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Suarez-Cuartin, Guillermo; Chalmers, James D.; Sibila, Oriol

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Diagnostic Challenges of Bronchiectasis

Guillermo Suarez-Cuartin [(1)], James D Chalmers [(2)], Oriol Sibila [(1)]

[(1)] Respiratory Department, Hospital de la Santa Creu i Sant Pau. Institute for Biomedical Research Sant Pau (IIB Sant Pau). Autonomous University of Barcelona. Barcelona, Spain.

[(2)] Scottish Centre for Respiratory Research, University of Dundee. Dundee, UK.

Corresponding author:

Dr. Oriol Sibila. Servei de Pneumologia, Hospital de la Santa Creu i Sant Pau. C/. Sant Antoni M. Claret 167, 08025 Barcelona (Spain). Tel.: +34 93 556 5964; Fax: +34 93 556 5601. E-mail: osibila@santpau.cat

ABSTRACT

Bronchiectasis is a condition of increasing incidence and prevalence around the world. Many different diseases have been associated with bronchiectasis, and their treatment can differ widely. Recent guidelines have helped to approach aetiological diagnosis but it is still a complex process. Identifying the cause of the bronchiectasis may determine a change in the treatment of a large group of subjects. That is one of the main reasons why the aetiological diagnosis is crucial in the proper management of bronchiectasis patients.

Postinfectious bronchiectasis is the most frequent entity among different studies, but a high percentage of cases still remain without a clear aetiology. Bronchiectasis related to allergic bronchopulmonary aspergillosis (ABPA), immunodeficiencies with antibody production deficiency, primary ciliary dyskinesia, cystic fibrosis and alpha-1-antitrypsin deficiency, among others, require a specific management that may improve quality of life and prognosis in a large group of individuals.

Therefore, the aim of this article is to review the main bronchiectasis related diseases and to simplify the aetiological diagnosis, in order to improve the management of bronchiectasis patients, especially in those where a specific treatment is available.

1. INTRODUCTION

Non-cystic fibrosis (CF) Bronchiectasis (henceforth referred as bronchiectasis) is a progressive disease characterized by a permanent dilatation of bronchi, retention of mucus and ciliary clearance impairment. These changes are a result of very diverse pulmonary or systemic diseases, which can influence the course of the disease. Therefore, aetiological investigation is one of the key aspects in the management of patients with bronchiectasis [1,2].

Causes of bronchiectasis are many and varied, making the aetiological diagnosis process difficult. The most common causes are previous lung infections such as pneumonia or pulmonary tuberculosis, primary and secondary immunodeficiencies, CF, abnormal ciliary function, allergic bronchopulmonary aspergillosis (ABPA) and connective tissue diseases. Bronchiectasis has also been associated with other chronic respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD)[3]. In addition, recent studies focusing on the aetiology of bronchiectasis has revealed a high percentage of patients with no identifiable cause despite undergoing extensive studies for this purpose that are considered idiopathic [4–7].

The treatment of diseases associated with bronchiectasis can differ widely among them. Some bronchiectasis aetiologies can determine a change in patient management such as initiating a specific treatment, closer follow-up, genetic testing for relatives or modifying risk factors [6,7]. Therefore, it is important to identify the aetiological cause of the bronchiectasis for a proper management. Current guidelines recommendations for the aetiolology of bronchiectasis include an extensive laboratory and instrumental workup, as well as lung function tests and microbiological evaluation [1,2]. The aim of this article is to review the main diseases associated with bronchiectasis in order to simplify the process of the aetiological diagnosis and therefore to help improving patient management when a treatable or modifiable cause is identified.

