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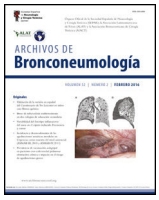

SEPAR's voice

Spanish Guidelines on the Evaluation and Diagnosis of Bronchiectasis in Adults☆

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ABSTRACT

In 2008, the Spanish Society of Pulmonology (SEPAR) published the first guidelines in the world on the diagnosis and treatment of bronchiectasis. Almost 10 years later, considerable scientific advances have been made in both the treatment and the evaluation and diagnosis of this disease, and the original guidelines have been updated to include the latest scientific knowledge on bronchiectasis. These new recommendations have been drafted following a strict methodological process designed to ensure the quality of content, and are linked to a large amount of online information that includes a wealth of references. These guidelines cover aspects ranging from a consensual definition of bronchiectasis to an evaluation of the natural course and prognosis of the disease. The topics of greatest interest and some new areas are addressed, including epidemiology and economic costs of bronchiectasis, pathophysiological aspects, the causes (placing particular emphasis on the relationship with other airway diseases such as chronic obstructive pulmonary disease and asthma), clinical and functional aspects, measurement of quality of life, radiological diagnosis and assessment, diagnostic algorithms, microbiological aspects (including the definition of key concepts, such as bacterial eradication or chronic bronchial infection), and the evaluation of severity and disease prognosis using recently published multidimensional tools.

Normativa sobre la valoración y el diagnóstico de las bronquiectasias en el adulto

Palabras clave:
Bronquiectasias
Infección bronquial
FACED
E-FACED
Pseudomonas aeruginosa
Tomografía computarizada de alta resolución

RESUMEN

En 2008 la Sociedad Española de Neumología y Cirugía Torácica (SEPAR) publicó las primeras normativas del mundo sobre el diagnóstico y tratamiento de las bronquiectasias. Tras casi una década muchos han sido los avances científicos en esta enfermedad, no solo en sus aspectos terapéuticos, sino también en su valoración y diagnóstico. Por ello, estas nuevas normativas sobre *la valoración y diagnóstico de las bronquiectasias* tratan de ofrecer al lector una actualización del conocimiento científico sobre las bronquiectasias basándose en un estricto procedimiento metodológico que asegura la calidad del contenido de las mismas, y en una amplia cantidad de información *online* que incluye abundante

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bibliografía. Estas normativas recogen desde una definición consensuada de bronquiectasias hasta la valoración de la historia natural y del pronóstico de la enfermedad. Se tratan los temas de mayor interés y algunos novedosos, como epidemiología y costes económicos de las bronquiectasias, aspectos fisiopatológicos, etiología (haciendo especial énfasis en la relación con otras enfermedades de la vía aérea como la enfermedad pulmonar obstructiva crónica y el asma), aspectos clínico-funcionales, medición de la calidad de vida, diagnóstico y valoración radiológica, algoritmo diagnóstico, aspectos microbiológicos (incluyendo la definición consensuada de conceptos clave como el de erradicación bacteriana o infección bronquial crónica), así como la valoración de la gravedad y el pronóstico de la enfermedad mediante el uso de las nuevas herramientas multidimensionales publicadas.

Introduction

Non-cystic fibrosis (CF) bronchiectasis (BE) is the third most common chronic inflammatory disease of the airways after asthma and chronic obstructive pulmonary disease (COPD), and is closely related to both. In 2008, the Spanish Society of Pulmonology and Thoracic Surgery (SEPAR) became the first scientific society to establish guidelines on the diagnosis and treatment of this disease, including CF.[1] More than 8 years later, the scientific evidence on BE has become clearer on a number of major issues, and the findings of recent studies have compelled us to publish these new guidelines, which, in order to provide the reader with more specific information, will focus solely on BE in adults. This first section will be devoted to the assessment and diagnosis of BE. The guidelines have been prepared with the advice of an expert in methodology. A Delphi system was used to create the list of topics, prioritizing the clinical questions (Annex 1, Methodology). Key clinical questions were structured according to the Patient-Intervention-Comparison-Outcome (PICO) system, and appear as an annex at the end of the manuscript (Annex 3).

Finally, the certainty of the evidence and the strength of the recommendations were established following the Grades of Recommendation Assessment, Development and Evaluation (GRADE) system (Annex 4 online. This annex contains an extensive set of literature references for each of the points discussed in these guidelines).

Definition

Bronchiectasis is a chronic inflammatory bronchial disease with irreversible dilatation of the bronchial lumen that can be caused by different etiologies. Clinically, it usually presents with chronic cough and expectoration, as well as recurrent infectious exacerbations. It can cause chronic bronchial infection and a progressive decline in lung function, all of which can lead to a deterioration in quality of life and increased morbidity and mortality. Traction BE, secondary to another lung disease (interstitial or emphysematous), is not considered in the present guidelines.

