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Impulse Oscillometry in the Evaluation of Non-Cystic Fibrosis Bronchiectasis in Adults: a Systematic Literature Review

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Impulse Oscillometry in the Evaluation of Non-Cystic Fibrosis Bronchiectasis in Adults: a Systematic Literature Review

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Declaração de Integridade Científica

Eu, Francisca de António Andrade, autora da presente dissertação intitulada *Impulse Oscillometry in the Evaluation of Non-Cystic Fibrosis Bronchiectasis in Adults: a Systematic Literature Review*, declaro, sob compromisso de honra, que este trabalho é original e que respeitei integralmente os princípios de honestidade e integridade científica ao longo de todas as fases de elaboração do mesmo. Declaro ainda que todas as fontes utilizadas foram devidamente identificadas e referenciadas, de acordo com as normas académicas em vigor.

Porto, junho de 2025

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Resumo

Introdução: As bronquiectasias não associadas à fibrose quística (BNFQ) constituem uma doença respiratória crónica caracterizada por uma dilatação irreversível da via aérea, inflamação persistente e infeções recorrentes. A oscilometria de impulso (IOS) tem emergido como uma técnica promissora, não invasiva, para a avaliação da função respiratória, sendo particularmente útil em doentes que não conseguem realizar as manobras expiratórias forçadas exigidas pela espirometria. No entanto, a sua utilidade na avaliação clínica das BNFQ permanece pouco explorada.

Objetivo: Esta revisão sistemática teve como objetivo avaliar o papel da IOS na avaliação de adultos com BNFQ, especificamente quanto ao seu valor diagnóstico, correlação com a gravidade da doença, capacidade de prever a reversibilidade da obstrução brônquica e associação com desfechos clínicos como exacerbações, hospitalizações e mortalidade.

Métodos: Foi realizada uma pesquisa sistemática da literatura em janeiro de 2025, nas bases de dados PubMed, Scopus, Web of Science e Cochrane, seguindo as diretrizes PRISMA. Foram incluídos estudos que avaliassem doentes adultos com BNFQ utilizando IOS, e que relatassem associações com desfechos clínicos, radiológicos ou funcionais. Apenas artigos com resumos acessíveis foram incluídos. A qualidade metodológica dos estudos selecionados foi avaliada utilizando a escala de Newcastle-Ottawa adaptada para estudos transversais.

Resultados: Foram incluídos sete estudos. A IOS demonstrou maior sensibilidade do que a espirometria na deteção de disfunção das pequenas vias aéreas, especialmente em casos iniciais ou ligeiros da doença. Vários parâmetros da IOS apresentaram correlações moderadas a fortes com *scores* de gravidade e achados radiológicos. No entanto, os resultados foram heterogéneos e as correlações com desfechos clínicos como exacerbações ou hospitalizações mostraram-se inconsistentes. Apenas um estudo avaliou a resposta à terapêutica com broncodilatador, identificando o parâmetro R5-R20 como um potencial preditor. Os parâmetros da IOS mantiveram-se relativamente estáveis entre diferentes fases da doença, limitando a sua utilidade na deteção de alterações agudas.

Conclusão: A IOS pode complementar as ferramentas tradicionais na avaliação de doentes com BNFQ, especialmente na identificação de alterações nas pequenas vias aéreas, mas é necessária uma maior padronização e investigação longitudinal futura.

Palavras-chave: bronquiectasias não associadas à fibrose quística, oscilometria de impulso, testes de função pulmonar, gravidade da doença, exacerbação, revisão sistemática.

Abstract

Background: Non-cystic fibrosis bronchiectasis (NCFB) is a chronic respiratory disease characterized by irreversible airway dilation, persistent inflammation, and recurrent infections. Impulse oscillometry (IOS) has emerged as a promising non-invasive technique for assessing respiratory function, particularly useful for patients unable to perform forced maneuvers required in spirometry. However, its clinical utility in NCFB remains underexplored.

Objective: This systematic review aimed to evaluate the role of IOS in assessing adult patients with NCFB, focusing on its diagnostic value, correlation with disease severity, ability to predict airway reversibility, and association with clinical outcomes such as exacerbations, hospitalizations, and mortality.