2. AETIOLOGIES

The causes most frequently identified in patients with bronchiectasis are summarized in **Table 1.** The entities that have been associated with the development of bronchiectasis are numerous, and their prevalence varies depending on the population studied. Most studies directed to characterising patients with bronchiectasis to date have focused on specific populations in the UK, which can make it difficult to extrapolate the results to other countries and outside of highly specialised centres[4–6]. Recently, Lonni and colleagues conducted an analysis of 1,258 patients from seven cohorts in different countries included in the European Bronchiectasis Registry (EMBARC) in the study directed to the most extensive identification of aetiologies of bronchiectasis to date[7]. This study has shown that the cause of bronchiectasis was identified in approximately 60% of individuals. Among these, the most frequent were postinfectious (20%), COPD-related bronchiectasis (15%), connective tissue disease-related (10%), immunodeficiencies (5.8%) and asthma-related bronchiectasis (3.3%)[7]. **Table 2** summarizes the distribution of aetiologies most frequently identified in recent studies.

Table 1. Aetiologies of bronchiectasis

Postinfectious
Necrotising pneumonia Tuberculosis and non-tuberculosis mycobacterium Viruses (adenovirus, measles and other childhood infections)
Immunodeficiencies
* *Primary:* antibody deficiency, combined immunodeficiency, neutrophil dysfunction, Wiskott-Aldrich syndrome, among others * *Secondary:* HIV infection, haematological malignancies, chemotherapy, transplant
Hypersensitivity
Allergic bronchopulmonary aspergillosis
Associated with lung diseases
Asthma COPD Swyer-James Syndrome
Diseases associated with connective tissue
Rheumatoid Arthritis Sjögren Syndrome *Other:* Ankylosing spondylitis systemic sclerosis, systemic lupus erythematosus, ankylosing spondylitis, relapsing polychondritis, sarcoidosis, Marfan syndrome and Ehlers-Danlos syndrome
Alteration of the mucociliary escalator
Cystic fibrosis Primary ciliary dyskinesia Young's syndrome
Inflammatory bowel disease
Ulcerative colitis Crohn's disease
Inflammatory pneumonitis
Aspiration and gastroesophageal reflux Toxic inhalation (drugs, gases, etc.)
Congenital defects of the airway
Tracheobronchomegaly (Mounier-Kuhn syndrome) Cartilage defects (Williams-Campbell syndrome) Pulmonary sequestration Tracheobronchomalacia
Bronchial Obstruction
* *Intrinsic:* scar stenosis, broncholithiasis, foreign body, tumour * *Extrinsic:* lymphadenopathy, tumour, aneurysm
Others
Alpha 1 antitrypsin deficiency Yellow nail syndrome Diffuse panbronchiolitis
Idiopathic or unknown aetiology

HIV: human immunodeficiency virus; COPD, chronic obstructive pulmonary disease

Table 2. Distribution of the aetiologies of bronchiectasis in recent studies.

	Pasteur et al. (n=150)	King et al. (n=103)	Shoemark et al. (n=165)	Anwar et al. (n=189)	Lonni et al. (n=1258)
Mean age (SD)	52,7 (15,2)	56 (14)	49 (16)	66,1 (11,5)	67 (58-75)*
Gender (% M/F)	38/62	37/63	35/65	49/51	40/60
Idiopathic (%)	53	74	26	43	40
Postinfectious (%)	29	10	32	24	20
Immunodeficiencies (%)	8	9	7	2	6
ABPA (%)	7	4	8	4	5
Connective tissue diseases (%)	3	2	2	5	10
COPD (%)	-	-	-	12	15
Asthma (%)	-	-	-	3	3
Inflammatory intestinal disease (%)	1	-	3	2	2
Cystic Fibrosis (%)	3	0	1	<1	0
Ciliary dysfunction (%)	2	1	10	1	2
AAT Deficiency (%)	0	0	0	1	<1
Aspiration / GER (%)	4	0	1	1	<1
Panbronchiolitis (%)	<1	0	2	0	0
Young's Syndrome (%)	3	1	3	<1	0
Yellow nail Syndrome (%)	-	-	2	-	<1
Congenital defect of the airway (%)	<1	0	-	-	<1
Pink's disease (%)	<1	-	-	<1	<1
Other (%)	-	-	Mycobacteria Infection: 2	-	Bronchial obstruction: <1

* Data presented as median (interquartile range).

