Respiratory Medicine 170 (2020) 105954

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: http://www.elsevier.com/locate/rmed

Review article

Diagnosis and quantification of bronchiectasis using computed tomography or magnetic resonance imaging: A systematic review

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ARTICLE INFO

Keywords:
Bronchiectasis
Tomography
X-ray computed
Magnetic resonance imaging
Systematic review

ABSTRACT

Background: Bronchiectasis is an irreversible dilatation of the airways caused by inflammation and infection. To diagnose bronchiectasis in clinical care and to use bronchiectasis as outcome parameter in clinical trials, a radiological definition with exact cut-off values along with image analysis methods to assess its severity are needed. The aim of this study was to review diagnostic criteria and quantification methods for bronchiectasis.
Methods: A systematic literature search was performed using Embase, Medline Ovid, Web of Science, Cochrane and Google Scholar. English written, clinical studies that included bronchiectasis as outcome measure and used image quantification methods were selected. Criteria for bronchiectasis, quantification methods, patient demographics, and data on image acquisition were extracted.
Results: We screened 4182 abstracts, selected 972 full texts, and included 122 studies. The most often used criterion for bronchiectasis was an inner airway-artery ratio ≥1.0 (42%), however no validation studies for this cut-off value were found. Importantly, studies showed that airway-artery ratios are influenced by age. To quantify bronchiectasis, 42 different scoring methods were described.
Conclusion: Different diagnostic criteria for bronchiectasis are being used, but no validation studies were found to support these criteria. To use bronchiectasis as outcome in future studies, validated and age-specific cut-off values are needed.

1. Introduction

Bronchiectasis is defined as an abnormal and permanent dilatation of the airways, usually sustained by local inflammation and chronic infection [1]. Bronchiectasis is associated with different genetic or acquired conditions including cystic fibrosis (CF), primary or secondary immune deficiencies, and ciliopathies, or can develop as a result of low respiratory tract infections [2,3]. However, in the majority of the patients, bronchiectasis is present without a clear underlying disease [3].

Chest computed tomography (CT) is considered the gold standard for the radiological diagnosis. To determine whether airways are dilated, airway diameters are usually compared with diameters of their adjacent arteries. To date, no exact radiological criteria of bronchiectasis exist. A widely accepted definition of bronchiectasis is described by the Fleischner society in the glossary of terms for thoracic imaging [4]. In this guideline bronchiectasis is defined as a "bronchial dilatation with respect to the adjacent pulmonary artery (signet ring sign), lack of tapering of bronchi, and identification of bronchi within 1 cm of the pleural surface" [4]. However, several challenges with this diagnosis might be identified. First, the threshold width for bronchiectasis of the airway compared to that of the artery is not specified. Second, it is unclear whether inner [luminal] or outer airway diameters should be measured. To use bronchiectasis as outcome measure in both daily care and clinical trials, precise criteria with clear cut-off values for

Abbreviations: CF, Cystic fibrosis; CT, Computed tomography; MRI, Magnetic resonance imaging; PRAGMA-CF, Perth-Rotterdam annotated grid morphometric analysis for cystic fibrosis.

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https://doi.org/10.1016/j.rmed.2020.105954
Received 4 November 2019; Received in revised form 27 March 2020; Accepted 31 March 2020
Available online 9 April 2020

bronchiectasis are needed.

In light of the absence of exact radiological criteria of bronchiectasis and the heterogeneity of definitions reported in literature, we decided to conduct a systematic review with the following objectives: 1) To identify the most common diagnostic criteria for bronchiectasis used in clinical trials, and 2) To evaluate how the severity and extent of bronchiectasis have been quantified.

2. Methods

2.1. Search

We conducted the initial literature search at December 9th, 2016, and an additional search was performed on July 11th, 2018. Literature search was conducted with help of a biomedical information specialist (dr. WM Bramer) using the following search terms: bronchiectasis, radiology, diagnostic imaging, magnetic resonance imaging (MRI), CT, X-ray, Röntgen. The search was restricted by papers written in English. The following databases were searched: Embase, Medline Ovid, Web of Science, Cochrane, and Google Scholar. Search queries are presented in e-Table 1.

2.2. Review registration

This review was registered at PROSPERO, registration number: CRD42017055001.

2.3. Review process

The systematic search was performed in two phases. First, title and abstract screening was done independently by two authors (JM and GV), and a consensus on selected papers was reached after face-to-face meetings. Second, a full text screening was done independently by the same authors, which was also followed by face-to-face meetings to reach a consensus on the selected papers.

A full list of inclusion and exclusion criteria is reported in Table 1. In short, we searched for clinical studies in which: 1) criteria to diagnose bronchiectasis were described; 2) bronchiectasis was used as an outcome measure; and 3) severity of bronchiectasis was measured.

Table 1
Inclusion and exclusion criteria.

Title abstract screening	
Inclusion criteria	Bronchiectasis
	Radiological assessment of bronchiectasis
	Clinical study
Exclusion criteria	Reviews
	Case reports n < 10
Full text screening	
Inclusion criteria	Clear criteria of bronchiectasis that are used in the study are presented
	Bronchiectasis is used as outcome measure
	Bronchiectasis outcomes are statistically validated against other clinical parameters or against a control group
	Underlying mechanism of the development of bronchiectasis is inflammation/infection of the bronchial wall (for example studies about traction bronchiectasis in case of fibrosis or widened airways due to collagen or cartilage disorder were not included)
	Imaging (X-ray, CT, bronchography or magnetic resonance imaging)
	Humans
	Original study
	English written
	If published more than once, the most recent study is selected
	Severity and/or extent of bronchiectasis is evaluated
Exclusion criteria	Reviews
	Case reports n < 10
	Papers of which the full text could not be found
	Papers that we did not have access to (Erasmus MC university database and no response or e-mail authors)

2.4. Missing papers

We searched for full texts in journals that were included in the licenses of the library of Erasmus Medical Centre. For journals not included in the licenses, we requested a copy of the paper by approaching the corresponding author by e-mail and/or ResearchGate. Papers that could not be found were excluded from the analysis.

2.5. Data extraction

The following data were extracted from the selected studies: criteria for bronchiectasis diagnosis; imaging modality; standardisation of lung volume; patient groups and characteristics (age, gender, race); scoring methods for bronchiectasis; and reproducibility measures.

2.6. Referring to multiple publications

Due to the large number of studies selected by this systematic review, references in relation to a specific topic that include more than ten studies are tabulated in Table 2.

3. Results

3.1. Search

A flowchart of the included and excluded papers along with the main reasons for exclusion of full texts are presented in Fig. 1. A total of 4182 papers were identified. After screening all titles and abstracts, 972 papers were selected for full text evaluation, and 122 were included in the analysis [5–126]

3.2. Radiological criteria to define bronchiectasis

Criteria for radiological diagnosis of bronchiectasis across 122 studies are reported in Table 3. The most used criterion, reported in 108 (89%) studies, was an increased ratio of the cross-sectional diameter of an airway and its adjacent artery [airway-artery ratio] with cut-off values ranging from 1.0 to 1.5. In 59 (48%) studies inner airway diameters were used to assess this ratio, and four studies (3%) used outer airway diameters [89,92,122,123].

