalence. Eur Respir J 2015;46(6):1805–7.
3. Monteagudo M, Rodríguez-Blanco T, Barrecheguren M, et al. Prevalence and incidence of bronchiectasis in Catalonia, Spain: a population-based study. Respir Med 2016;121:26–31.
4. Sakula ARTH. Laënnec 1781–1826 his life and work: a bicentenary appreciation. Thorax 1981;36(2):81–90.
5. Aliberti S, Goeminne PC, O'Donnell AE, et al. Criteria and definitions for the radiological and clinical diagnosis of bronchiectasis in adults for use in clinical trials: international consensus recommendations. Lancet Respir Med 2021. https://doi.org/10.1016/S2213-2600(21)00277-0.
6. Dimakou K, Triantafillidou C, Toumbis M, et al. Non CF-bronchiectasis: aetiologic approach, clinical, radiological, microbiological and functional profile in 277 patients. Respir Med 2016;116:1–7.

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

7. Eden E, Choate R, Barker A, et al. The clinical features of bronchiectasis associated with alpha-1 antitrypsin deficiency, common variable immunodeficiency and primary ciliary dyskinesia–results from the U.S. Bronchiectasis research registry. Chronic Obstr Pulm Dis (Miami) 2019;6(2):145–53.
8. Aliberti S, Lonni S, Dore S, et al. Clinical phenotypes in adult patients with bronchiectasis. Eur Respir J 2016;47(4):1113–22.
9. Hill AT, Haworth CS, Aliberti S, et al. Pulmonary exacerbation in adults with bronchiectasis: a consensus definition for clinical research. Eur Respir J 2017;49(6). https://doi.org/10.1183/13993003.00051-2017.
10. Aksamit TR, O'Donnell AE, Barker A, et al. Adult patients with bronchiectasis: a first look at the US bronchiectasis research registry. Chest 2017;151(5):982–92.
11. Dhar R, Singh S, Talwar D, et al. Bronchiectasis in India: results from the European multicentre bronchiectasis audit and research collaboration (EMBARC) and respiratory research Network of India registry. Lancet Glob Health 2019;7(9):e1269–79.
12. McDonnell MJ, Aliberti S, Goeminne PC, et al. Comorbidities and the risk of mortality in patients with bronchiectasis: an international multicentre cohort study. Lancet Respir Med 2016;4(12):969–79.
13. Porsbjerg C, Menzies-Gow A. Co-morbidities in severe asthma: clinical impact and management. Respirology 2017;22(4):651–61.
14. Dimakou K, Gousiou A, Toumbis M, et al. Investigation of bronchiectasis in severe uncontrolled asthma. Clin Respir J 2018;12(3):1212–8.
15. Tan WC, Hague CJ, Leipsic J, et al. Findings on thoracic computed tomography scans and respiratory outcomes in persons with and without chronic obstructive pulmonary disease: a population-based cohort study. PLoS One 2016;11(11):e0166745.
16. Martínez-García MÁ, Soler-Cataluña JJ, Donat Sanz Y, et al. Factors associated with bronchiectasis in patients with COPD. Chest 2011;140(5):1130–7.
17. Polverino E, Dimakou K, Hurst J, et al. The overlap between bronchiectasis and chronic airway diseases: state of the art and future directions. Eur Respir J 2018;52(3). https://doi.org/10.1183/13993003.00328-2018.