SD: standard deviation; ABPA: allergic bronchopulmonary aspergillosis; COPD, chronic obstructive pulmonary disease; AAT: Alpha-1 antitrypsin; gastro-oesophageal reflux (GER)

2.1 Postinfectious

This is the most frequently identified aetiology in most studies with a prevalence of 10-32%[4–8]. This variability may be due to a higher prevalence of postinfectious aetiology in the most disadvantaged communities[9]. Infections that have been associated with the presence of bronchiectasis are bacterial or viral pneumonia, pulmonary tuberculosis and childhood infections such as measles and whooping cough[10–12].

Identifying this aetiology is often complicated because there may be biases in the data collection. Sometimes patients cannot recall previous infections or their severity, making it difficult to establish a temporal relationship between these infections and bronchiectasis. Shoemark et al. observed an important delay in the diagnostic of bronchiectasis. While the average age of onset of symptoms in these patients was 7 years, the average age for the diagnostic study of bronchiectasis was 49 years[5]. Therefore, in patients for whom the connection between the antecedent infection and the onset of symptoms of bronchiectasis is unclear, a more comprehensive aetiological study is recommended[2].

The incidence of bronchiectasis caused by non-tuberculosis mycobacterial (NTM) infections is a controversial point[11]. Although the presence of bronchiectasis predisposes colonization by opportunistic microorganisms such as NTM, it is also suggested that they play a role in the development of these bronchial disorders. Fujita et al. retrospectively evaluated resected lung specimens from 9 patients infected with *Mycobacterium avium* complex[13]. In all the cases they identified destruction of bronchial cartilage and of the smooth muscle layer as well as bronchial mucosa ulcerations and the presence of airway granulomas. Given these histopathological changes, the authors concluded that NTM infection could be a cause rather

than a consequence of the appearance of bronchiectasis[13]. It has been suggested that certain host factors may increase the risk to develop pulmonary NTM infection [14]. Kartalija et al studied 103 patients with NTM infection and found that they were taller, had a significantly lower body mass index and body fat, and a higher prevalence of scoliosis and pectus excavatum than the 101 uninfected control subjects. Also, abnormal serum leptin and adiponectin levels were measured in NTM infected patients, resulting in suppressed blood IFN-γ and IL-10 levels [15]. Patients with *M. avium* infection classically are middle aged and elderly female patients with middle lobe bronchiectasis, who may have little cough (the so called, "Lady Windemere" syndrome), although disease associated with NTM should be considered in all patients.

2.2 Immunodeficiencies

Immunodeficiency is defined as the partial or complete failure to conduct an effective immune response to an infectious agent. It is classified as primary (or congenital) and secondary (or acquired). It comprises a heterogeneous group of conditions that can occur in both childhood and adulthood. In patients with primary or secondary immunodeficiencies, bronchiectasis may be the result of a state of persistent systemic and airway inflammation due to recurrent infectious episodes[16,17]. A study from Hurst et al. observed greater airway and systemic inflammation in patients with primary antibody deficiency compared to immunocompetent bronchiectasis controls. The severity of this systemic inflammatory response correlated with the rate of progression of lung disease and also to airway inflammation [17].

The presence of an immune deficiency in patients with bronchiectasis varies from 2-18% depending on the population studied[6,18]. The deficiency in the function or production of one or more kinds of immunoglobulines is the most common and clinically important manifestation

of primary immunodeficiencies. Common variable immunodeficiency, X-linked agammaglobulinemia or immunoglobulin A deficiency are therefore common causes of bronchiectasis[4,19]. Other secondary immunodeficiences related to bronchiectasis are infection by the human immunodeficiency virus, immunosuppressive therapy or chemotherapy, and patients with haematological malignancies.