Epidemiology and Costs

Although the actual prevalence of BE is unknown, it is estimated to be between 42 and 566 cases per 100 000 population (higher in women and the elderly), although it is recognized as being significantly underdiagnosed. These figures confirm that it is not a rare disease, as it exceeds the 5 cases per 10 000 population established in the definition of orphan disease in Europe. We are currently witnessing a major increase in the number of cases diagnosed with BE, possibly due to the growing longevity of the population, the chronic nature of underlying diseases, the recently observed association between BE and other highly prevalent entities (such as asthma or COPD) and, above all, the widespread use of imaging techniques to confirm diagnosis (chest high-resolution computed tomography [HRCT]). The cost of BE is high (the average cost of annual treatment in Spain is estimated to be close to €4700), and is greater the more severe the disease (around €10 000 annually in severe cases), if there is coexisting COPD, a higher number of exacerbations, and when there is chronic bronchial *Pseudomonas aeruginosa* infection. Most of the cost is due to exacerbations and inhaled antibiotic treatment in severe BE. Cost-effectiveness studies of currently available treatments for BE are needed.[2,3]

Physiopathology

BE is the result of a complex vicious circle consisting of lesion of the mucociliary system, inflammation, infection and airway repair, which differ according to the specific etiology that triggers the initial abnormality. Damage to the mucociliary system makes it difficult to eliminate secretions and facilitates bacterial growth and bronchial inflammation, with the latter 2 being responsible for the bronchial structural damage and perpetuation of the vicious pathogenic circle (Fig. 1). An imbalance between pro- and anti-inflammatory products, and persistent infection and inflammation despite the immune response and treatment, could play an important role in disease progression. Inflammation of the airways has a neutrophilic profile. A high percentage of patients with BE also present systemic inflammation in the stable phase of the disease, which has been related with more severe forms.[4,5]

Etiology

BE can be caused by a number of different etiologies, both pulmonary and systemic. The relative frequency of these etiologies depends on the geographical area in which it is studied, the characteristics of the patient and the clinic attended (general or specialized clinics). The post-infection forms are the most common in most series (Table 1). *BEs of unknown origin (or idiopathic)* are considered to be those in which the cause is unknown despite a comprehensive etiological study (Fig. 2, diagnostic algorithm), and could account for between 25% and 45% of cases, according to the series.[6–8] It is believed that a significant percentage of these BE could be due to selective immune deficiencies, gastroesophageal reflux, infections not reported by the patient or other airway diseases such as COPD or asthma.

Relationship Between Bronchiectasis and Chronic Obstructive Pulmonary Disease

Between 30% and 50% of patients with severe COPD have BE, and its prevalence increases with the severity of the COPD, while 5%–10% of patients with BE have associated COPD.[6–8] Patients with COPD and BE make up a clinical group or phenotype with its own characteristics (greater production and purulence of sputum, more dyspnea and a higher number of exacerbations), worse prognosis and possible therapeutic implications. HRCT should be performed to rule out the presence of BE in patients with moderate or severe

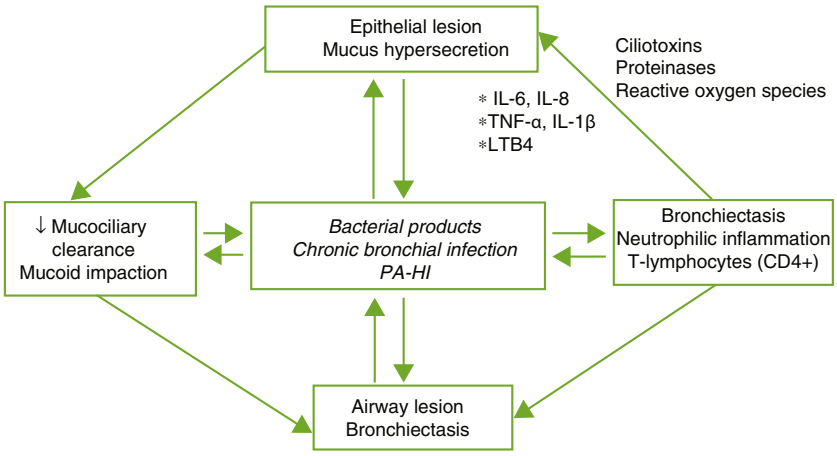


Fig. 1. Pathogenesis of bronchiectasis. HI: *Haemophilus influenzae*; IL: interleukin; LTB4: leukotriene B4; PA: *Pseudomonas aeruginosa*; TNF: tumor necrosis factor. *Adapted from: Fuschillo et al.*[4]

Table 1
Etiology and Diseases Associated With Bronchiectasis.

