Diagnostic delay in bronchiectasis: an Italian perspective

Received: 25 Sept 2023
Accepted: 10 Dec 2023

To the Editor:

Bronchiectasis is a chronic respiratory disease characterised by an abnormal dilation of the bronchi associated with a clinical syndrome of daily productive cough and a history of frequent exacerbations [1]. Although bronchiectasis awareness has increased over the past decades, underestimation of this disease still exists across different settings and healthcare professionals [2]. A diagnostic delay seems to exist in bronchiectasis, ranging from 12 to 17 years, and this might lead to disease progression and worsen patients' outcomes [3, 4, 5]. So far, no studies have evaluated specific reasons for diagnostic delay as well as patients' journeys before bronchiectasis diagnosis. To assess the length and reasons for diagnostic delay in bronchiectasis, a multicentre, observational, point-prevalence study was conducted across seven Italian hospitals from November 2022 to May 2023. Ethical committee approval was obtained from each study site and written consent was obtained from each patient. Consecutive adults (age ⩾18 years) with a clinical and radiological diagnosis of bronchiectasis were recruited [1]. Patients with cystic fibrosis or those with traction bronchiectasis due to pulmonary fibrosis were excluded. Demographic, aetiological, clinical, radiological, functional, microbiological and treatment data were collected. Dates of symptom onset, physician visit, first chest computed tomography (CT) scan performed, bronchiectasis diagnosis and referral to a bronchiectasis clinic were collected. In addition, patients were invited to indicate which healthcare professional they consulted initially, if a misdiagnosis of respiratory diseases other than bronchiectasis was made, and if they experienced a worsening of symptoms because of the diagnostic delay. According to the arbitrary assumption that a reasonable time for bronchiectasis diagnosis is 1 year, patients were divided into two groups: those with a diagnostic delay ⩽365 days (group 1) *versus* those with a diagnostic delay >365 days (group 2). The primary objective of the study was the assessment of time from onset of symptoms to the diagnosis of bronchiectasis as a disease. Qualitative variables were summarised using absolute and relative (percentage) frequencies. Sample characteristics were described using descriptive statistics. Comparison of quantitative variables was evaluated using Mann–Whitney U-tests; Pearson's Chi-squared or Fisher's exact tests were used for qualitative ones. A two-tailed p-value <0.05 was considered statistically significant.

232 bronchiectasis patients (72.0% female, median (interquartile range (IQR)) age 63 (51–70) years) were enrolled. The aetiology of bronchiectasis was idiopathic in 52.3% of cases, post-infective in 17.2%, asthma-associated in 6.5%, associated with COPD in 6.5%, due to primary immunodeficiencies in 3.7% and due to primary ciliary dyskinesia in 3.3%. Among comorbidities, the most prevalent one was gastro-oesophageal reflux disease (42.7%), followed by arterial hypertension (30.3%), chronic rhinosinusitis (29.0%), asthma (26.7%), COPD (18.5%), anxiety (11.7%) and depression (9.5%). The median (IQR) value of the Reiff score was 4 (3–6), while the bronchiectasis severity index (BSI) was 6 (3–10). 23.1% of patients experienced at least three exacerbations in the year prior to enrolment. The most prevalent symptoms at onset included daily productive cough and frequent exacerbations. Patients went to a physician after a median (IQR) 9 (0–60) days from symptoms onset. General practitioners (72.4%) and pulmonologists (54.7%) were the healthcare professionals most seen by patients at symptom onset (table 1). Physicians recognised only respiratory symptoms (documenting only the symptoms; for example, productive cough without a diagnosis of a specific respiratory disease) in 17.2%; whereas a wrong diagnosis of asthma or COPD was made in 19.0% and 9.1%, respectively (table 1), while a coexistence of bronchiectasis with asthma or COPD was diagnosed in 62 (26.7%) and 43 (18.5%) patients, respectively. A chest CT was performed after a median (IQR) 885.5 (136.5–5019.0) days from symptom onset. The diagnosis of bronchiectasis as a chronic respiratory disease was made after a median (IQR) 1316 (243.5–5697.5) days, ∼3.5 years, from symptoms onset. Pulmonologists, including those with an expertise in bronchiectasis, were the healthcare professionals who made the diagnosis of bronchiectasis more frequently. Patients' access to a bronchiectasis clinic occurred after a median (IQR) 3303 (786.5–7874.5) days, ∼9 years, from symptom onset. Finally, more than half of the patients (58.7%) felt that the diagnostic