There is often a history of recurrent respiratory (pneumonias, sinusitis) and non-respiratory (otitis, meningitis, diarrhea) infections, but in many cases impaired immunity can be identified in apparently healthy subjects, which may produce a delay in diagnosis in these patients[20]. A history of frequent non-respiratory infections can give a clue to the presence of an underlying immunodeficiency. Treatment with immunoglobulin have demonstrated an improvement in lung function in patients with hypogammaglobulinemia[21]. Therefore, identifying these patients and initiating early specific treatment is essential in cases that require it to avoid the appearance of bronchiectasis and to slow down the progression of the disease.

2.3 Chronic obstructive pulmonary disease (COPD)

The presence of bronchiectasis associated with COPD is the aetiology that has generated most interest and controversy in recent years. It is due to the high prevalence of patients with COPD and to the undertaking of more routine chest CT in these patients[22]. The prevalence of this bronchiectasis-COPD association differs depending on whether the studied population is a bronchiectasis series or a COPD series. Recent studies have found that about 12-15% of patients with bronchiectasis have a diagnosis of associated COPD[6,7]. However, it is believed that this association may be even greater when looking at COPD series. In a meta-analysis performed by Ni et al including six observational studies with 881 COPD patients, the mean prevalence of

bronchiectasis was 54,3% [23]. A study in the UK showed that 29% of patients with COPD followed in primary care had morphological alterations of airway potentially classifiable as bronchiectasis[24]. A recent population study on 18,793 patients diagnosed with bronchiectasis also in the UK during 2004-2013 has shown that 36% of individuals had a diagnosis of COPD[25]. The prevalence of smoking history is also different depending on the studied population. In bronchiectasis series, 17-36% of patients were smokers or ex-smokers [5–8,18,26], while in COPD studies almost all patients included had a smoking history, since this is one of the main causes related to this disease.

The factors associated with the presence of bronchiectasis in COPD are severe airflow obstruction, isolation of potentially pathogenic microorganisms and at least one hospital admission due to an exacerbation of COPD in the last year[27]. In addition, the association of these diseases has shown a worse prognosis. Goeminne et al. observed that in patients with bronchiectasis and COPD mortality was almost three times higher than in patients with bronchiectasis without COPD (55% vs. 20%)[28]. Moreover, in patients with COPD and bronchiectasis on high resolution chest tomography, an increase in the number of exacerbations and hospitalizations as well as five-year mortality has been detected[29–31]. Martinez-Garcia and colleagues studied 201 patients diagnosed with COPD, of whom 57% had associated bronchiectasis. They noted that the coexistence of these entities is associated with a high risk of mortality from all causes in the group of patients with moderate to severe COPD[30].

These smaller studies may have overestimated the prevalence of bronchiectasis in COPD, as larger studies suggest a lower prevalence. In the ECLIPSE study (N=2161), an international multicentre COPD cohort, bronchiectasis was reported in only 2% of males with GOLD II COPD (<1% of females), increasing to 9% of females and 7% of males in very severe COPD (GOLD IV) [32].

Whether the diagnosis is bronchiectasis with fixed airflow obstruction or COPD with suggestive anatomical abnormalities of bronchiectasis, this "overlap syndrome" has a significant impact on the management of both diseases and requires more studies to help understand its natural history and therefore to optimize the treatment given to date.

2.4 Asthma

The relationship between bronchiectasis and bronchial asthma is not clearly defined. Anwar et al. and Lonni et al. observed a prevalence of bronchiectasis associated with bronchial asthma of about 3%[6,7]. Nevertheless, studies aimed at the characterisation of radiological alterations of asthma have found bronchiectasis on chest high-resolution computed tomography (HRCT) in 17-35% of asthma patients[33–36]. These alterations have been associated more frequently with cases of non-allergic asthma and more severe forms of the disease[34,35]. However, a study performed by Menzies et al. also found a 2.01 increased hazard ratio of bronchiectasis among asthma patients with sensitization to *Aspergillus fumigatus* not meeting the diagnostic criteria for ABPA [36].