Post-infectious (30%)	Bacteria, Tuberculosis, NTM, viruses and fungi
Associated with chronic respiratory disease (6.3%–13.7%)	COPD (3.9%–7.8%), bronchial asthma (1.4%–5.4%), α-1 antitrypsin deficiency
Immune deficiencies (5%–9.4%)	Primary: humoral, cellular or combined quantitative or qualitative deficiencies. Secondary: neoplasms, HIV, other viruses, biological and immunosuppressant treatment
Associated with systemic diseases (1.4%–3.8%)	Rheumatoid arthritis, lupus, Sjögren syndrome, Marfan syndrome, recurrent polychondritis, ankylosing spondylitis, sarcoidosis, inflammatory bowel disease
Hypersensitivity (0.9%–2.6%)	Allergic bronchopulmonary aspergillosis
Ciliary dyskinesias (2.5%–29%)	Primary ciliary dyskinesia, Young syndrome
Local causes (obstructive) (<1%)	Intrinsic (tumors, foreign bodies, stenosis). Extrinsic (tumors, lymphadenopathies)
Post-transplant (<1%)	Bronchiolitis obliterans or graft-*versus*-host disease
Post-inflammatory pneumonitis (<1%)	Aspiration, gastroesophageal reflux, radiotherapy, inhalation of toxic gases or drugs
Others (<1%)	Yellow nail syndrome, diffuse panbronchiolitis, Swyer-James syndrome, congenital defects of the tracheobronchial tree, endometriosis, amyloidosis
Unknown etiology (24.2%–44.8%)	

COPD: chronic obstructive pulmonary disease; HIV: human immunodeficiency virus; NTM: non-tuberculous mycobacteria.
Percentages based on Gao et al.[6] and Olveira et al.[8]

COPD with multiple exacerbations, and/or repeated isolation of potentially pathogenic microorganisms (PPM) in respiratory samples (or *Pseudomonas aeruginosa* only) in a clinically stable phase. Although a causality relationship between both entities has not been studied, it is biologically plausible that this is the case.[9,10]

Relationship Between Bronchiectasis and Asthma

The prevalence of BE in severe or uncontrolled asthma is 20%–30%. The possible impact of BE on asthma is unknown, although it usually appears in severe, uncontrolled or neutrophilic asthma.[11] Similarly, the pathophysiological mechanism of these entities and the existence of a causality relationship are unknown. In patients with central BE who present with symptoms suggestive of asthma, allergic bronchopulmonary aspergillosis (ABPA) should be ruled out.

Diagnosis

Clinical Aspects

Forms of Presentation

Patients with BE usually present clinically with chronic cough (41%–100%), chronic (46%–76%) or intermittent expectoration (20%–38%), and repeated respiratory infections, but can remain asymptomatic between these episodes. Other symptoms that often present are dyspnea, hemoptysis of varying intensity, intermittent chest pain and fatigue. Acropachy is rare and usually appears in advanced stages. Sinusitis is common, especially in primary ciliary dyskinesia and in primary immune deficiencies.

Anamnesis

This should include the most common symptoms of BE mentioned in the previous section, as well as tests aimed at identifying a specific cause (Fig. 2, diagnostic algorithm). It is useful to quantify the daily volume (semi-quantitatively, marked by the patient in a graduated container) and color of the sputum (Murray scale, Fig. 3).[12]

Differential Diagnosis

Other chronic respiratory diseases with similar symptoms or diffuse cystic lung diseases, or diseases that may present radiologically with cavitation should be considered in the differential diagnosis of BE (Table 2).

Functional Aspects

The most common functional abnormality in BE is chronic persistent airflow obstruction (with normal or slightly reduced forced vital capacity), more marked in smokers or COPD patients. Mixed patterns can appear in the post-tuberculous, fibrotic or destructive forms, although a pure restrictive pattern is rare. A slight decrease may be observed in the diffusing capacity of the lungs for carbon