Shareable abstract (@ERSpublications)
It takes ∼3.5 years to reach a diagnosis of bronchiectasis from onset of symptoms: the long patient's journey in Italy https://bit.ly/46XMWAz

Cite this article as: Chessari C, Simonetta E, Amati F, *et al*. Diagnostic delay in bronchiectasis: an Italian perspective. *ERJ Open Res* 2024; 10: 00713-2023 [DOI: 10.1183/23120541.00713-2023].

TABLE 1 Patients' symptoms at disease onset; initial healthcare professional consulted at symptom onset; misdiagnosis; and patients' perception of diagnostic delay

	Study population	Group 1: delay ⩽365 days	Group 2: delay >365 days	p-value
Patients	232	73	159	
Patients' symptoms at disease onset				
Daily cough	155 (66.8)	46 (63.0)	109 (68.6)	0.41
Frequent exacerbations	112 (48.3)	25 (34.3)	87 (54.7)	0.004
Daily sputum	101 (43.5)	32 (43.8)	69 (43.4)	0.95
Frequent pneumonia	63 (27.2)	15 (20.6)	48 (30.2)	0.13
Fatigue	58 (25.0)	20 (27.4)	38 (23.9)	0.57
Exertional dyspnoea	58 (25.0)	21 (28.8)	37 (23.42	0.38
Sputum most days of the week	49 (21.1)	14 (19.2)	35 (22.0)	0.62
Cough most days of the week	45 (19.4)	17 (23.3)	28 (17.6)	0.31
Chest pain	39 (16.8)	16 (21.9)	23 (14.5)	0.16
Haemoptysis	34 (14.7)	17 (23.3)	17 (10.7)	0.01
Dyspnoea at rest	29 (12.6)	12 (16.4)	17 (10.8)	0.23
Weight loss	21 (9.1)	6 (8.2)	15 (9.4)	0.77
Fever	18 (7.8)	5 (6.9)	13 (8.2)	0.73
Other(s)	7 (3.0)	0 (0.0)	7 (4.5)	0.07
Healthcare professionals consulted at symptom onset[#]				
General practitioner	168 (72.4)	48 (65.8)	120 (75.5)	0.12
Pulmonologist	127 (54.7)	47 (64.4)	80 (50.3)	0.05
Paediatrician	23 (9.9)	3 (4.1)	20 (12.6)	0.05
Emergency room physician	22 (9.5)	8 (11.0)	14 (8.8)	0.60
Otolaryngologist	14 (6.0)	4 (5.5)	10 (6.3)	1.00
Allergist or immunologist	12 (5.2)	4 (5.5)	8 (5.0)	1.00
Pulmonologist expert in bronchiectasis	10 (4.3)	4 (5.5)	6 (3.8)	0.51
Cardiologist	7 (3.0)	1 (1.4)	6 (3.8)	0.44
Infectious disease physician	5 (2.2)	1 (1.4)	4 (2.5)	1.00
Other(s)	10 (4.3)	7 (9.6)	3 (1.9)	0.01
Misdiagnosis at symptom onset				
Chronic bronchitis	119 (51.3)	28 (38.4)	91 (57.2)	0.008
Asthma	44 (19.0)	14 (19.2)	30 (18.9)	0.96
COPD	21 (9.1)	6 (8.2)	15 (9.4)	0.77
Pneumonia or recurrent pneumonia	20 (8.6)	7 (9.6)	13 (8.2)	0.72
Gastro-oesophageal reflux disease	17 (7.3)	5 (6.9)	12 (7.6)	0.85
Chronic sinusitis	7 (3.0)	1 (1.4)	6 (3.8)	0.44
Tuberculosis	3 (1.3)	1 (1.4)	2 (1.3)	1.00
Cystic fibrosis	3 (1.3)	2 (2.7)	1 (0.6)	0.23
Other	4 (1.7)	0 (0.0)	4 (2.5)	0.31
No disease, only symptom(s)	40 (17.2)	23 (31.5)	17 (10.7)	<0.0001
Physician who made the diagnosis of bronchiectasis				0.64
Pulmonologist	155 (66.8)	51 (69.9)	104 (65.4)	
Pulmonologist expert in bronchiectasis	60 (25.9)	28 (27.4)	40 (25.2)	
Paediatrician	9 (3.9)	1 (1.34)	8 (5.0)	
General practitioner	3 (1.3)	0 (0.0)	3 (1.9)	
Other	5 (2.0)	1 (0.6)	4 (2.4)	
Feeling about the diagnostic delay				0.23
My illness is unchanged	89 (38.4)	35 (48.0)	54 (34.0)	
My illness has worsened reversibly	86 (37.1)	22 (30.1)	64 (40.3)	
My illness has worsened irreversibly	50 (21.6)	14 (19.2)	36 (22.6)	
My illness has improved	7 (3.0)	2 (2.7)	5 (3.1)	