Unlike other aetiologies, morphological alterations of patients with asthma may affect all lung lobes, and both proximal and distal zones[37]. Finally, in a recent population study in the UK, the diagnosis of asthma was again found to be associated with a large number of patients with bronchiectasis, namely 42.5% [25]. It is difficult to define in which cases is bronchiectasis secondary to asthma and not the primary disease. Therefore, further studies are needed to better characterise this relationship and determine the impact on the prognosis of both diseases.

2.5 Allergic bronchopulmonary aspergillosis (ABPA)

This is a lung disease that occurs as a result of a hypersensitivity reaction to bronchial colonization by *Aspergillus fumigatus*[38]. The diagnosis of ABPA is performed using clinical and immunological criteria which are summarized in **Table 3** [38]. The percentage of bronchiectasis associated with ABPA varies depending on the population analysed, from 1% in a study conducted in the US[18] to 7-8% in studies in the United Kingdom[5–7]. In some cases, it is difficult to make the diagnosis of ABPA because the result of serology tests such as total IgE and IgE specific to *Aspergillus fumigatus* can be similar to that observed in bronchial asthma[39]. Moreover, it is possible that the patient is in a stable phase at the time of the study and that structural damage occurred years before and that specific tests may give results that are normal or near normal[2]. In these cases, the identification of central bronchiectasis along with predominant impact on the upper lung lobes in chest HRCT can support the diagnosis of ABPA[40]. Chronic isolation of *Staphylococcus aureus* in bronchiectasis patients could also suggest ABPA as an aetiology, as this association has been reported in a previous study from Shah *et al* [41]. Its routine screening is recommended, since the identification of this disease implies specific management[2].

Table 3. Criteria used by the American Academy of Allergy, Asthma, and Immunology (AAAAI) for the diagnosis of allergic bronchopulmonary aspergillosis

ABPA diagnostic criteria
Minimum criteria ● Asthma or CF with impaired lung function ● Immediate skin reaction to the *Aspergillus* antigen ● Total serum IgE of 1000ng/ml (416 iu/ml) or greater ● High levels of specific IgG and IgE for *Aspergillus* in serum ● Pulmonary infiltrates on chest radiograph Additional criteria ● Peripheral blood eosinophilia ● Presence of precipitating antibodies for *Aspergillus* in serum ● Central bronchiectasis ● Isolation of *Aspergillus* in mucus plugs Classified as ABPA-CB or ABPA-S (seropositive) according to the presence or absence of central bronchiectasis, respectively.

CF: Cystic fibrosis; Ig: Immunoglobulin; ABPA: allergic bronchopulmonary aspergillosis

2.6 Connective tissue diseases

Bronchiectasis have been associated with multiple systemic diseases and connective tissue disease is thought to be the cause in up to 10-16% of patients in studies in Europe and the US[7,18]. Among the more notable are connective tissue diseases such as rheumatoid arthritis (RA) and Sjögren's syndrome, although bronchiectasis has been identified in patients with systemic sclerosis, systemic lupus erythematosus, ankylosing spondylitis, relapsing polychondritis, Marfan syndrome and Ehlers Danlos syndrome[42]. The association of bronchiectasis with RA is the most studied among these systemic diseases. An incidence of bronchiectasis of approximately 5% in patients with RA and respiratory symptoms has been reported, which is higher than the incidence of pulmonary fibrosis in those patients[43]. Like

other pleuropulmonary manifestations of RA, bronchiectasis precedes articular manifestations in a large number of patients. This supports the hypothesis that chronic bronchial infection could be one of the triggers of RA[44]. Remy-Jardin *et al*. observed that approximately 30% of patients with RA who underwent chest HRCT had bronchiectasis. Although this finding was more frequent in patients with respiratory symptoms, about 8% of patients were asymptomatic[45]. A recent study by Perry et al. found that patients with RA and bronchiectasis present higher activity and severity of the disease and higher levels of anti-citullinated peptide antibodies when compared with patients with RA only[46].