Methods: A systematic literature search was conducted in January 2025 across PubMed, Scopus, Web of Science, and Cochrane databases, following PRISMA guidelines. Studies were included if they assessed adult NCFB patients using IOS and reported associations with clinical, radiological, or functional outcomes. Only peer-reviewed articles with accessible abstracts were considered. Study quality was assessed using the Newcastle-Ottawa Scale adapted for cross-sectional studies.

Results: Seven studies were included. IOS showed greater sensitivity than spirometry in detecting small-airway dysfunction, especially in early or mild disease. Several IOS parameters correlated moderately to strongly with radiological and severity scores. However, the findings were heterogeneous, and associations with outcomes such as exacerbations and hospitalizations were inconsistent. Only one study evaluated bronchodilator response, highlighting R5-R20 as a potential predictor. IOS parameters remained relatively stable across disease stages, limiting their value in acute monitoring.

Conclusion: IOS may complement traditional tools in NCFB evaluation, particularly for identifying small-airway abnormalities, but standardization and further longitudinal research are needed.

Keywords: non-cystic fibrosis bronchiectasis, impulse oscillometry, pulmonary function tests, disease severity, exacerbation, systematic review.

List of Abbreviations

AUC: Area Under the Curve

AX: Area of Reactance

BSI: Bronchiectasis Severity Index

CF: Cystic Fibrosis

E-FACED: Exacerbation-FACED Score (Multidimensional severity score for bronchiectasis that includes exacerbations)

FACED: FEV_1, Age, Colonization, Extension, Dyspnea (Multidimensional severity score for bronchiectasis)

FEV_1: Forced Expiratory Volume in 1 Second

FOT: Forced Oscillation Technique

Fres Resonant Frequency

FVC: Forced Vital Capacity

HRCT: High-Resolution Computed Tomography

IOS: Impulse Oscillometry System

MeSH: Medical Subject Headings

MRC: Medical Research Council

NCFB: Non-Cystic Fibrosis Bronchiectasis

PCD: Primary Ciliary Dyskinesia

PECOS: Patient, Exposure, Comparator, Outcome, Study Design

PEF: Peak Expiratory Flow

PFTs: Pulmonary Function Tests

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

R20: Resistance at 20 Hz (central airway resistance)

R5: Resistance at 5 Hz (total airway resistance)

R5-R20: Difference between R5 and R20 (peripheral airway resistance)

ROC: Receiver Operating Characteristic Curve

Rrs: Respiratory Resistance

VC: Vital Capacity

X5: Reactance at 5 Hz

Xrs: Respiratory Reactance

Zrs: Respiratory Impedance

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Introduction

Bronchiectasis is a chronic respiratory disease characterized by abnormal and irreversible bronchial dilation, resulting from the combination of local inflammatory and infectious processes, along with inadequate secretion clearance, airway obstruction, immunodeficiency, genetic disorders (such as cystic fibrosis (CF) and primary ciliary dyskinesia (PCD)), systemic and autoimmune diseases (such as inflammatory bowel disease and rheumatoid arthritis) and chronic aspiration.[1,2] These mechanisms interact in a self-perpetuating cycle known as the "vicious vortex", where airway infection, chronic inflammation, mucociliary dysfunction, and lung damage continuously potentiate each other. This dynamic interaction better represents the pathophysiology of bronchiectasis, leading to persistent lung inflammation, recurrent infections, and progressive lung damage, ultimately impairing lung function. The complexity and multiplicity of the underlying pathophysiological mechanisms warrant a multimodal therapeutic approach, posing significant challenges in disease management.[1,3]

As a result of these pathological processes, patients with bronchiectasis commonly present with a chronic cough with abundant sputum production and recurrent chest infections. The condition is typically diagnosed based on clinical symptoms and confirmed by chest high-resolution computed tomography (HRCT), which reveals characteristic radiographic features such as bronchial enlargement and wall thickening. [1,4]

Epidemiological data regarding the prevalence of bronchiectasis in the general population are heterogeneous, ranging from 52.3 to over 1000 per 100000 individuals. Nevertheless, it is estimated that the incidence and prevalence of bronchiectasis has been increasing globally, resulting in not only a higher socioeconomic burden associated with healthcare for this condition but also a significant psychosocial impact on the lives of these patients.[5,6]