Data are presented as n or n (%), unless otherwise stated. [#]: more than one answer allowed.

delay worsened their respiratory status (table 1). 73 (31.5%) and 159 (68.5%) patients belonged to group 1 and 2, respectively. Patients with three or more exacerbations per year were more prevalent in group 1. Patients in group 1 had a higher prevalence of both anxiety (19.2% *versus* 8.2%; p=0.02) and depression (15.1% *versus* 7.0%; p=0.05) than those in group 2. Patients in group 2 had a higher median (IQR) Reiff score (5 (3.0–7.5) *versus* 4 (2–6); p=0.02), while there was no significant difference in the BSI between the two groups (median (IQR) 6 (4–10) in group 1 *versus* 6 (3–9) in group 2; p=0.17). Patients in group 1 consulted a pulmonologist more frequently (64.4% *versus* 50.3%; p=0.05) than group 2. A history

of haemoptysis was more frequent in group 1 than group 2 (23.3% *versus* 10.7%; p=0.01). Group 1 included a higher proportion of patients lacking a specific diagnosis compared to group 2 (31.5% *versus* 10.7%; p<0.0001). Patients in group 2 more frequently had a misdiagnosis of bronchitis (54.7% *versus* 34.3%; p=0.004) and nonspecific chronic bronchitis (57.2% *versus* 38.4%; p=0.008) compared to group 1.