Exact measurements of airway-artery ratios were presented in eight (7%) studies. Four (3%) studies presented mean inner airway-artery ratios in healthy adults, being 0.68 (n = 85), 0.70 (n = 33), 0.71 (n = 42), and 0.79 (n = 106) [24,25,54,69]. Four other studies (3%) studied airway-artery ratios of children with CF or common variable immunodeficiency disorders [60,84,123,124]. Long et al. reported significantly different inner airway-artery ratios in CF patients (n = 23) and controls (n = 20), of 0.77 and 0.55 respectively [60]. Perez et al. reported that outer airway-artery ratios of diseased and control subjects were significantly different (1.17 versus 1.02 respectively); while inner airway-artery ratios were not [84]. Kuo et al. also reported that outer airway-artery ratios were more precise than inner airway-artery ratios, and presented cut-off values for outer airway-artery ratios of 1.06 for children younger than six years [124], and 1.11 for children above six years of age [123].

The second most used criterion to define bronchiectasis was the lack of tapering of the airways, which was mentioned in 37 (30%) studies.

The third most used criterion was the visibility of airways in the periphery of the lung, reported in 25 (20%) studies. The following cut-

Table 2
Reference legend for topics that include to more than ten studies.

Topic	Studies
Studies in which the inner diameter of the airway was used to assess the airway - artery ratio	[1-59]
Studies in which it was not stated whether the inner or outer wall of the airway was used for the airway - artery ratio	[60-104]
Lack of tapering included in definition of bronchiectasis	[1,2,4,7,9-11,13-16,21,26,27,33,36,37,43,44,47,49,50,52,53,55,56,58,63,65,71,73,74,85,86,93,103,105]
Definition visibility of airway 1 cm from pleura	[1,2,4,9,10,15,16,21,26,52,58,63,65,71,103]
Studies that referred to Naidich et al for a description of bronchiectasis [106]	[35,52,53,58,107-117]
The in- or expiratory level of the lungs during scanning was discussed	[1-3,5-11,14-17,22-24,28,29,31,34,35,37,38,40-43,45,46,49-55,57-59,61,62,64-66,69-71,75-77,80-85,87,90,93-97,99-104,108-111,113,114,118-123]
CT scanning was performed during inspiratory breath hold without further specification	[2,3,5-11,14-17,22-24,28,29,31,35,37,38,40,41,45,46,49,50,52,53,55,57,61,62,64-66,69,71,75-77,82,83,85,90,93,94,99,100,102,103,109-111,113,114,118,119]
Volume standardisation during CT scanning was pressured controlled under general	[11,34,54,58,70,80,95,101,104,122,123]
Did not mention the level of inspiration	[4,12,13,18-21,25-27,30,32,33,36,39,44,47,48,56,60,63,67,68,72-74,78,79,86,88,89,91,92,98,105,107,112,115-117]
Lungs were also scanned after maximal expiration	[1,4-6,10,11,14,17,29,37,42,44,52,59,61,65,66,70,75,77,80-82,85,87,89,90,95-97,99,101-103,108,121-123]
Only adults in study	[2,4,5,7-9,12,15-22,25-28,30-33,35-39,45,48-53,55-58,60,62,67,69,71,73,74,76,78,83,87,89,92,93,100,103,107-113,115-117]
Only children in study	[11,13,14,34,64-66,70,72,80,82,84,85,95,97,99,101,102,104,114,118-123]
Both adults and children in study	[3,6,10,23,24,29,40-42,46,59,61,63,68,75,77,79,81,86,88,90,91,94,96,98,105]
Patients with bronchiectasis that was either post-infective, idiopathic or not further specified were included	[1,7,11,13,19-22,25-28,31-33,35,36,40,41,43,44,47,49,53,54,56,57,61,71,72,74,76,78,85,87,89,93,100,103,107,109-117]
Patients with cystic fibrosis were included	[3,4,6,10,14,23,24,29,34,35,39,42,46,59,64-66,68,70,75,77,80-82,84,85,88,90,92,94-99,101-105,111,118-123]
Patients with primary ciliary dyskinesia were included	[7,13,26,32,33,35,40,41,43,47,48,63,71,72,79,85,86,91,93,111,113,114,116]
Patients with immune deficiencies were included	[7,11,13,17-21,33,40,41,43,47,67,71,72,84,89,93,111,113,116]
Patients with chronic obstructive pulmonary disease were included	[5,15,16,19-22,45,52,58,61,62,69,71,73,103,111]
Patients with asthma were included	[19-22,47,50,55,60,61,72,103]
Patients with allergic bronchopulmonary aspergillosis were included	[7,32,33,60,71,89,107,110,113,116]
Actual measurements of airways	[4,8,9,30,34,38,59,80,84,102-104,119-121]
Airway – artery ratios were measured	[8,9,30,34,38,80,84,103,104,119-121]
Used Brody or CF-CT method	[4,14,63-66,68,75,77,79-82,84,88-91,94,96-99,102,118-120]
Used Bhalla scoring method	[3,6,10,13,23,24,26,27,29,31-33,40,41,46,49,52-54,58,76,78,81,86,118]
Bronchiectasis scores validated against spirometry	[1-3,5,6,8,9,11,13,14,16-19,21-27,31,35-37,39,40,42,44,48-53,57,59-65,67,68,72,73,75,77-79,81-83,85-94,97,99,102,103,105,108,110,114,117-119]
Bronchiectasis scores validated against clinical symptoms	[8,16,23,36,37,44,52-55,58,69,72,73,75,76,83,97,98,105,107,110,113]
Bronchiectasis scores validated against bacterial infections	[14-16,31,36,45,48,52,53,55,56,64,73,86,91,95,97,101,113,116]
Bronchiectasis scores validated against inflammatory markers	[6,12,18,24,28,45,52,57,60,70,72,73,88,95,102,122]
Bronchiectasis scores validated against pulmonary exacerbations	[44,45,52,53,64,73,74,77,94,96,97,107]
Bronchiectasis scores validated against mortality or survival	[7,16,24,33,43,47,54,71,100,107,111,115]
Longitudinal studies with bronchiectasis as outcome measure	[18,67,68,79,81,94,99,100,104,118,119]
Scoring was performed by 1 observer	[2,4,6,8,9,11-13,21,28,32,38,44,48,63,70,72,77,82,84,86,95-101,104,111,116,118-122]
Scoring was performed by 2 observers	[1,5,7,10,15-18,22-25,27,29-31,33-37,39-41,43,45,49-53,55,57,58,60-62,64,65,67-69,71,73,76,79,80,83,85,88,89,92-94,102,103,108-110,113-115,117]
The final score was decided upon consensus	[5,7,10,15-17,22-24,29-31,35-37,40-42,45,46,49,51-53,57,58,60,65,67,73,81,93,103,115,117]
The mean score of the observers was used	[27,33,39,61,62,64,68,76,78,83,85,87,105,108,113]
Reported inter- observer agreement for bronchiectasis score	[11,17,27,49,50,53,64,65,68,79,82,84,85,87-89,91,93-95,108-110,113]
Reported intra- and inter-observer agreement for bronchiectasis score	[8,9,14,34,44,63,66,77,80,96,119,121,122]

off values for a pathognomonic distance of visible airways with respect to the pleura were described: 1.0 cm (n = 15, 12%); 2.0 cm (n = 1, 1%) [107]; 3.0 cm (n = 3, 2%) [58,79,99]; and the peripheral $^1/_3$ of the lung (n = 3, 2%) [80,85,86].

3.3. Imaging modality

All evaluated studies used chest CT to diagnose bronchiectasis. No chest X-ray or bronchography studies were found. In four (3%) studies, bronchiectasis outcomes of MRI scans were compared with those of CT scans [73,74,87,105]. Puderbach et al. concluded that MRI overall performed well, but that subtle morphologic changes such as peripheral bronchiectasis were missed [87]. Montella et al. showed good to excellent agreement between MRI and CT bronchiectasis scores [73,74]. Tepper et al. reported an overestimation of bronchiectasis scores when comparing MRI with CT [105]. All studies emphasised that longitudinal trials are needed to further validate the use of MRI.