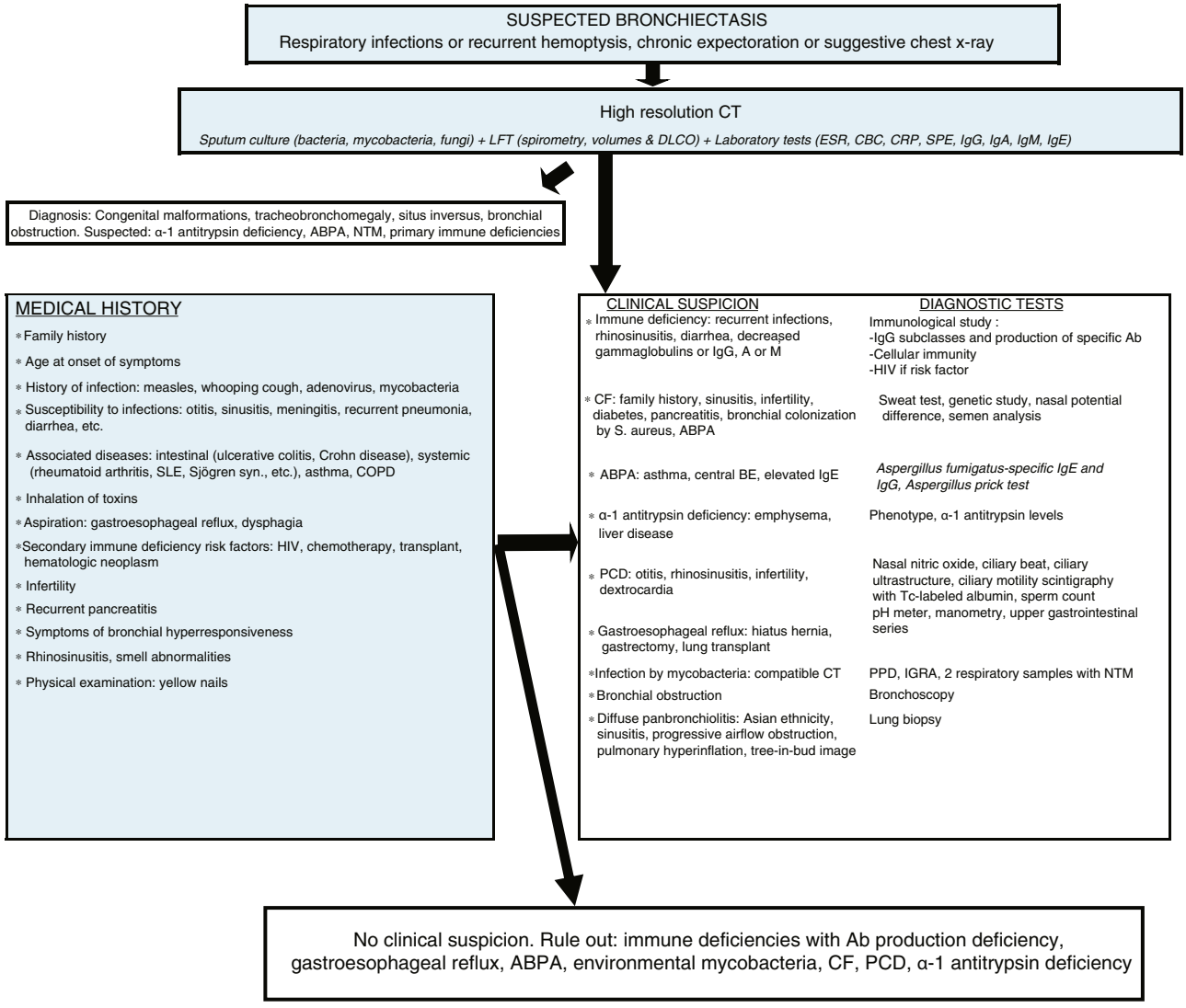


Fig. 2. Diagnostic algorithm. Ab: antibodies; ABPA: allergic bronchopulmonary aspergillosis; BE: bronchiectasis; CBC: complete blood count; CF: cystic fibrosis; COPD: chronic obstructive pulmonary disease; CRP: C-reactive protein; CT: computed tomography; PCD: primary ciliary dyskinesia; DLCO: diffusing capacity of the lungs for carbon monoxide; ESR: erythrocyte sedimentation rate; FEV_1: forced expiratory volume in the first second; HIV: human immunodeficiency virus; Ig: immunoglobulin; IGRA: interferon gamma release assay; LFT: lung function tests; NTM: non-tuberculous mycobacteria; PPD: purified protein derivative skin test; S: *Staphylococcus*; SLE: systemic lupus erythematosus; SPE: serum protein electrophoresis; Syn: syndrome; Tc: technetium; UGI: upper gastrointestinal.

dioxide (DLCO). Bronchial hyperresponsiveness (BHR) has been observed in 30%–69% of cases.