Other collagenopathies have been much less studied. Studies aimed at characterizing the radiological changes of the lung by chest HRCT in patients with systemic sclerosis and systemic lupus erythematosus identified bronchiectasis in 59% and 21% respectively[47,48]. More studies are needed to elucidate the pathogenesis of the association between bronchiectasis and these diseases, as well as to determine the clinical impact that these bronchial abnormalities have on the course of the different systemic diseases.

It has been reported that connective tissue disease and in particular RA associated bronchiectasis is associated with a poorer prognosis, requiring more intensive monitoring. Whether this reflects the nature of the disease or the impact of the immunosuppressive drugs frequently used to treat RA is unclear[49].

2.7 Inflammatory bowel disease (IBD)

Bronchiectasis are the most common pulmonary manifestation of IBD[50]. They have been associated with IBD in approximately 1-3% depending on the population studied[4–7,18]. Among these, ulcerative colitis has the most clearly established relationship, but an association

has also been suggested with Crohn's disease [42]. The most common form of presentation is the appearance of coughing with chronic bronchorrhea in patients with IBD, many after being colectomised[51]. One of the proposed theories suggests that this is because inflammatory mediators change from the resected intestine to the lung due to their common embryological origin[52]. In some cases, treatment with inhaled and oral glucocorticosteroids has been effective, including their instillation via bronchoalveolar lavage[42], but there is insufficient evidence to prescribe this treatment routinely[1,2].

2.8 Ciliary dysfunction

Primary ciliary dyskinesia (PCD) is a rare aetiology characterised by early onset. It is a hereditary transmitted disease and about 30 associated genes have been isolated, which can determine the heterogeneity and severity of the presentation between individuals[53,54]. It usually appears in childhood in the form of neonatal respiratory distress syndrome, chronic cough and/or chronic nasal congestion in more than 80% of cases[54]. Other frequent findings include chronic rhinosinusitis, dextrocardia, chronic otitis media, hearing loss, anosmia, infertility and diffuse bronchiectasis.

In screening patients with suspected PCD, the saccharin test has many limitations on the undergoing and interpretation of results, so new techniques have been studied to improve the diagnosis of this condition [53]. Nasal nitric oxide (nNO) levels are usually low in PCD patients (around 10-20% of normal values) [53,55]. Therefore, its use as a diagnostic test has grown as more specialized centres have standardized protocols and availability for this technique [53]. Measuring nNO levels has been proven useful in the diagnosis of PCD in adults and children over 5 years of age, but since the technique requires patients to perform trained velum closure or

to exhale against resistance (in order to limit contamination with air from lower airways), reproducibility is limited in younger children [55]. However, low nNO levels can also be found in CF, acute upper airways infections, sinusitis and nasal polyposis, so it should not be used as single diagnostic test [56]. The gold standard for diagnosis is electron microscopy, although it is recommended that the workup be conducted combining various tests such as the frequency and pattern of ciliary beating and the determination of nNO to support the diagnosis [57]. Currently there is no specific treatment for PCD, and few data is available to support strong recommendations on the management of patients with this disease. Nevertheless, the European Respiratory Society task force recommends that patients with PCD should be evaluated and closely followed in centres specializing in this disease by a multidisciplinary team, including education in airway clearance techniques, based on CF guidelines [58].

2.9 Alpha-1-antitrypsin (AAT) deficiency

The association between AAT deficiency and bronchiectasis remains controversial. The prevalence of bronchiectasis in patients with AAT deficiency varies greatly between studies, probably because other aetiologies were not studied in many of them[59,60]. Screening of AAT deficiency is not recommended in the study of bronchiectasis, except in cases in which emphysema on chest HRCT is identified, particularly in a panlobular or basal distribution[2]. Although specific treatment for AAT deficiency is available and it is likely to improve the natural history of bronchiectasis, more evidence is needed to prove its benefit on these patients.