3.4. Standardisation of lung volume

Lung volume, *i.e.* the level of inspiration during scanning was discussed in 82 (67%) studies. In 59 (48%) studies CT scanning was performed during inspiratory breath hold without further specification. In 11 (9%) paediatric studies lung volume was pressure controlled, using a manometer to assess transpulmonary pressure while the patient was under general anaesthesia. In ten (8%) studies breath hold practise sessions were held before CT scanning [5,43,77–79,90,104,105,109,112]. Four (3%) studies used a spirometer to establish lung volume [84,89,122,123]. Expiratory CT scans were made in 38 (31%) studies, mostly to detect trapped air. However, two (2%) studies also used expiratory scans to assess bronchiectasis. Both Mott et al. and Do Amaral et al. concluded, in a paediatric and adult study respectively, that expiratory scans were inferior to inspiratory scans to assess bronchiectasis since fewer airways were detected [75,120].

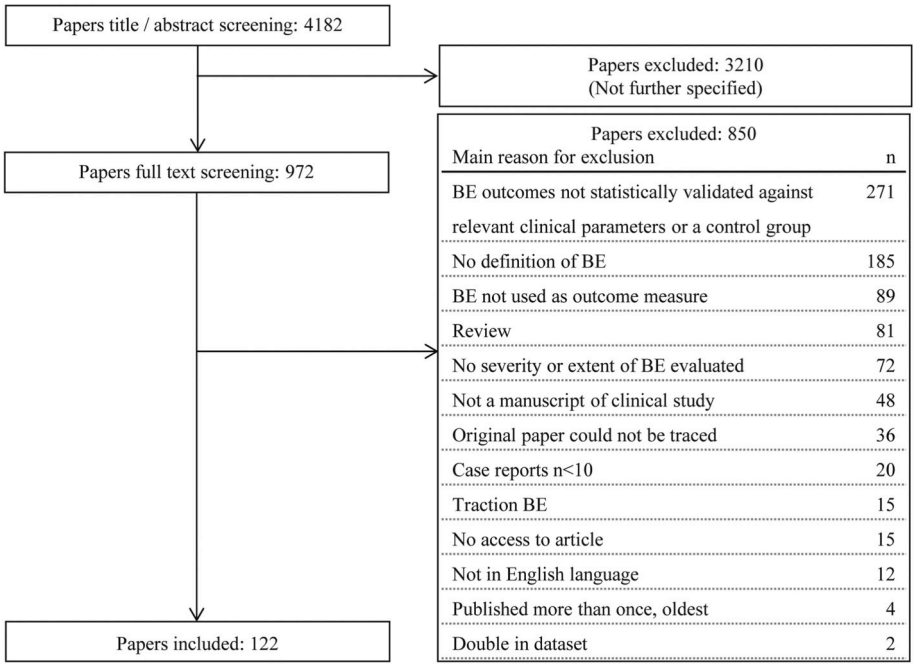

Fig. 1. Flowchart inclusions and exclusions. BE = bronchiectasis. Two reasons for exclusion require extra explanation. Firstly, 48 selected papers were not a manuscript of clinical study, meaning that these papers were not full manuscripts of clinical studies, but poster-presentations or meeting abstracts. Secondly, we had no access to paper in 15 cases, neither via the journal licence of the Erasmus Medical Centre university library, nor after sending request for a copy of the paper to the corresponding author by e-mail or ResearchGate.

Table 3
Criteria for bronchiectasis.

Criterion	n studies (%)
Airway-artery ratio	108 (89%)
≥1.0	
inner airway diameter	52 (43%)
outer airway diameter	4 (3%)
not specified	42 (34%)
≥1.1	
inner airway diameter	7 (6%)
outer airway diameter	0 (0%)
not specified	1 (1%)
≥1.5	
inner airway diameter	1 (1%)
outer airway diameter	0 (0%)
not specified	2 (2%)
Lack of tapering	37 (30%)
Visibility of airways in periphery	25 (20%)

Footnotes: The most frequent used criteria to diagnose bronchiectasis are presented. Airway-artery ratios are calculated by dividing the cross-sectional diameter of an airway by that of its adjacent artery.

3.5. Patient groups and age characteristics

A total of 11,581 subjects were described in 122 evaluated studies, of which 51% were female, 44% were male, and in 5% gender was not specified. Only nine (7%) studies reported the race of the subjects; in these studies the majority of patients was Caucasian [24,25,36,37,79,81,82,95,100]. Median size of study population was 60 [IQR range 30–102]. Enrolled populations contained only adults in 65 studies (53%), only children in 26 studies (21%), and both in 26 studies (21%). As the remaining studies reported mean ages around 50 years, it is likely that only adults were included [5,79,80,88,117].

Bronchiectasis aetiology of enrolled subjects (reported in ten or more studies) was post-infective or idiopathic/not further specified bronchiectasis (49 studies, 40%), CF (47 studies, 38%), primary ciliary dyskinesia (23 studies, 19%), immune deficiencies (22 studies, 18%), chronic obstructive pulmonary disease (17 studies, 14%), asthma (11 studies, 8%), and ten (8%) studies included patients with allergic bronchopulmonary aspergillosis.

3.6. Scoring methods for bronchiectasis

To quantify bronchiectasis 42 different scoring methods have been reported across the 122 included studies. Two approaches to quantify bronchiectasis were identified: exact measurements and semi-quantified scoring methods.

Fifteen (12%) studies assessed the amount of bronchiectasis with exact measurements:

1) Airway-artery ratios were calculated in 12 (10%) studies. Measurements were done manually in all studies, and both manually and automatically in one study [84].
2) Airway dimensions were measured in three (2%) studies and expressed in cumulative airway diameters [12], total airway surfaces of bronchiectic airways [120], or mean airway diameters [109].
3) The total number of airways visible on CT was counted in three (2%) studies [109,122,124].

In semi-quantified scoring methods, amount of extent or severity of structural abnormalities are rated by an observer. An overview from 42 scoring methods, divided in extent and severity of dilatation, is presented in e-Tables 2a and 2b. The two most frequently reported scoring methods were both developed for CF lung disease. Twenty-seven (22%) studies used a method published in 2004 by Brody et al., [14] or an upgraded version, the CF-CT method [127]. Twenty-five (20%) studies used the Bhalla method [10].

3.7. Reproducibility of scoring

Measures to determine inter- and intra-observer agreement of bronchiectasis scores were reported in 36 (30%) studies: five (4%) studies reported only intra-observer agreement [33,105,116,122,124], 24 (20%) studies only inter-observer agreement, and 13 (11%) studies reported both. Intra-class correlation coefficients (ICCs) for bronchiectasis ranged between 0.73 and 0.95 and Cohen's kappa values ranged between 0.47 and 0.88. Roughly, both methods can be interpreted as follows: <0.4 = poor; 0.4–0.6 = fair; 0.6–0.8 = good; >0.8 = excellent.

4. Discussion

We assessed radiological criteria and quantification methods for bronchiectasis in 122 clinical studies. The main findings of the present review are: a) there are no validated criteria to diagnose bronchiectasis; b) cut-off values to diagnose bronchiectasis should be age-specific; c) many different scoring methods are being used to quantify bronchiectasis; d) image acquisition and analysis is often not standardised.