Quality of Life

Patients with BE have poorer quality of life scores than the general population. This deterioration has been related to a larger extent with age, chronic bronchial *P. aeruginosa* infection, grade of dyspnea, number of exacerbations, poorer lung function, presence of BHR, greater structural damage, chronic bronchorrhea, presence of respiratory failure and symptoms of depression and anxiety. The only questionnaires designed specifically for use in BE are the Quality of Life-Bronchiectasis[13] questionnaire and the recently published Bronchiectasis Health Questionnaire. Other validated questionnaires are: St. George's Respiratory Questionnaire[14] and the Leicester Cough Questionnaire,[15] the latter for the specific assessment of the impact of cough. The Quality of Life-Bronchiectasis questionnaire is useful to assess the patient's perception of severity on an annual basis (http://www.psy.miami.edu/qol_b/qol_measures01.phtml).

Analytical Aspects

Some systemic inflammatory markers, such as the peripheral neutrophil count, C-reactive protein (CRP) level and erythrocyte sedimentation rate are associated with accelerated loss of lung function and greater radiological extension; determination of CRP has been shown to be most useful.

Radiological Aspects

Chest radiograph shows low sensitivity and specificity for the diagnosis of BE. It should be performed when complications (such as pneumonia, pneumothorax or atelectasis) are suspected. HRCT is currently the gold standard for both diagnosis and to assess disease morphology, extent and progression (*strong recommendation, high quality evidence*). It also helps in therapeutic decision-making and the diagnosis of concomitant findings. Low-dose (<1 mSv) volumetric acquisition protocols without contrast are commonly used, with a high resolution reconstruction algorithm with 1–1.25 mm slices every 10 mm in maximum inspiration. The expiration images

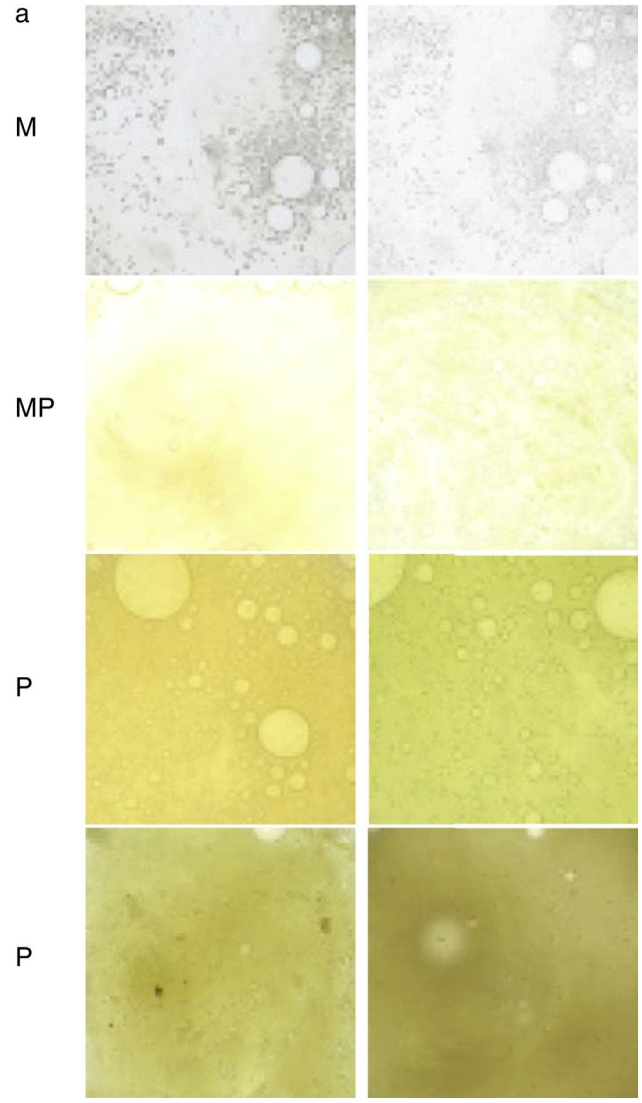


Fig. 3. Table to assess the color of sputum from least to most purulent. M: mucous; MP: mucopurulent; P: purulent.
Source: Murray et al.[12]

usually help to assess the presence of air trapping, bronchomalacia and small airway abnormalities. The criteria described by Naidich et al. (Fig. 4)[16] are recommended for the radiological diagnosis of BE. The cardinal sign is the presentation of a bronchial dilatation, taking the diameter of the adjacent bronchial artery as a reference, although up to 20% of healthy elderly individuals may present this radiological criterion. In some cases, HRCT can reveal the etiology (Fig. 2). Diffuse BE suggests an underlying systemic problem, those due to tuberculosis predominate in upper fields and those secondary to ABPA are usually central. The presence of associated multiple small nodules, predominantly in the lingula and middle lobe, suggests non-tuberculous mycobacteria (NTM) infection.