Moreover, bronchiectasis is a complex and heterogeneous condition with diverse etiologies, highlighting the importance of a thorough etiological investigation, and a variable prognosis. Some patients experience a relatively stable disease course, while others exhibit rapid progression marked by frequent exacerbations, accelerated lung function decline, and an increased risk of hospital admissions.[1,7] Accurate assessment of bronchiectasis severity is crucial for optimizing clinical management, predicting outcomes, and guiding therapeutic interventions.[8] While no universally accepted definition of bronchiectasis severity exists, several validated scoring systems have been developed, including the Bronchiectasis Severity Index (BSI), FACED, and E-FACED scores. These tools effectively predict clinical outcomes such as mortality and hospitalization, but require extensive clinical history, microbiological data, and exacerbation records, limiting their use in initial assessments. [7,9–11]

Consequently, pulmonary function tests (PFTs) remain central to evaluating bronchiectasis severity. In fact, PFTs are fundamental tools for diagnosing and monitoring chronic respiratory diseases, and maximizing their utility is crucial for improving patient care. Among these, spirometry is recognized in guidelines as the gold standard for assessing airflow limitation.[12–14] However, spirometry's

requirement for forceful breathing maneuvers poses practical challenges for individuals with physical frailty, severe disease, or limited cooperation, such as young children or older adults.[15] Compared to chest HRCT, PFTs may be more appropriate as a first-line approach in patients with suspected bronchiectasis, given that they are more accessible, less costly, and free from radiation exposure. However, spirometry has some limitations in detecting early lung function impairment, and the delay between disease onset and radiological diagnosis can compromise timely intervention, reinforcing the need for alternative, non-invasive techniques that can reliably assess lung function and improve early detection.[15–17]

In this context, the Impulse Oscillometry System (IOS) has emerged as a promising non-invasive alternative technique for assessing respiratory function in patients with bronchiectasis, and it is particularly suitable for individuals who have difficulty performing spirometry. IOS measures respiratory impedance (Zrs), which includes both respiratory resistance (Rrs) and respiratory reactance (Xrs), by imposing multiple-frequency sound waves over normal tidal breathing, offering a comprehensive assessment of lung function. [18–20] Among the key parameters measured, resistance at 5 Hz (R5) reflects total respiratory resistance, resistance at 20 Hz (R20) represents central airway resistance, and R5-R20 reflects the resistance of the peripheral airways. As for reactance, reactance at 5 Hz (X5) reflects the elastic properties of the peripheral airways (with lower values indicating decreased lung elasticity), while the area of reactance (AX) provides a measure of lung elasticity and is particularly useful for assessing small airway obstruction. The resonant frequency (Fres), the point where reactance crosses zero, differentiates between low and high-frequency reactance. [18,19,21]

IOS offers advantages in assessing respiratory function by providing complementary information to traditional spirometry, as it can, for instance, differentiate between central and peripheral airway resistance. This is particularly relevant because in obstructive airway diseases, the earliest changes often occur in the smaller, more distal airways, which offer minimal resistance at high lung volumes and may not significantly impact maximal airflow measured by FEV_1. As such, spirometry is a suboptimal PFT for the evaluation of early airway disease.[22,23] Consequently, IOS may be a useful complementary tool for the evaluation of lung function in this context. [19,24,25]

Despite its potential advantages, IOS remains underutilized in routine bronchiectasis care due to uncertainties surrounding its clinical application and the lack of standardized cut-offs for defining abnormal IOS results. Moreover, to the best of our knowledge, no systematic reviews to date have evaluated the role of IOS in predicting exacerbations, treatment response, and long-term clinical outcomes.

Given the increasing prevalence of bronchiectasis worldwide and the growing recognition of bronchiectasis as a clinically relevant entity in the field of respiratory medicine, effective strategies for predicting exacerbation risk and guiding disease management are essential. As a non-invasive and accessible tool, IOS presents a valuable opportunity for improving bronchiectasis assessment in clinical practice.