18. Shteinberg M, Nassrallah N, Jrbashyan J, et al. Upper airway involvement in bronchiectasis is marked by early onset and allergic features. ERJ Open Res 2018;4(1). https://doi.org/10.1183/23120541.00115-2017.
19. De Soyza A, McDonnell MJ, Goeminne PC, et al. Bronchiectasis rheumatoid overlap syndrome is an independent risk factor for mortality in patients with bronchiectasis: a multicenter cohort study. Chest 2017;151(6):1247–54.
20. Perry E, Eggleton P, De Soyza A, et al. Increased disease activity, severity and autoantibody positivity in rheumatoid arthritis patients with co-existent bronchiectasis. Int J Rheum Dis 2015. https://doi.org/10.1111/1756-185X.12702.
21. Soto-Cardenas MJ, Perez-De-Lis M, Bove A, et al. Bronchiectasis in primary Sjögren's syndrome: prevalence and clinical significance. Clin Exp Rheumatol 2010;28(5):647–53.
22. Lhote R, Chilles M, Groh M, et al. Spectrum and prognosis of antineutrophil cytoplasmic antibody-associated vasculitis-related bronchiectasis: data from 61 patients. J Rheumatol 2020;47(10):1522–31.
23. Kelly MG, Frizelle FA, Thornley PT, et al. Inflammatory bowel disease and the lung: is there a link between surgery and bronchiectasis? Int J Colorectal Dis 2006;21(8):754–7.
24. Araújo D, Shteinberg M, Aliberti S, et al. Standardised classification of the aetiology of bronchiectasis using an objective algorithm. Eur Respir J 2017;50(6). https://doi.org/10.1183/13993003.01289-2017.
25. Murray MP, Pentland JL, Turnbull K, et al. Sputum colour: a useful clinical tool in non-cystic fibrosis bronchiectasis. Eur Respir J 2009;34(2):361–4.
26. Bestall JC, Paul EA, Garrod R, et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax 1999;54(7):581–6.
27. Hansell DM, Bankier AA, MacMahon H, et al. Fleischner Society: glossary of terms for thoracic imaging. Radiology 2008;246(3):697–722.
28. Diaz AA, Young TP, Maselli DJ, et al. Bronchoarterial ratio in never-smokers adults: implications for bronchial dilation definition. Respirology 2017;22(1):108–13.
29. Aksamit T, Bandel T-J, Criollo M, et al. The RESPIRE trials: two phase III, randomized, multicentre, placebo-controlled trials of Ciprofloxacin Dry Powder for Inhalation (Ciprofloxacin DPI) in non-cystic fibrosis bronchiectasis. Contemp Clin Trials 2017;58:78–85.
30. Martínez-García MÁ, de Gracia J, Vendrell Relat M, et al. Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. Eur Respir J 2014;43(5):1357–67.
31. Onen ZP, Gulbay BE, Sen E, et al. Analysis of the factors related to mortality in patients with bronchiectasis. Respir Med 2007;101(7):1390–7.
32. Dettmer S, Ringshausen F, Vogel-Claussen J, et al. Computed tomography in adult patients with primary ciliary dyskinesia: typical imaging findings. PLoS One 2018;13(2):e0191457.
33. Eisenberg I, Yasin A, Fuks L, et al. Radiologic characteristics of non-tuberculous mycobacteria