Validation studies containing normal values of criteria for bronchiectasis, i.e. means and standard deviations of airway-artery ratios or tapering of the healthy population, were not found. Cut-off values for airway-artery ratios that can be used to label airways as bronchiectasis are essential. Reported studies on bronchiectasis mainly included relatively small populations of patients with airways disease and even fewer smaller studies reported data airway-artery ratios on healthy volunteers. Clearly such studies are valuable as starting point but their generalisability is doubtful. For other clinical parameters used in respiratory medicine such as spirometry data, reference values have been extensively studied and means and standard deviations are published per age, sex and race. Ideally, similar studies are needed to generate reference values for airway-artery ratios and tapering. However, due to radiation risk, population-based studies using CT scanning have not being conducted to date. As radiation dose needed for chest CT scans have come down considerably in the last decade such studies might become feasible. Similar for MRI reference values have to be generated. Also for MRI being a radiation free alternative no proper reference data for bronchiectasis are available. Until proper validation studies have been performed, it is important to take this limitation into consideration when interpreting data on bronchiectasis patients.

The most used criterion for a radiological diagnosis of bronchiectasis is an airway-artery ratio of more than 1.0, although no study validated the use of this specific cut-off value.

Reported cut-off for airway-artery ratios values varied between 1.0 and 1.5, and no consensus exists on whether inner or outer airway diameters should be used to compute this ratio. The use of inner diameters probably originates from the time that bronchography was used to diagnose bronchiectasis, as the acquired images only revealed inner diameters [128]. However, in diseased lungs airway walls are often thickened, reducing inner diameters as seen on CT. This may lead to false-negative diagnoses of bronchiectasis. Until larger comparison studies have been performed, we suggest to take both the inner and the outer diameter of the airways into account.

Furthermore, optimal cut-off values to detect bronchiectasis seem to be age-dependent [69,122,124]. In older age the ratio seem to increase [129], which is thought to be the result of loss of elastic recoil of the ageing airways [130]. A population based cohort study would be suitable to assess this phenomenon.

While using airway-artery ratios, we assume that artery diameters are unaffected by the underlying disease. Importantly, this assumption has been challenged, as Diaz et al. showed that airway-artery ratios can be altered from the perspective of the arteries in case of smoking, due to local hypoxia [25].

A large number of scoring methods for bronchiectasis have been described. For scientific purposes, scoring methods need to be well validated. Actual measurements are likely more accurate to assess bronchiectasis than semi-quantitative scoring methods. Unfortunately, manual measurements are time consuming. Furthermore, also for these measurements diagnostic criteria and cut-off values should be defined.

Semi-quantitative scoring methods are often not suitable for automated analysis. However, the PRAGMA-CF method, used in three studies [89,92,122], provides scaled outcomes. Eventually, automated systems will replace labour-intensive manual scoring systems, as they are more reproducible, faster, and probably cheaper.

Although chest CT is the current gold standard to detect bronchiectasis, a major disadvantage is the radiation risk. The potential damage of ionising radiation is cumulative, and younger patients are more vulnerable to this effect. This issue is especially important for chronic diseases such as CF as many patients will have multiple CT scans during lifetime often starting from a young age. Even though the lifelong radiation risk for monitoring CF lung disease using biennial chest CT is considered to be low it restricts its use [131]. For this reason MRI being a radiation free imaging modality is an interesting but still technical challenging alternative for chest CT for the sensitive diagnosis of bronchiectasis. In this review, against 122 CT based studies, we identified only four that additionally collected MRI scans, of which the authors' preferences pointed towards CT due to its high sensitivity [73,74,87,105]. More sensitive chest MRI protocols are in development. Importantly, validation of these protocols is needed before MRI can be used as imaging modality for diagnosis of bronchiectasis.

Standardisation of lung volume is not routinely pursued in clinical trials, even though airway-artery ratios, and consequently the detection of bronchiectasis, are dependent on lung volume. It is highly likely that in such studies CT scans were acquired with suboptimal lung volumes. In one study of 20 subjects with CF it was shown that when patients were asked to inhale maximally without any further training and monitoring, CT scans were acquired on average at volume levels of 77% total lung capacity [132], which is a strong argument to introduce standardisation of lung volume for chest CT.

Data of reproducibility of used scoring methods were reported in only 44% of the studies. Providing data on inter- or intra-observer agreement belong to transparent data sharing and strengthens the credibility of the research reports [133]. Published intra- and inter-agreement scores showed overall good results.

Many aetiologies of bronchiectasis were described. Nowadays bronchiectasis is acknowledged as disease entity by itself. The large amount of recent publications between our initial search in December 2016 and our final search July 2018 indicates a growing interest in bronchiectasis. The development of the European patient registry for bronchiectasis patients (www.bronchiectasis.eu) will contribute importantly to improve our knowledge and facilitate new clinical trials in bronchiectasis patients [134].

Limitations of this systematic review were the following. First of all,

Table 4
Research implications and hypotheses on how to diagnose and quantify bronchiectasis.

Topic	Hypotheses	Research implications
Airway-artery ratio	Airway-artery ratios are age specific The use of inner airway – artery diameters results in different outcomes than the use of outer airway – artery ratios	Studies including a large number of diseased and healthy subjects from infancy into adulthood in which airway-artery ratios are measured and receiver operating characteristic curves are plotted on a larger scale
Tapering	Lack of tapering is difficult to detect by eye, but is suitable for automated analysis	Studies using objective automated methods to quantify tapering
Imaging modality	Standardised, volume controlled MRI is suitable to diagnose bronchiectasis	Longitudinal studies with standardised MRI protocols that compare MRI outcomes with other clinical parameters
Scoring methods	Bronchiectasis scoring methods can serve as sensitive outcome measure in clinical studies	Longitudinal studies in which bronchiectasis is scored with standardised methods, of which both sensitivity to monitor changes in disease as well as reproducibility are being assessed

some studies seemed to have used overlapping data. Only if exactly the same studies were published twice, we excluded older versions. However, the literature is reported in a descriptive manner and no statistical analyses were performed.

The lack of a meta analysis of outcomes is another limitation. Due to the use of many different scoring methods and incomplete description of image acquisition and analyses, we felt that we were unable to perform such analyses. Therefore, we made five hypotheses along with research implications on how to diagnose and quantify bronchiectasis (Table 4).

To conclude, different radiological criteria for bronchiectasis are being used but we found no validation studies supporting these criteria. Longitudinal studies including various bronchiectasis patient populations are needed to further validate bronchiectasis criteria and quantification methods. To set up validated criteria for the radiological diagnosis of bronchiectasis, an international taskforce of experts including both pulmonologists and radiologists would be needed.

Source of funding

This work was supported by the Innovative Medicines Initiative (IMI) and EFPIA companies under the European Commission funded project, iABC (grant 115721). The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: J. Meerburg and G. Veerman declare no conflicts of interest. S. Aliberti reports grants and personal fees from Bayer Healthcare, Aradigm Corporation, Grifols, Chiesi, INSMED, personal fees from Astra Zeneca, Basilea, Zambon, Novartis, Raptor, Actavis UK Ltd, and Horizon outside the submitted work; H. Tiddens reports grants from Roche, Novartis, CFF, Vertex, Gilead and Chiesi outside the submitted work, has a patent PRAGMA-CF scoring system issued and is heading the Erasmus Medical Centre -Sophia Children's Hospital core laboratory LungAnalysis.

Acknowledgments

We would like to acknowledge Wichor Bramer, biomedical information specialist of the medical library of Erasmus Medical Center for his help with the literature search.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmed.2020.105954.