2.10 Gastrointestinal aspiration

The aspiration of gastrointestinal contents have been reported as the cause of bronchiectasis in some studies[4–7,18]. Although few studies exist which aim to analyse this relationship, Lee and colleagues found a prevalence of gastroesophageal reflux (GER) in 40% of patients with bronchiectasis[61]. In the same vein, a recent study by McDonnell et al. observed a high prevalence of hiatus hernia and GER symptoms in individuals with bronchiectasis in stable phase[62]. The presence of GER has been also associated with greater severity of bronchiectasis and a worse outcome of the disease[7,62]. Whether GER is a common cause of bronchiectasis or not it seems reasonable to treat GER where it is identified.

2.11 Cystic fibrosis

Although the majority of cystic fibrosis is diagnosed by neonatal screening or presents during childhood, we continue to identify some cases of CF presenting with apparently idiopathic bronchiectasis during adulthood. Features suggesting the need to exclude CF will include early age at presentation, the presence of non-respiratory features such as malabsorption or infertility, the early presence of *Pseudomonas aeruginosa*, *Burkholderia cepacia* or *Staphylococcus aureus* and the presence of an upper lobe distribution on CT. Whether heterozygosity for CFTR mutations contribute to the development of bronchiectasis is unclear. Investigation is with sweat test and genetic screening.

2.12 Idiopathic causes

This category encompasses all patients with bronchiectasis in whom it was not possible to identify a cause despite a full aetiological study. The prevalence of this group varies greatly

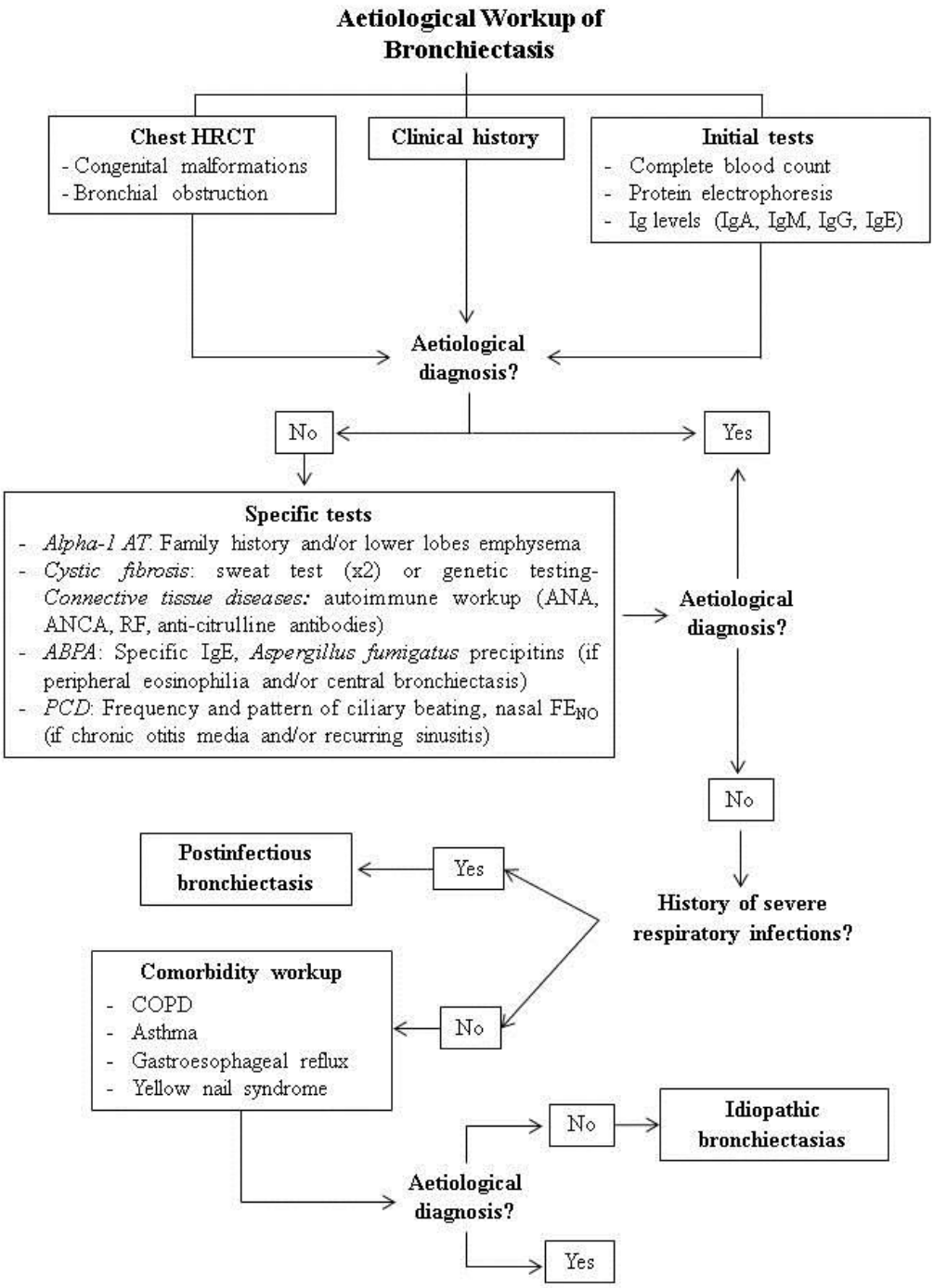
depending on the population and the rigour of the diagnostic study, and lies between 26-74%[6]. A sub-analysis by Shoemark et al. reported an older mean age at diagnosis and predominant involvement of lower lobes in individuals with idiopathic bronchiectasis compared with patients with post infectious bronchiectasis, who had a mean age at diagnosis of 7 years and more diffuse lung involvement[5]. Lonni and colleagues also noted that the group of patients without a definite cause had more mild to moderate bronchiectasis compared to the other subjects[7]. Despite these findings, it is still a very heterogeneous group and more studies are needed to understand and identify the causative mechanisms of bronchiectasis in these patients.