This systematic review aims to address these gaps by examining the available literature on the role of IOS in evaluating non-cystic fibrosis bronchiectasis (NCFB) in adults. Specifically, this review will assess the diagnostic value of IOS parameters in NCFB, their correlation with disease severity, their predictive

potential for airway obstruction reversibility, and their association with key clinical outcomes like hospital admissions and mortality. Additionally, this review will explore the variability of IOS parameters across different disease stages, including acute exacerbations, while also identifying limitations in IOS's predictive capabilities and clinical utility.

By synthesizing current evidence, this systematic review aims to provide insights into the potential of IOS as a practical, non-invasive tool for NCFB assessment and management, enhancing clinical decision-making and improving patient care.

Methods

Eligibility criteria:

The PECOS (P-patient; E-exposure; C-comparator; O-outcome; S-study design) framework was followed to select the studies to include in the present systematic review.

The inclusion criteria for this systematic review encompassed published peer-reviewed studies involving adult patients (aged 18 years or older) diagnosed with NCFB, and who underwent IOS for disease evaluation. Only studies in which the primary focus was the assessment of NCFB in clinical practice were included.

Studies were only included if there was at least one association between IOS and one of the following outcome measures: diagnostic accuracy for distinguishing patients with NCFB from healthy individuals; correlation of IOS parameters (R5, R20, R5–R20, X5, AX, Fres) with disease severity (as assessed by chest HRCT, BSI, or FACED scores); feasibility and clinical applicability of IOS compared to other pulmonary function tests (e.g., spirometry) and prediction of airway reversibility or clinical outcomes such as exacerbation frequency, hospital admissions or mortality.

Experimental studies, such as randomized clinical trials, as well as observational studies, including cohort, case-control, and cross-sectional studies, were included for a comprehensive gathering of available data on IOS in the assessment of NCFB. However, only articles with accessible abstracts were included.

Exclusion criteria were applied to studies that focused exclusively on bronchiectasis resulting from CF, traction bronchiectasis or pseudobronchiectasis. Studies that utilized non-IOS forced oscillation techniques (FOT) to evaluate bronchiectasis were also excluded. Furthermore, review articles, study protocols, or studies that did not explicitly mention bronchiectasis in the title or abstract were not considered for inclusion.

No restrictions were applied based on language, geographic location, or publication date.

Information sources:

This systematic review was conducted in strict adherence to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. [26]

Since all data used in this review were obtained from previously published peer-reviewed studies, no ethical approval or patient consent was necessary.

The databases searched were PubMed, Scopus, Cochrane and Web of Science. The last search was conducted in January 2025.

Search strategy:

To explore the current state of the art regarding IOS in the assessment of NCFB, an initial search was conducted using the query “impulse oscillometry and bronchiectasis.” Subsequently, to further align with the objectives of this systematic review, additional searches were performed employing relevant search terms that were developed from Medical Subject Headings (MeSH), and keywords generated from the subject headings.

In general, the following search query was used across the four databases, targeting the title, abstract, and keyword fields: ("Impulse oscillometry" OR "Oscillometric" OR IOS OR Oscillometry OR Oscillometries) AND ("Non-cystic fibrosis bronchiectasis" OR "Non-CF bronchiectasis" OR Bronchiectasis). Minor adjustments were made according to the specific search requirements of each database.

Study selection:

The study selection process began with a screening phase in which two reviewers (FA and MHR) independently conducted searches across the four databases. Each reviewer then compiled a list of potentially eligible studies, based on the title and abstract, with any discrepancies regarding article inclusion being resolved by a third reviewer (TO). Following the removal of duplicate records and studies that did not meet inclusion criteria, the full texts of the remaining potentially eligible papers were retrieved and thoroughly reviewed. Finally, exclusion criteria were applied, and all reviewers reached a consensus on the final list of included studies.

Quality assessment of the individual studies:

Given that all selected studies were cross-sectional in design, quality assessment was conducted using the Newcastle-Ottawa Scale adapted for cross-sectional studies, which is available in the supplementary materials of the referenced article.[27] This scale is designed to assess the quality of non-randomized studies to be included in a systematic review, and it is recommended by Cochrane and PRISMA guidelines for observational studies.[26,28] Using a star-rating system, it evaluates studies across three key domains: the selection of study groups; the comparability of these groups; and the

assessment of the outcome of interest. Each study was independently assessed by two reviewers, FA and MHR. Any discrepancies identified during the evaluation were discussed, and a consensus table was developed (Table I). A scoring system ranging from 0 to 10 was applied (Very Good Studies: 9–10 stars; Good Studies: 7–8 stars; Satisfactory Studies: 5–6 stars; Unsatisfactory Studies: 0–4 stars).