Etiological Aspects (Fig. 2)

In all patients, regardless of clinical suspicion of the cause that precipitates the BE, a detailed clinical history should be taken, and a microbiological study including bacteria, mycobacteria and fungi together with laboratory tests that include serum protein electrophoresis (SPE) and IgG, IgA, IgM and IgE immunoglobulin (Ig) levels should be performed. The results of these tests can shed light on most causes, and rationally indicate the diagnostic tests needed for confirmation. If an etiological diagnosis cannot be reached, causes requiring specific management or treatment must always be ruled out. IgG subclass deficiency should be confirmed with an antibody production study; this can only be omitted in cases with very low IgG_2 levels.[17] The study of autoimmune diseases and HIV infection should only be done in the case of clinical suspicion, because BE is rarely the first manifestation. A post-infectious cause should only be considered when BE symptoms present after an episode of acute respiratory infection or pneumonia, provided other causes have been previously excluded. The diagnosis of immune deficiencies with defective antibody production, CF and primary ciliary dyskinesia should be confirmed in specialized centers.

Microbiological Aspects

Colonization and Infection in Bronchiectasis

It is preferable to use the term "pathogenic colonization" which is usually expressed as "bronchial infection" and not as "bronchial colonization". This is a "passive pathogenesis" model caused by the growth of microorganisms on the surface of the respiratory mucosa without invading the adjacent tissues and which causes a local inflammatory effect. Different stages in the infection can be distinguished in BE, which are important in clinical management and antimicrobial treatment (Table 3).

Concept of Eradication

Eradication of a certain PPM is the absence of cultures positive for the microorganism in at least 3 sputum samples taken at least 1 month apart over a period of 6 months. Colony count in the culture is not common practice, but can help assess treatment efficacy.[18]

Potentially Pathogenic Microorganisms and Microbiome

Bronchial infection in BE is normally caused by so-called PPMs, which include non-typeable *Haemophilus influenzae*, *P. aeruginosa*, *Streptococcus pneumoniae*, *Moraxella catharralis* and *Staphylococcus aureus*, the latter being more common in CF; of these, *P. aeruginosa* has been associated with a worse prognosis. Recent improvements in microbiological methods have led to an increase in the isolation of enterobacteria, Gram-negative non-fermenting bacteria such as *Achromobacter* (*Alcaligenes*) *xylosoxidans* and *Stenotrophomonas maltophilia*, *Nocardia* spp., fungi (essentially *Candida albicans* and *Aspergillus fumigatus*, although also *Scedosporium apiospermum*) and NTM, some of which can have negative clinical and prognostic consequences for the patient (*Mycobacterium abscessus*). As yet, few studies have investigated methicillin-resistant *S. aureus* (MRSA) in BE, although its incidence may be rising.

Routine cultures for the detection of PPM, mycobacteria and fungi (yeasts and filamentous) are generally carried out in stable patients, and whenever there is an exacerbation, preferably before taking antibiotics. Furthermore, NTM culture should be performed in patients with fibronodular lesions in the radiological follow-up who do not respond to standard treatment and in whom clinical deterioration is noted, as well as in patients scheduled to start macrolide treatment.

There are still few studies on the microbiome associated with BE, and as yet insufficient scientific evidence to support routine studies of the respiratory microbiome or the search for anaerobic bacteria.[19]

Microbiological Diagnosis of the Bronchial Infection

The microscopic examination of sputum should exclude contamination from the upper respiratory tract, so >25 leukocytes and <10 epithelial cells should be observed. Samples must be collected, transported and processed within 6 h. If this is not possible, they

Table 2
Respiratory Diseases Included in Clinical or Radiological Differential Diagnosis With Bronchiectasis.

Clinical Differential Diagnosis	Radiological Differential Diagnosis
COPD	**Cystic diseases**
Asthma	*Histiocytosis X*
Cystic fibrosis	*Lymphangioleiomyomatosis*
Bronchiolitis obliterans	*Tuberous sclerosis*
Chronic bronchitis	*Lymphocytic interstitial pneumonia*
Slowly-resolving lung infections	
	Destruction of lung parenchyma
	Advanced interstitial disease
	Centriacinar pulmonary emphysema
	Multiple bullae
	Possible cavitation
	Infections
	Multiple pulmonary abscesses
	Pneumonia caused by *Pneumocystis jiroveci*
	Pneumonia caused by *Staphylococcus aureus* (pneumatoceles)
	Pneumonia caused by mycobacteria
	Other infections: coccidioidomycosis, paragonimiasis, recurrent respiratory papillomatosis
	Malignant lesions
	Bronchoalveolar carcinoma
	Cystic pulmonary metastases (sarcomas, meningioma, urothelial carcinoma, blastomas, adenocarcinomas)
	Pulmonary lymphoma
	Others
	Amyloidosis
	Desquamative interstitial pneumonia
	Light chain deposition disease
	Neurofibromatosis
	Granulomatosis with polyangiitis
	Septic pulmonary embolisms
	Post-traumatic pseudocysts
	Extrinsic allergic alveolitis