4. APPROACHES TO AETIOLOGICAL DIAGNOSIS

Bronchiectasis may be related to many diseases and many of them may require specific treatment. Identifying the cause of this bronchial disease may determine patient management or the need for genetic testing of individuals and their relatives in 7-13% of cases[6,7]. Therefore, it is recommended to try determining the diagnosis of the cause of bronchiectasis in all cases where possible.

Some aetiologies must be ruled out in all patients with bronchiectasis due to clinical implications in the management and prognosis. These include immunodeficiencies with antibody production deficiency, ABPA, primary ciliary dyskinesia, gastroesophageal reflux disease, mycobacterial infection, alpha-1 antitrypsin deficiency and CF[1]. **Figure 1** summarises the proposed algorithm for addressing the aetiologic diagnosis[1,2].

Figure 1. Proposed algorithm for establishing the aetiologic diagnosis of bronchiectasis



HRCT: high-resolution computed tomography; Ig: Immunoglobulin; Alpha-1-AT: Alpha-1 antitrypsin; ANA: antinuclear antibodies; ANCA: anti neutrophil cytoplasmic antibodies; RF: rheumatoid factor; ABPA: allergic bronchopulmonary aspergillosis; PCD: Primary ciliary dyskinesia; $FE_{NO:}$ Fraction of exhaled nitric oxide, COPD, Chronic obstructive pulmonary disease.

In summary, all bronchiectasis patients should undergo a detailed medical background assessment and at least a basic study of immunoglobulin levels. If no immunodeficiency is detected, specific tests must be performed according to clinical history. The diagnosis of postinfectious bronchiectasis is made when other aetiologies have been ruled out and a history of severe respiratory infections exists. Finally, idiopathic bronchiectasis can be diagnosed only after a negative thorough aetiological study and no other bronchiectasis-related comorbidities are identified.

CONCLUSIONS

Identifying the aetiology of bronchiectasis is challenging, but important as early identification of treatable underlying disorders can lead to a change in management. We advocate a systematic approach to investigation for every patient with careful exclusion of each of the underlying conditions listed above. Continued improvements in the investigation and management of bronchiectasis will lead to better long term outcomes.

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