References

[1] E. Polverino, P.C. Goeminne, M.J. McDonnell, et al., European Respiratory Society guidelines for the management of adult bronchiectasis, Eur. Respir. J. 50 (3) (2017).
[2] K.S. Brower, M.T. Del Vecchio, S.C. Aronoff, The etiologies of non-CF bronchiectasis in childhood: a systematic review of 989 subjects, BMC Pediatr. 14 (1) (2014).
[3] R. Chandrasekaran, M. Mac Aogain, J.D. Chalmers, et al., Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis, BMC Pulm. Med. 18 (1) (2018) 83.
[4] D.M. Hansell, A.A. Bankier, H. MacMahon, et al., Fleischner Society: glossary of terms for thoracic imaging, Radiology 246 (3) (2008) 697–722.
[5] A. Alzeer, HRCT score in bronchiectasis: correlation with pulmonary function tests and pulmonary artery pressure, Ann. Thorac. Med. 3 (3) (2008) 82–86.
[6] A.P. Andonopoulos, S. Yarmenitis, P. Georgiou, et al., Bronchiectasis in systemic sclerosis. A study using high resolution computed tomography, Clin. Exp. Rheumatol. 19 (2) (2001) 187–190.
[7] R.M. Angus, M.L. Davies, M.D. Cowan, et al., Computed tomographic scanning of the lung in patients with allergic bronchopulmonary aspergillosis and in asthmatic patients with a positive skin test to Aspergillus fumigatus, Thorax 49 (6) (1994) 586–589.
[8] H. Arakawa, K. Fujimoto, Y. Fukushima, et al., Thin-section CT imaging that correlates with pulmonary function tests in obstructive airway disease, Eur. J. Radiol. 80 (2) (2011) e157–e163.
[9] Z.A. Aziz, A.U. Wells, S.R. Desai, et al., Functional impairment in emphysema: contribution of airway abnormalities and distribution of parenchymal disease, Am. J. Roentgenol. 185 (6) (2005) 1509–1515.
[10] M. Bhalla, N. Turcios, V. Aponte, et al., Cystic fibrosis: scoring system with thin-section CT, Radiology 179 (3) (1991) 783–788.
[11] M. Boon, F.L. Vermeulen, W. Gysemans, et al., Lung structure-function correlation in patients with primary ciliary dyskinesia, Thorax 70 (4) (2015) 339–345.
[12] M. Boon, S.E. Verleden, B. Bosch, et al., Morphometric analysis of explant lungs in cystic fibrosis, Am. J. Respir. Crit. Care Med. 193 (5) (2016) 516–526.
[13] C.F. Bortoluzzi, S. Volpi, C. D'Orazio, et al., Bronchiectases at early chest computed tomography in children with cystic fibrosis are associated with increased risk of subsequent pulmonary exacerbations and chronic pseudomonas infection, J. Cyst. Fibros. 13 (5) (2014) 564–571.
[14] A.S. Brody, J.S. Klein, P.L. Molina, et al., High-resolution computed tomography in young patients with cystic fibrosis: distribution of abnormalities and correlation with pulmonary function tests, J. Pediatr. 145 (1) (2004) 32–38.
[15] A.S. Brody, M.R. Kosorok, Z. Li, et al., Reproducibility of a scoring system for computed tomography scanning in cystic fibrosis, J. Thorac. Imag. 21 (1) (2006) 14–21.
[16] J.D. Chalmers, P. Goeminne, S. Aliberti, et al., The bronchiectasis severity index an international derivation and validation study, Am. J. Respir. Crit. Care Med. 189 (5) (2014) 576–585.
[17] S.M.D. da Silva, I.A. Paschoal, E.M. de Capitani, et al., COPD phenotypes on computed tomography and its correlation with selected lung function variables in severe patients, Int J COPD 11 (1) (2016) 503–513.
[18] C.J. Dakin, J.K. Pereira, R.L. Henry, et al., Relationship between sputum inflammatory markers, lung function, and lung pathology on high-resolution computed tomography in children with cystic fibrosis, Pediatr. Pulmonol. 33 (6) (2002) 475–482.
[19] J. de Gracia, M. Vendrell, A. Alvarez, et al., Immunoglobulin therapy to control lung damage in patients with common variable immunodeficiency, Int. Immunopharm. 4 (6) (2004) 745–753.
[20] P.A. de Jong, Y. Nakano, M.H. Lequin, et al., Progressive damage on high resolution computed tomography despite stable lung function in cystic fibrosis, Eur. Respir. J. 23 (1) (2004) 93–97.
[21] P.A. De Jong, Y. Nakano, W.C. Hop, et al., Changes in airway dimensions on computed tomography scans of children with cystic fibrosis, Am. J. Respir. Crit. Care Med. 172 (2) (2005) 218–224.
[22] P.A. De Jong, A. Lindblad, L. Rubin, et al., Progression of lung disease on computed tomography and pulmonary function tests in children and adults with cystic fibrosis, Thorax 61 (1) (2006) 80–85.
[23] A. Devaraj, A.U. Wells, M.G. Meister, et al., Pulmonary hypertension in patients with bronchiectasis: prognostic significance of CT signs, Am. J. Roentgenol. 196 (6) (2011) 1300–1304.
[24] A.A. Diaz, T.P. Young, D.J. Maselli, et al., Quantitative CT measures of bronchiectasis in smokers, Chest 151 (6) (2017) 1255–1262.
[25] A.A. Diaz, T.P. Young, D.J. Maselli, et al., Bronchoarterial ratio in never-smokers adults: implications for bronchial dilation definition, Respirology 22 (1) (2017) 108–113.
[26] J.D. Dodd, S.C. Barry, R.B.M. Barry, et al., Thin-section CT in patients with cystic fibrosis: correlation with peak exercise capacity and body mass index, Radiology 240 (1) (2006) 236–245.
[27] E.A. Edwards, R. Metcalfe, D.G. Milne, et al., Retrospective review of children presenting with non cystic fibrosis bronchiectasis: HRCT features and clinical relationships, Pediatr. Pulmonol. 36 (2) (2003) 87–93.
[28] A. Ekici, E. Bulcun, T. Karakoc, et al., Factors associated with quality of life in subjects with stable COPD, Respir. Care 60 (11) (2015) 1585–1591.
[29] A. Emad, Y. Emad, CD4/CD8 ratio and cytokine levels of the BAL fluid in patients with bronchiectasis caused by sulfur mustard gas inhalation, J. Inflamm. 4 (2007), 2.
[30] E. Erdem, R. Ersu, B. Karadag, et al., Effect of night symptoms and disease severity on subjective sleep quality in children with non-cystic-fibrosis bronchiectasis, Pediatr. Pulmonol. 46 (9) (2011) 919–926.
[31] P.M. Farrell, J. Collins, L.S. Broderick, et al., Association between mucoid Pseudomonas infection and bronchiectasis in children with cystic fibrosis, Radiology 252 (2) (2009) 534–543.
[32] M. Gallego, X. Pomares, M. Espasa, et al., Pseudomonas aeruginosa isolates in severe chronic obstructive pulmonary disease: characterization and risk factors, BMC Pulm. Med. 14 (1) (2014) 103.
[33] L.W. Garratt, E.N. Sutanto, K.M. Ling, et al., Matrix metalloproteinase activation by free neutrophil elastase contributes to bronchiectasis progression in early cystic fibrosis, Eur. Respir. J. 46 (2) (2015) 384–394.
[34] T. Gatheral, N. Kumar, B. Sansom, et al., COPD-related bronchiectasis; independent impact on disease course and outcomes, COPD 11 (6) (2014) 605–614.
[35] P.C. Goeminne, T.S. Nawrot, D. Ruttens, et al., Mortality in non-cystic fibrosis bronchiectasis: a prospective cohort analysis, Respir. Med. 108 (2) (2014) 287–296.