should be kept for no longer than 24 h at room temperature, preferably stored at 4 °C rather than −20 °C. For longer periods, they should be kept at −80 °C. General differential and selective media should be included in the culture to increase yield. Routine bacterial counts are controversial due to the time needed to perform them, and the potential usefulness of the information obtained. Nevertheless, they should be used in the evaluation of new treatments, including combinations of antimicrobials, and to assess the eradication of PPMs. Different morphotypes of the same microorganism can appear in cultures and should be detected using specific antibiotic susceptibility testing (AST) in each case.

Although AST results are the gold standard in antimicrobial treatment, correlation between conventional *in vitro* sensitivity and *in vivo* response can be poor, especially with microorganisms that grow in biofilms, or while using inhaled antibiotics that reach very high concentrations in the bronchial mucosa. Therapeutic decisions, therefore, should be guided by the clinical response.

NTMs require culture with special media and must be expressly requested. An acid-fast stain (Ziehl-Neelsen or, preferably, auramine–rhodamine fluorescence staining) may be useful. If a positive stain is obtained, it should be confirmed and identified using molecular techniques, and AST should be carried out. Suspected *Nocardia* spp. infection should be discussed with the microbiologist to facilitate identification. Finally, the determination of anti-pseudomonas antibodies is unnecessary in bacterial cultures.

Severity and Prognostic Factors

Radiological Scores

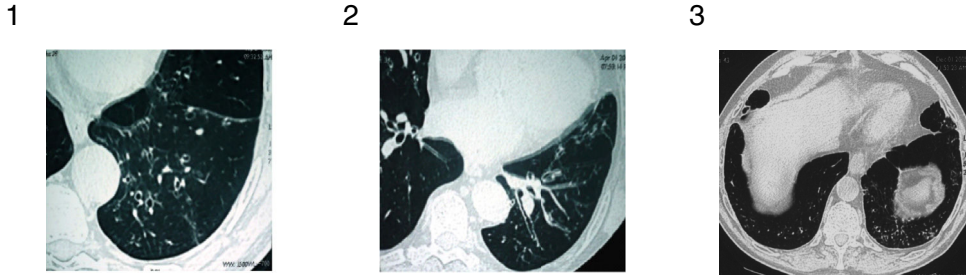
Of the many radiological score systems, the modified Reiff score is recommended for its simplicity.[20] This score is based on the diameter of the bronchial lumen/diameter of the adjacent vessel (0 points≤1; 1 point=1–2; 2 points=2–3; 3 points≥3) in each of the 6 lung lobes. The modified Bhalla score system (Table 4)[21] is recommended if more extensive or detailed radiological information is needed. The correlation between both scores is very high.

Multidimensional Clinical Scores

Two multidimensional scores are used to assess the prognosis and initial severity of BE: the FACED[22] and the Bronchiectasis Severity Index (BSI),[23] as well as a modification of the former (E-FACED),[24] which also includes the number and severity of exacerbations in the previous year. For the initial clinical management and assessment of the patient, the E-FACED score is recommended for its simplicity (Table 5). The variables should be collected as close as possible to the time of diagnosis. Both the FACED and E-FACED have shown good prognostic capacity for mortality. E-FACED also presents a good prognostic capacity for the number and severity of exacerbations. The E-FACED should be obtained annually to assess clinical progression of the disease (*strong recommendation, moderate quality evidence*). Although the BSI (www.bronchiectasisseverity.com/) is more complex, it has also shown good prognostic capacity for quality of life and lung function decline.

Natural Evolution

BE is an irreversible, chronic disease with variable progression. As the disease progresses, a greater number of exacerbations and hospital admissions, progressive airflow obstruction, chronic bronchial infection caused by *P. aeruginosa* and other multiresistant PPMs, progressive dyspnea, respiratory failure, cor pulmonale and death (especially due to respiratory exacerbations) usually appear. The presence of systemic inflammation, chronic bronchial *P. aeruginosa* infection and severe exacerbations have been associated with more rapid progression of BE.[25]



DIRECT SIGNS
-1.Bronchial dilatation: bronchoarterial ratio greater than 1
Abnormal bronchial contour
Signet ring sign (transverse slice)
Tram-track sign (horizontal slice)
String of pearls sign (horizontal slice)
Bunch of grapes sign
-2.Lack of bronchial tapering
-3.Visualization of peripheral bronchi
Within 1 cm of the costal pleura
In contact with the mediastinal pleura

INDIRECT SIGNS
-Peribronchial thickening
-Mucoid impaction
Tubular or Y-shaped structures
Rounded or branching opacities (transverse slice
Air-fluid levels
-Mosaic pattern
-Centrilobular nodules, tree-in-bud nodules
-Focal areas of air trapping
-Atelectasis/consolidation

Fig. 4. Radiological signs of bronchiectasis (images above the table of the 3 principle criteria or direct signs of Naidich et al.).
Source: Webb et al.[16]

Table 3
Stages of Bronchial Infection (Pathogenic Colonization) in Bronchiectasis.