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

infection in patients with bronchiectasis. Lung 2020; 198(4):715–22.
34. Halpin DMG, Criner GJ, Papi A, et al. Global initiative for the diagnosis, management, and prevention of chronic obstructive lung disease. The 2020 GOLD Science Committee Report on COVID-19 and Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med 2021;203(1):24–36.
35. Radovanovic D, Santus P, Blasi F, et al. A comprehensive approach to lung function in bronchiectasis. Respir Med 2018;145:120–9.
36. Chang AB, Bell SC, Torzillo PJ, et al. Chronic suppurative lung disease and bronchiectasis in children and adults in Australia and New Zealand Thoracic Society of Australia and New Zealand guidelines. Med J Aust 2015;202(1):21–3.
37. Chang AB, Bush A, Grimwood K. Bronchiectasis in children: diagnosis and treatment. Lancet 2018; 392(10150):866–79.
38. Visser SK, Bye PTP, Fox GJ, et al. Australian adults with bronchiectasis: the first report from the Australian Bronchiectasis Registry. Respir Med 2019;155: 97–103.
39. Gao Y-H, Guan W-J, Liu S-X, et al. Aetiology of bronchiectasis in adults: a systematic literature review. Respirology 2016;21(8):1376–83.
40. Polverino E, Goeminne PC, McDonnell MJ, et al. European Respiratory Society guidelines for the management of adult bronchiectasis. Eur Respir J 2017; 50(3). https://doi.org/10.1183/13993003.00629-2017.
41. Martínez-García MÁ, Máiz L, Olveira C, et al. Spanish guidelines on the evaluation and diagnosis of bronchiectasis in adults. Arch Bronconeumol 2018; 54(2):79–87.
42. Hill AT, Sullivan AL, Chalmers JD, et al. British thoracic society guideline for bronchiectasis in adults. Thorax 2019;74(Suppl 1):1–69.
43. Padoan R, Quattrucci S, Amato A, et al. The diagnosis of cystic fibrosis in adult age. Data from the Italian registry. Diagnostics (Basel) 2021;11(2). https://doi.org/10.3390/diagnostics11020321.
44. De Boeck K, Wilschanski M, Castellani C, et al. Cystic fibrosis: terminology and diagnostic algorithms. Thorax 2006;61(7):627–35.
45. CFTR-, clinical and functional translation of CFTR, CFTR2@Johns Hopkins - https://cftr2.org.
46. Aalbers BL, Yaakov Y, Derichs N, et al. Nasal potential difference in suspected cystic fibrosis patients with 5T polymorphism. J Cyst Fibros 2020;19(4):627–31.
47. De Boeck K, Vermeulen F, Dupont L. The diagnosis of cystic fibrosis. Presse Med 2017;46(6 Pt 2):e97–108.
48. Villanueva G, Marceniuk G, Murphy MS, et al, Guideline Committee. Diagnosis and management of cystic fibrosis: summary of NICE guidance. BMJ 2017;359:j4574.
49. Shapiro AJ, Davis SD, Polineni D, et al. Diagnosis of primary ciliary dyskinesia. an official american thoracic society clinical practice guideline. Am J Respir Crit Care Med 2018;197(12):e24–39.
50. Lucas JS, Barbato A, Collins SA, et al. European Respiratory Society guidelines for the diagnosis of primary ciliary dyskinesia. Eur Respir J 2017;49(1). https://doi.org/10.1183/13993003.01090-2016.
51. Mitchelmore P, Polverino E, Rademacher J, et al. Immunodeficiency associated bronchiectasis in the European bronchiectasis registry (EMBARC). In: Allergy and immunology. European Respiratory Society; 2020. p. 2057. https://doi.org/10.1183/13993003.congress-2020.2057.
52. Loebinger M, Aliberti S, Menendez R, et al. Alpha-1 antitrypsin deficiency in patients with bronchiectasis: data from the European Bronchiectasis Registry EMBARC. In: Respiratory infections. European Respiratory Society; 2020. p. 3330. https://doi.org/10.1183/13993003.congress-2020.3330.
53. Cazzola M, Stolz D, Rogliani P, et al. α1-Antitrypsin deficiency and chronic respiratory disorders. Eur Respir Rev 2020;29(155). https://doi.org/10.1183/16000617.0073-2019.
54. De Soyza A, McDonnell MJ, Davidson J, et al. Rheumatoid arthritis is a common and important comorbidity in bronchiectasis: data from the EMBARC European bronchiectasis registry. In: 10.1 respiratory infections. European Respiratory Society; 2016. p. PA1541. https://doi.org/10.1183/13993003.congress-2016.PA1541.
55. Huang S, Doyle TJ, Hammer MM, et al. Rheumatoid arthritis-related lung disease detected on clinical chest computed tomography imaging: prevalence, risk factors, and impact on mortality. Semin Arthritis Rheum 2020;50(6):1216–25.
56. Maglione M, Aksamit T, Santamaria F. Paediatric and adult bronchiectasis: specific management with coexisting asthma, COPD, rheumatological disease and inflammatory bowel disease. Respirology 2019;24(11):1063–72.
57. Perry E, Stenton C, Kelly C, et al. RA autoantibodies as predictors of rheumatoid arthritis in non-cystic fibrosis bronchiectasis patients. Eur Respir J 2014; 44(4):1082–5.
58. Clarke A, Perry E, Kelly C, et al. Heightened autoantibody immune response to citrullinated calreticulin in bronchiectasis: implications for rheumatoid arthritis. Int J Biochem Cell Biol 2017;89:199–206.
59. Loebinger MR, Wells AU, Hansell DM, et al. Mortality in bronchiectasis: a long-term study assessing the factors influencing survival. Eur Respir J 2009; 34(4):843–9.
60. Martínez-García MA, Soler-Cataluña J-J, Perpiñá-Tordera M, et al. Factors associated with lung function decline in adult patients with stable non-cystic fibrosis bronchiectasis. Chest 2007;132(5):1565–72.
61. Araújo D, Shteinberg M, Aliberti S, et al. The independent contribution of Pseudomonas aeruginosa