[36] S. Gregersen, T.M. Aaløkken, G. Mynarek, et al., High resolution computed tomography and pulmonary function in common variable immunodeficiency, Respir. Med. 103 (6) (2009) 873–880.
[37] S. Gregersen, T.M. Aaløkken, G. Mynarek, et al., Development of pulmonary abnormalities in patients with common variable immunodeficiency: associations with clinical and immunologic factors, Ann. Allergy Asthma Immunol. 104 (6) (2010) 503–510.
[38] W.J. Guan, Y.H. Gao, G. Xu, et al., Characterization of lung function impairment in adults with bronchiectasis, PloS One 9 (11) (2014), e113373.
[39] W.J. Guan, Y.H. Gao, G. Xu, et al., Six-minute walk test in Chinese adults with clinically stable bronchiectasis: association with clinical indices and determinants, Curr. Med. Res. Opin. 31 (4) (2015) 843–852.
[40] W.J. Guan, J.J. Yuan, Y.H. Gao, et al., Maximal mid-expiratory flow is a surrogate marker of lung clearance index for assessment of adults with bronchiectasis, Sci. Rep. 6 (2016) 28467.
[41] T. Guran, R. Ersu, B. Karadag, et al., Association between inflammatory markers in induced sputum and clinical characteristics in children with non-cystic fibrosis bronchiectasis, Pediatr. Pulmonol. 42 (4) (2007) 362–369.
[42] M.A. Habesoglu, F. Tercan, U. Ozkan, et al., Effect of radiological extent and severity of bronchiectasis on pulmonary function, Multidiscip Resp Med 6 (5) (2011) 284–290.
[43] D.M. Hansell, M.B. Rubens, S.P.G. Padley, et al., Obliterative bronchiolitis: individual CT signs of small airways disease and functional correlation, Radiology 203 (3) (1997) 721–726.
[44] T.H. Helbich, G. Heinz-Peer, D. Fleischmann, et al., Evolution of CT findings in patients with cystic fibrosis, AJR Am. J. Roentgenol. 173 (1) (1999) 81–88.
[45] T.H. Helbich, G. Heinz-Peer, I. Eichler, et al., Cystic fibrosis: CT assessment of lung involvement in children and adults, Radiology 213 (2) (1999) 537–544.
[46] T.C. Hung, H.C. Lin, K.J. Lin, et al., 133Xenon ventilation scan as a functional assessment in bronchiectasis, Chang Gung Med. J. 21 (4) (1998) 403–408.
[47] R.M. Ibrahim, A. Elnekeidy, A. Rizk, et al., Correlation between a proposed MDCT severity score of bronchiectasis and pulmonary function tests, Egypt J Radiol Nucl Med 47 (2) (2016) 413–420.
[48] J. Jin, W. Yu, S. Li, et al., Factors associated with bronchiectasis in patients with moderate-severe chronic obstructive pulmonary disease, Medicine 95 (29) (2016).
[49] W.S. Jong, W.J. Koh, S.L. Kyung, et al., High-resolution CT findings of Mycobacterium avium-intracellulare complex pulmonary disease: correlation with pulmonary function test results, Am. J. Roentgenol. 191 (4) (2008) W160–W166.
[50] T. Kadowaki, S. Yano, K. Wakabayashi, et al., An analysis of etiology, causal pathogens, imaging patterns, and treatment of Japanese patients with bronchiectasis, Respir Invest 53 (1) (2015) 37–44.
[51] S. Khalilzadeh, S. Kahkouee, M. Hassanzad, et al., The correlation of brody high resolution computed tomography scoring system with clinical status and pulmonary function test in patients with cystic fibrosis, Iran. J. Med. Sci. 36 (1) (2011) 18–23.
[52] S.A. Kharitonov, A.U. Wells, B.J. O'Connor, et al., Elevated levels of exhaled nitric oxide in bronchiectasis, Am. J. Respir. Crit. Care Med. 151 (6) (1995) 1889–1893.
[53] A. Kilcoyne, L.P. Lavelle, C.J. McCarthy, et al., Chest CT abnormalities and quality of life: relationship in adult cystic fibrosis, Ann. Transl. Med. 4 (5) (2016), 87.
[54] J.S. Kim, N.L. Muller, C.S. Park, et al., Bronchoarterial ratio on thin section CT: comparison between high altitude and sea level, J. Comput. Assist. Tomogr. 21 (2) (1997) 306–311.
[55] M. Kosar, A. Kurt, S. Keskin, et al., Evaluation of effects of bronchiectasis on bronchial artery diameter with multidetector computed tomography, Acta Radiol. 55 (2) (2014) 171–178.
[56] J.H. Lee, Y.K. Kim, H.J. Kwag, et al., Relationships between high-resolution computed tomography, lung function and bacteriology in stable bronchiectasis, J. Kor. Med. Sci. 19 (1) (2004) 62–68.
[57] A.L. Lee, B.M. Button, S. Ellis, et al., Clinical determinants of the 6-minute walk test in bronchiectasis, Respir. Med. 103 (5) (2009) 780–785.
[58] M.R. Loebinger, A.U. Wells, D.M. Hansell, et al., Mortality in bronchiectasis: a long-term study assessing the factors influencing survival, Eur. Respir. J. 34 (4) (2009) 843–849.
[59] M. Loeve, K. Gerbrands, W.C. Hop, et al., Bronchiectasis and pulmonary exacerbations in children and young adults with cystic fibrosis, Chest 140 (1) (2011) 178–185.
[60] F.R. Long, R.S. Williams, R.G. Castile, Structural airway abnormalities in infants and young children with cystic fibrosis, J. Pediatr. 144 (2) (2004) 154–161.
[61] A.J. Lopes, G.B. Camilo, S.L.S. de Menezes, et al., Impact of different etiologies of bronchiectasis on the pulmonary function tests, Clin. Med. Res. 13 (1) (2015) 12–19.
[62] D.A. Lynch, J. Newell, V. Hale, et al., Correlation of CT findings with clinical evaluations in 261 patients with symptomatic bronchiectasis, Am. J. Roentgenol. 173 (1) (1999) 53–58.
[63] K. Maekawa, Y. Ito, T. Oga, et al., High-resolution computed tomography and health-related quality of life in Mycobacterium avium complex disease, Int. J. Tubercul. Lung Dis. 17 (6) (2013) 829–835.
[64] M. Maglione, A. Bush, S. Montella, et al., Progression of lung disease in primary ciliary dyskinesia: is spirometry less accurate than CT? Pediatr. Pulmonol. 47 (5) (2012) 498–504.
[65] R. Mahadeva, G. Walsh, C.D.R. Flower, et al., Clinical and radiological characteristics of lung disease in inflammatory bowel disease, Eur. Respir. J. 15 (1) (2000) 41–48.
[66] M.A. Martinez-Garcia, M. Perpina-Tordera, P. Roman-Sanchez, et al., Quality-of-life determinants in patients with clinically stable bronchiectasis, Chest 128 (2) (2005) 739–745.