The diagnostic delay in our bronchiectasis cohort (3.5 years) is lower when compared with both Spanish and English cohorts in which diagnostic delays of 12 and 17 years were reported, respectively [3, 4]. However, it is much longer than in COPD. A Chinese COPD study quantified the average diagnostic delay of 230 (IQR 50–720) days [6], while a large United Kingdom study reported that in COPD at an earlier stage, diagnostic opportunities are often lost [7]. An American study of 29 patients with α1-antitrypsin deficiency quantified the median diagnostic delay as 2.9 years and showed that it was associated with worse symptoms and functional status [8]. Comparing prevalence and incidence in similar geographic areas, bronchiectasis prevalence in primary care in Italy in 2015 was 163 per 100 000 inhabitants [2], while in Catalonia (Spain) in 2016 it was 362 cases per 100 000 inhabitants [9]. According to this difference, we might speculate that bronchiectasis awareness in primary care in Italy is low and this could explain both the diagnostic delay and especially the high rate of misdiagnosis we found in our study. A chest CT scan performed >1 year before the diagnosis and a diagnosis of bronchiectasis as a chronic respiratory disease made after >3 years from symptom onset seem unacceptable. The delayed chest CT scan could be explained by a misdiagnosis of chronic bronchitis, asthma or COPD. These findings are in line with data from the European Registry showing that >50% of bronchiectasis patients are treated with inhaled corticosteroids [10]. Factors associated with an earlier diagnosis of bronchiectasis were the presence of haemoptysis, a high rate of exacerbations and the coexistence of both anxiety and depression. Our study is limited by the inclusion of an Italian sample exclusively; different characteristics can be found in non-Italian bronchiectasis patients. Furthermore, in our experience, subjects enrolled belonged to a selected population of patients across secondary care bronchiectasis programmes and no data were collected on first *Pseudomonas* isolation. In addition, we should acknowledge that using date of symptom onset as a surrogate time to diagnosis may not be entirely reliable, because some symptoms, such as cough, may not be specific to bronchiectasis, while others, such as haemoptysis, may make the diagnosis of bronchiectasis more likely. In addition, since symptom onset was reported by the patients, a recall bias should be acknowledged. Finally, outcome data according to diagnostic delay are missing and many patients had the perception that their disease worsened due to the diagnostic delay; however, objective clinical, radiological and functional measurements of disease trajectory are missing in our experience and should be collected in further longitudinal, prospective studies. The strengths of our study are its multicentre design and a detailed collection of dates and characteristics linked to the delay. At present, diagnostic delay in bronchiectasis in Italy is still unacceptable with a high percentage of patients misdiagnosed with chronic bronchitis, asthma or COPD. Increasing bronchiectasis awareness, comprehensive history taking and proper examination are priorities especially in the community. A close partnership with bronchiectasis patient associations and general practitioners is key, along with a greater dissemination and implementation of international guidelines among pulmonologists [11, 12].

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Provenance: Submitted article, peer reviewed.

Ethics statement: Ethical committee approval was obtained at each study site.

Conflict of interest: G. Sotgiu is an associate editor of this journal. A. Gramegna reports consulting fees from Vertex and Zambon, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from Vertex, Chiesi and Insmed, outside the submitted work; support for attending meetings and/or travel from Neupharma, Chiesi and Insmed, outside the submitted work; participation on a Data Safety Monitoring Board or Advisory Board for Vertex, outside the submitted work. F. Blasi reports grants or contracts from AstraZeneca, Chiesi, GlaxoSmithKline and Insmed, outside the submitted work; consulting fees from GlaxoSmithKline, Menarini and OM Pharma, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from AstraZeneca, Chiesi, GlaxoSmithKline, Grifols, Insmed, Menarini, Om Pharma, Pfizer, Sanofi, Vertex, Viatris and Zambon, outside the submitted work. C. Crimi reports payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from GSK, Sanofi, AstraZeneca, F&P, ResMed and Novartis, outside the submitted work; and patent pending number 102023000013077 not related to the submitted work. S. Aliberti reports grants or contracts from Insmed Incorporated, Chiesi, Fisher & Paykel and GSK, outside the submitted work; royalties or licenses from McGraw Hill, outside the submitted work; consulting fees from Insmed Incorporated, Insmed Italy, Insmed Ireland Ltd, Zambon Spa, AstraZeneca UK Limited, AstraZeneca Pharmaceutical LP, CSL Behring GmbH, Grifols, Fondazione Internazionale Menarini, Moderna, Chiesi, MSD Italia S.r.l., BRAHMS, Physioassist SAS and GlaxoSmithKline Spa, outside the submitted work; payment or honoraria for lectures, presentations, speakers' bureaus, manuscript writing or educational events from GlaxoSmithKline Spa, Thermofisher Scientific, Insmed Italy, Insmed Ireland Ltd, Zambon and Fondazione Internazionale Menarini, outside the submitted work; and participation on a Data Safety Monitoring Board or Advisory Board for Insmed Incorporated, Insmed Italy, AstraZeneca UK Limited and MSD Italia S.r.l, outside the submitted work. The remaining authors have nothing to disclose.

Support statement: This work was partially supported by "Ricerca Corrente" funding from the Italian Ministry of Health to IRCCS Humanitas Research Hospital.

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