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.

infection to long-term clinical outcomes in bronchiectasis. Eur Respir J 2018;51(2). https://doi.org/10.1183/13993003.01953-2017.
62. Martínez-García MA, Perpiñá-Tordera M, Román-Sánchez P, et al. Quality-of-life determinants in patients with clinically stable bronchiectasis. Chest 2005;128(2):739–45.
63. Goeminne PC, Nawrot TS, Ruttens D, et al. Mortality in non-cystic fibrosis bronchiectasis: a prospective cohort analysis. Respir Med 2014;108(2):287–96.
64. Swinson DR, Symmons D, Suresh U, et al. Decreased survival in patients with co-existent rheumatoid arthritis and bronchiectasis. Br J Rheumatol 1997;36(6):689–91.
65. Martinez-Garcia MA, Athanazio RA, Girón R, et al. Predicting high risk of exacerbations in bronchiectasis: the E-FACED score. Int J Chron Obstruct Pulmon Dis 2017;12:275–84.
66. Chalmers JD, Goeminne P, Aliberti S, et al. The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med 2014;189(5):576–85.
67. Gao Y-H, Abo Leyah H, Finch S, et al. Relationship between symptoms, exacerbations, and treatment response in bronchiectasis. Am J Respir Crit Care Med 2020;201(12):1499–507.
68. Bilton D, Tino G, Barker AF, et al. Inhaled mannitol for non-cystic fibrosis bronchiectasis: a randomised, controlled trial. Thorax 2014;69(12):1073–9.
69. Wilson CB, Jones PW, O'Leary CJ, et al. Validation of the St. George's respiratory questionnaire in bronchiectasis. Am J Respir Crit Care Med 1997;156(2 Pt 1):536–41.
70. Spinou A, Fragkos KC, Lee KK, et al. The validity of health-related quality of life questionnaires in bronchiectasis: a systematic review and meta-analysis. Thorax 2016;71(8):683–94.
71. Finch S, Laska IF, Abo-Leyah H, et al. Validation of the COPD assessment test (CAT) as an outcome measure in bronchiectasis. Chest 2020;157(4):815–23.
72. Mac Aogáin M, Chandrasekaran R, Lim AYH, et al. Immunological corollary of the pulmonary mycobiome in bronchiectasis: the CAMEB study. Eur Respir J 2018;52(1). https://doi.org/10.1183/13993003.00766-2018.
73. Máiz L, Vendrell M, Olveira C, et al. Prevalence and factors associated with isolation of Aspergillus and Candida from sputum in patients with non-cystic fibrosis bronchiectasis. Respiration 2015;89(5):396–403.
74. Chotirmall SH, Martin-Gomez MT. Aspergillus Species in bronchiectasis: challenges in the cystic fibrosis and non-cystic fibrosis airways. Mycopathologia 2018;183(1):45–59.
75. Miller JM, Binnicker MJ, Campbell S, et al. A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the infectious diseases society of America and the american society for microbiology. Clin Infect Dis 2018;67(6):e1–94.
76. Popova G, Boskovska K, Arnaudova-Danevska I, et al. Sputum quality assessment regarding sputum culture for diagnosing lower respiratory tract infections in children. Open Access Maced J Med Sci 2019;7(12):1926–30.
77. Chalmers JD, Aliberti S, Polverino E, et al. The EMBARC European Bronchiectasis Registry: protocol for an international observational study. ERJ Open Res 2016;2(1). https://doi.org/10.1183/23120541.00081-2015.
78. McCullough AR, Tunney MM, Stuart Elborn J, et al. Predictors of adherence to treatment in bronchiectasis. Respir Med 2015;109(7):838–45.
79. McCullough A, Thomas ET, Ryan C, et al. Interventions for enhancing adherence to treatment in adults with bronchiectasis. Cochrane Database Syst Rev 2015;11:CD011023.

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en marzo 16, 2022. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2022. Elsevier Inc. Todos los derechos reservados.