[67] M.A. Martínez-García, M. Perpiñá-Tordera, J.J. Soler-Cataluña, et al., Dissociation of lung function, dyspnea ratings and pulmonary extension in bronchiectasis, Respir. Med. 101 (11) (2007) 2248–2253.
[68] M.A. Martínez-García, J. De Gracia, M.V. Relat, et al., Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score, Eur. Respir. J. 43 (5) (2014) 1357–1367.
[69] S. Matsuoka, K. Uchiyama, H. Shima, et al., Bronchoarterial ratio and bronchial wall thickness on high-resolution CT in asymptomatic subjects: correlation with age and smoking, Am. J. Roentgenol. 180 (2) (2003) 513–518.
[70] M.J. McDonnell, S. Aliberti, P.C. Goeminne, et al., Comorbidities and the risk of mortality in patients with bronchiectasis: an international multicentre cohort study, Lancet Respir Med 4 (12) (2016) 969–979.
[71] C.J. McMahon, J.D. Dodd, C. Hill, et al., Hyperpolarized 3helium magnetic resonance ventilation imaging of the lung in cystic fibrosis: comparison with high resolution CT and spirometry, Eur. Radiol. 16 (11) (2006) 2483–2490.
[72] K.A. Miszkiel, A.U. Wells, M.B. Rubens, et al., Effects of airway infection by Pseudomonas aeruginosa: a computed tomographic study, Thorax 52 (3) (1997) 260–264.
[73] S. Montella, F. Santamaria, M. Salvatore, et al., Assessment of chest high-field magnetic resonance imaging in children and young adults with noncystic fibrosis chronic lung disease: comparison to high-resolution computed tomography and correlation with pulmonary function, Invest. Radiol. 44 (9) (2009) 532–538.
[74] S. Montella, M. Maglione, D. Bruzzese, et al., Magnetic resonance imaging is an accurate and reliable method to evaluate non-cystic fibrosis paediatric lung disease, Respirology 17 (1) (2012) 87–91.
[75] L.S. Mott, K.G. Graniel, J. Park, et al., Assessment of early bronchiectasis in young children with cystic fibrosis is dependent on lung volume, Chest 144 (4) (2013) 1193–1198.
[76] I. Nathanson, K. Conboy, S. Murphy, et al., Ultrafast computerized tomography of the chest in cystic fibrosis: a new scoring system, Pediatr. Pulmonol. 11 (1) (1991) 81–86.
[77] A. Oikonomou, J. Manavis, P. Karagianni, et al., Loss of FEV1 in cystic fibrosis: correlation with HRCT features, Eur. Radiol. 12 (9) (2002) 2229–2235.
[78] A. Oikonomou, J. Tsanakas, E. Hatziagorou, et al., High resolution computed tomography of the chest in cystic fibrosis (CF): is simplification of scoring systems feasible? Eur. Radiol. 18 (3) (2008) 538–547.
[79] Z.P. Onen, B. Eris Gulbay, E. Sen, et al., Analysis of the factors related to mortality in patients with bronchiectasis, Respir. Med. 101 (7) (2007) 1390–1397.
[80] G.C. Ooi, P.L. Khong, M. Chan-Yeung, et al., High-Resolution CT quantification of bronchiectasis: clinical and functional correlation 1, Radiology 225 (3) (2002) 663–672.
[81] C.M. Owens, P. Aurora, S. Stanojevic, et al., Lung clearance index and HRCT are complementary markers of lung abnormalities in young children with CF, Thorax 66 (6) (2011) 481–488.
[82] D.G. Parr, P.G. Guest, J.H. Reynolds, et al., Prevalence and impact of bronchiectasis in α1-antitrypsin deficiency, Am. J. Respir. Crit. Care Med. 176 (12) (2007) 1215–1221.
[83] I.S. Patel, I. Vlahos, T.M.A. Wilkinson, et al., Bronchiectasis, exacerbation indices, and inflammation in chronic obstructive pulmonary disease, Am. J. Respir. Crit. Care Med. 170 (4) (2004) 400–407.
[84] A. Perez-Rovira, W. Kuo, J. Petersen, et al., Automatic airway-artery analysis on lung CT to quantify airway wall thickening and bronchiectasis, Med. Phys. 43 (10) (2016) 5736–5744.
[85] M. Pifferi, D. Caramella, A. Bulleri, et al., Pediatric bronchiectasis: correlation of HRCT, ventilation and perfusion scintigraphy, and pulmonary function testing, Pediatr. Pulmonol. 38 (4) (2004) 298–303.
[86] M. Pifferi, A. Bush, G. Pioggia, et al., Evaluation of pulmonary disease using static lung volumes in primary ciliary dyskinesia, Thorax 67 (11) (2012) 993–999.
[87] M. Puderbach, M. Eichinger, J. Gahr, et al., Proton MRI appearance of cystic fibrosis: comparison to CT, Eur. Radiol. 17 (3) (2007) 716–724.
[88] Q. Qi, T. Li, J.C. Li, et al., Association of body mass index with disease severity and prognosis in patients with non-cystic fibrosis bronchiectasis, Braz. J. Med. Biol. Res. 48 (8) (2015) 715–724.
[89] K.A. Ramsey, T. Rosenow, L. Turkovic, et al., Lung clearance index and structural lung disease on computed tomography in early cystic fibrosis, Am. J. Respir. Crit. Care Med. 193 (1) (2016) 60–67.
[90] H.R. Roberts, A.U. Wells, D.G. Milne, et al., Airflow obstruction in bronchiectasis: correlation between computed tomography features and pulmonary function tests, Thorax 55 (3) (2000) 198–204.
[91] C.M.H.H.T. Robroeks, M.H. Roozeboom, P.A. De Jong, et al., Structural lung changes, lung function, and non-invasive inflammatory markers in cystic fibrosis, Pediatr. Allergy Immunol. : official publication of the European Society of Pediatric Allergy and Immunology 21 (3) (2010) 493–500.
[92] T. Rosenow, M.C. Oudraad, C.P. Murray, et al., PRAGMA-CF. A quantitative structural lung disease computed tomography outcome in young children with cystic fibrosis, Am. J. Respir. Crit. Care Med. 191 (10) (2015) 1158–1165.
[93] S.A. Rowan, J.M. Bradley, I. Bradbury, et al., Lung clearance index is a repeatable and sensitive indicator of radiological changes in bronchiectasis, Am. J. Respir. Crit. Care Med. 189 (5) (2014) 586–592.
[94] D.B. Sanders, Z.H. Li, A.S. Brody, et al., Chest computed tomography scores of severity are associated with future lung disease progression in children with cystic fibrosis, Am. J. Respir. Crit. Care Med. 184 (7) (2011) 816–821.