Stage	Microbiological Criteria[a]	Comments
Initial infection	First culture positive for a PPM not isolated in previous periodic cultures	Clinical manifestations do not usually appear, although there may be an inflammatory response
Intermittent infection	Positive and negative cultures for the same PPM in consecutive samples taken at least one month after the initial infection	Generally indicates chronic infection with low quantitative values not always detectable in the culture It usually occurs in patients who do not receive specific antibiotic treatment against the PPM
Chronic infection	Three or more consecutive cultures positive for the same PPM within a period of at least 6 months in samples taken at least 1 month apart	It induces an inflammatory response that usually manifests with persistent purulent expectoration. May be accompanied by systemic infection, low-grade fever, asthenia and/or weight loss

PPM: potentially pathogenic microorganisms.
[a] Referring to sputum cultures.

Conflict of Interests

Miguel Ángel Martínez has participated in training sessions sponsored by Gilead, Novartis, Glaxo, Praxis, Teva and Zambon. He has also been the principal investigator in projects funded by Praxis and Zambon, and has participated in meetings analyzing clinical trial outcomes organized by Bayer and Grifols.

Luis Máiz has participated in training sessions sponsored by Gilead, Novartis, Zambon and Praxis.

Casilda Olveira has participated in training activities or expert committees sponsored by Gilead, Praxis, Novartis, Teva and Zambon.

Rosa Maria Girón Moreno has participated in training sessions sponsored by Gilead, Teva and Zambon.

Marina Blanco Aparicio has participated in training sessions sponsored by Zambon and Praxis Pharmaceutical, and has been principal investigator in a clinical trial on inhaled antibiotic therapy sponsored by Bayer.

Table 4
Modified Bhalla Scoring System.

Parameter	Score			
	0	1	2	3
Severity of bronchiectasis	Absent	Mild: lumen slightly greater than adjacent vessel	Moderate: lumen 2×to 3×adjacent vessel	Severe: lumen >3×adjacent vessel
Peribronchial thickening	Absent	Mild: airwall thickness equal to adjacent vessel	Moderate: airwall thickness ≤2×adjacent vessel	Severe: airwall thickness >2×adjacent vessel
Extent of bronchiectasis (no. of BPS)	Absent	1–5	6–9	>9
Extent of mucous plugging (no. of BPS)	Absent	1–5	6–9	>9
Sacculation or abscesses (no. of BPS)	Absent	1–5	6–9	9
Generations of bronchial divisions affected (bronchiectasis/plugging)	Absent	Up to 4th generation	Up to 5th generation	Up to 6th generation and distal
No. of bullae	Absent	Unilateral (not >4)	Bilateral (not >4)	>4
Air trapping (no. of BPS)	Absent	1–5	>5	
Collapse/consolidation	Absent	Subsegmental	Segmental/lobar	

Adapted from: Bhalla et al.[21]
The 3 parameters selected for the simplified scale are shown in bold.
In the original Bhalla scoring system, air trapping is replaced by the presence of emphysema, but with the same score.
BPS: bronchopulmonary segments.

Table 5
E-FACED Multidimensional Scoring System.

Variable	Values	Score
Exacerbaciones with hospital admission (previous year)	No	0
	At least 1	2
FEV$_1$ (% predicted)	At least 50%	0
	Less than 50%	2
Age	Less than 70 years	0
	At least 70 years	2
Chronic bronchial infection (***C***olonization) by *P. aeruginosa*	No	0
	Yes	1
Radiological ***E***xtension (no. of lobes)[a]	1–2 lobes	0
	More than 2 lobes	1
Dyspnea (modified MRC scale)	0–II	0
	III–IV	1

Adapted from: Martínez-García et al.[24]
FEV$_1$: forced expiratory volume in the first second; MRC: *Medical Research Council*.
Total range of growing severity: 0–9 points (E-FACED).
E-FACED classification of severity.
0–3 points: mild bronchiectasis.
4–6 points: moderate bronchiectasis.
7–9 points: severe bronchiectasis.
[a] Middle lobe and lingula considered as independent lobes.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbr.2017.07.013.

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