[95] F. Santamaria, S. Montella, L. Camera, et al., Lung structure abnormalities, but normal lung function in pediatric bronchiectasis, Chest 130 (2) (2006) 480–486.
[96] F. Santamaria, S. Montella, H.A.W.M. Tiddens, et al., Structural and functional lung disease in primary ciliary dyskinesia, Chest 134 (2) (2008) 351–357.
[97] R. Shah, W. Sexauer, B.J. Ostrum, et al., High-resolution CT in the acute exacerbation of cystic fibrosis: evaluation of acute findings, reversibility of those findings, and clinical correlation, Am. J. Roentgenol. 169 (2) (1997) 375–380.
[98] A. Shah, A. Shoemark, S.J. MacNeill, et al., A longitudinal study characterising a large adult primary ciliary dyskinesia population, Eur. Respir. J. 48 (2) (2016) 441–450.
[99] R.E. Sheehan, A.U. Wells, S.J. Copley, et al., A comparison of serial computed tomography and functional change in bronchiectasis, Eur. Respir. J. 20 (3) (2002) 581–587.
[100] S.I. Sheikh, F.R. Long, K.S. McCoy, et al., Computed tomography correlates with improvement with ivacaftor in cystic fibrosis patients with G551D mutation, J. Cyst. Fibros. 14 (1) (2015) 84–89.
[101] J.W. Song, W.J. Koh, K.S. Lee, et al., High-resolution CT findings of Mycobacterium avium-intracellulare complex pulmonary disease: correlation with pulmonary function test results, AJR Am. J. Roentgenol. 191 (4) (2008) 1070.
[102] S.M. Stick, S. Brennan, C. Murray, et al., Bronchiectasis in infants and preschool children diagnosed with cystic fibrosis after newborn screening, J. Pediatr. 155 (5) (2009) 623–628 e1.
[103] X. Tang, J. Bi, D. Yang, et al., Emphysema is an independent risk factor for 5-year mortality in patients with bronchiectasis, Clin. Res. J 11 (6) (2017) 887–894.
[104] L.A. Tepper, E.M. Utens, D. Caudri, et al., Impact of bronchiectasis and trapped air on quality of life and exacerbations in cystic fibrosis, Eur. Respir. J. 42 (2) (2013) 371–379.
[105] L.A. Tepper, P. Ciet, D. Caudri, et al., Validating chest MRI to detect and monitor cystic fibrosis lung disease in a pediatric cohort, Pediatr. Pulmonol. 51 (1) (2016) 34–41.
[106] L. Van Der Giessen, M. Loeve, J. De Jongste, et al., Nocturnal cough in children with stable cystic fibrosis, Pediatr. Pulmonol. 44 (9) (2009) 859–865.
[107] D. Wang, J. Luo, W. Du, et al., A morphologic study of the airway structure abnormalities in patients with asthma by high-resolution computed tomography, J. Thorac. Dis. 8 (10) (2016) 2697–2708.
[108] J. Widger, S. Ranganathan, P.J. Robinson, Progression of structural lung disease on CT scans in children with cystic fibrosis related diabetes, J. Cyst. Fibros. 12 (3) (2013) 216–221.
[109] M.O. Wielputz, M. Eichinger, O. Weinheimer, et al., Automatic airway analysis on multidetector computed tomography in cystic fibrosis: correlation with pulmonary function testing, J. Thorac. Imag. 28 (2) (2013) 104–113.
[110] C.B. Wilson, P.W. Jones, C.J. O'Leary, et al., Effect of sputum bacteriology on the quality of life of patients with bronchiectasis, Eur. Respir. J. 10 (8) (1997) 1754–1760.
[111] J.J. Wong-You-Cheong, B.C. Leahy, P.M. Taylor, et al., Airways obstruction and bronchiectasis: correlation with duration of symptoms and extent of bronchiectasis on computed tomography, Clin. Radiol. 45 (4) (1992) 256–259.
[112] C.F. Yang, M.T. Wu, A.A. Chiang, et al., Correlation of high-resolution CT and pulmonary function in bronchiolitis obliterans: a study based on 24 patients associated with consumption of Sauropus androgynus, Am. J. Roentgenol. 168 (4) (1997) 1045–1050.
[113] Z. Zoumot, A.K. Boutou, S.S. Gill, et al., Mycobacterium avium complex infection in non-cystic fibrosis bronchiectasis, Respirology 19 (5) (2014) 714–722.
[114] S.H. Bak, S. Kim, Y. Hong, et al., Quantitative computed tomography features and clinical manifestations associated with the extent of bronchiectasis in patients with moderate-to-severe COPD, Int J COPD 13 (2018) 1421–1431.
[115] P. Bedi, J.D. Chalmers, P.C. Goeminne, et al., The BRICS (bronchiectasis radiologically indexed CT score): a multicenter study score for use in idiopathic and postinfective bronchiectasis, Chest 153 (5) (2018) 1177–1186.
[116] D. Caudri, L. Turkovic, J. Ng, et al., The association between Staphylococcus aureus and subsequent bronchiectasis in children with cystic fibrosis, J. Cyst. Fibros. 17 (4) (2018) 462–469.
[117] F. Çiftci, E. Şen, S.B. Saryal, et al., The factors affecting survival in patients with bronchiectasis, Turk. J. Med. Sci. 46 (6) (2016) 1838–1845.
[118] E.M. DeBoer, M.E. Kroehl, B.D. Wagner, et al., Proteomic profiling identifies novel circulating markers associated with bronchiectasis in cystic fibrosis, Proteonomics Clin. Appl. 11 (9–10) (2017).
[119] K. Dimakou, A. Gousiou, M. Toumbis, et al., Investigation of bronchiectasis in severe uncontrolled asthma, Clin. Res. J 12 (3) (2018) 1212–1218.
[120] R.H. do Amaral, C.S. Nin, V.V.S. de Souza, et al., Computed tomography findings of bronchiectasis in different respiratory phases correlate with pulmonary function test data in adults, Lung 195 (3) (2017) 347–351.
[121] Y.H. Gao, W.J. Guan, Y.N. Zhu, et al., Antibiotic-resistant Pseudomonas aeruginosa infection in patients with bronchiectasis: prevalence, risk factors and prognostic implications, Int J COPD 13 (2018) 237–246.
[122] W. Kuo, E.R. Andrinopoulou, A. Perez-Rovira, et al., Objective airway artery dimensions compared to CT scoring methods assessing structural cystic fibrosis lung disease, J. Cyst. Fibros. 16 (1) (2017) 116–123.
[123] W. Kuo, M. de Bruijne, J. Petersen, et al., Diagnosis of bronchiectasis and airway wall thickening in children with cystic fibrosis: objective airway-artery quantification, Eur. Radiol. 27 (11) (2017) 4680–4689.
[124] W. Kuo, T. Soffers, E.R. Andrinopoulou, et al., Quantitative assessment of airway dimensions in young children with cystic fibrosis lung disease using chest computed tomography, Pediatr. Pulmonol. 52 (11) (2017) 1414–1423.
[125] S. Tsikrika, K. Dimakou, A.I. Papaioannou, et al., The role of non-invasive modalities for assessing inflammation in patients with non-cystic fibrosis bronchiectasis, Cytokine 99 (2017) 281–286.
[126] X. Yang, Y. Xu, J. Jin, et al., Chronic rhinosinusitis is associated with higher prevalence and severity of bronchiectasis in patients with COPD, Int J COPD 12 (2017) 655–662.
[127] C.E. Wainwright, S. Vidmar, D.S. Armstrong, et al., Effect of bronchoalveolar lavage-directed therapy on Pseudomonas aeruginosa infection and structural lung injury in children with cystic fibrosis: a randomized trial, Jama 306 (2) (2011) 163–171.
[128] R.S. Joress Mmh, The diagnosis of bronchiectasis: clinical and roentgenological observations, Chest 10 (6) (1944) 489–508.
[129] S.J. Copley, A.U. Wells, K.E. Hawtin, et al., Lung morphology in the elderly: comparative CT study of subjects over 75 years old versus those under 55 years old, Radiology 251 (2) (2009) 566–573.
[130] J.P. Janssens, J.C. Pache, L.P. Nicod, Physiological changes in respiratory function associated with ageing, Eur. Respir. J. 13 (1) (1999) 197–205.
[131] W. Kuo, P. Ciet, H.A. Tiddens, et al., Monitoring cystic fibrosis lung disease by computed tomography. Radiation risk in perspective, Am. J. Respir. Crit. Care Med. 189 (11) (2014) 1328–1336.
[132] M. Loeve, M.H. Lequin, M. De Bruijne, et al., Cystic fibrosis: are volumetric ultra-low-dose expiratory CT scans sufficient for monitoring related lung disease? Radiology 253 (1) (2009) 223–229.
[133] R. Szczesniak, L. Turkovic, E.R. Andrinopoulou, et al., Chest imaging in cystic fibrosis studies: what counts, and can be counted? J. Cyst. Fibros. 16 (2) (2017) 175–185.
[134] S.H. Chotirmall, J.D. Chalmers, Bronchiectasis: an emerging global epidemic, BMC Pulm. Med. 18 (1) (2018) 76.