In general, most studies were rated as good or very good. Overall, study samples were deemed reasonably representative of the general population, although most studies did not report a formal sample size calculation. The majority of studies provided clear exclusion criteria and accounted for excluded participants, for which we assigned one star in the “non-respondents” assessment category. Study results were obtained based on hospital records and validated measurement tools. The studies adjusted for important confounding factors, including age, body mass index, disease severity, and comorbidities, using multivariable regression models. Independent blind assessment and appropriate statistical methods were employed, with p-values and confidence intervals clearly reported.

Results

This systematic review included seven studies investigating the diagnostic and prognostic utility of IOS in patients with NCFB. All studies explored associations between IOS parameters and clinical, radiological, or functional outcomes. The findings are presented according to the predefined outcome categories. The study selection process is illustrated in Figure 1.

Characteristics of the included studies:

A comprehensive table (Table II) was constructed to synthesize the key data extracted from the selected studies. The information included variables such as study design and population characteristics, namely sample size, number of patients and controls, and participants' mean age. The tools used to assess bronchiectasis severity and the IOS system employed in each study were also documented. Additionally, details regarding the pulmonary function assessment methods used in comparison with IOS (e.g., chest HRCT, spirometry) were recorded. Finally, the table included the outcomes measured, specifically the IOS parameters.

Diagnostic value of IOS in bronchiectasis

Several studies demonstrated that IOS is a sensitive tool for detecting early-stage or mild bronchiectasis, particularly in patients with a normal spirometry. Guan et al. (2015) found that IOS was more sensitive than FEV_1 in identifying airflow limitation and small-airway involvement, particularly in patients with milder radiological involvement (chest HRCT scores ≤5). Similarly, Guan et al. (2016) reported that small-airway abnormalities detected by IOS were evident in mild bronchiectasis cases.[29,30]

Liang et al. (2022) identified R5 z-score as the most accurate IOS parameter for detecting respiratory diseases, including bronchiectasis, with specificities over 80%, but with low sensitivity, making it less ideal for diagnostic purposes. In fact, traditional spirometric parameters remained superior for diagnostic precision, with FEV_1 and FEV_1/FVC z-scores showing the highest sensitivity and specificity.[31]

Perossi et al. (2022) emphasized the value of IOS and chest HRCT analysis in identifying early abnormalities, especially in patients with less advanced disease.[32]

IOS parameters and disease severity correlation

IOS parameters showed significant correlations with both clinical and radiological markers of disease severity. Guan et al. (2015, 2016) reported that IOS parameters (except R20) were significantly

associated with chest HRCT scores and the BSI. Additionally, Guan et al. (2015) observed that elevated IOS parameters were found in patients with *Pseudomonas aeruginosa* chronic bronchial infection, ventilation dyshomogeneity, more bronchiectatic lung lobes and cystic bronchiectasis (all $p < 0.05$), while higher 24-hour sputum volume was linked to lower X5, and higher Fres and AX (all $p < 0.05$). Although IOS small-airway parameters, like R5-R20, demonstrated moderate correlations with both the BSI and the chest HRCT total score, Guan et al. (2016) highlighted that in patients with milder radiological involvement (chest HRCT score < 6), these correlations became non-significant.[29,30]

Tan et. al (2022) found that patients with *Pseudomonas aeruginosa* chronic bronchial infection had longer disease duration, more acute exacerbations and lower FVC, VC, and PEF values. However, there were no significant differences in IOS parameters between *Pseudomonas aeruginosa* positive and negative subgroups. Also, Guan et al. (2016) noted that IOS abnormalities were more closely related to cystic bronchiectasis and ventilation dyshomogeneity than to the isolation of *Pseudomonas aeruginosa* or predominantly middle/lower lobe bronchiectasis.[30,33]

Tan et al. (2022) found significant differences in IOS parameters (R5, R5-R20, Rp, Fres and Z5) across severity groups (mild, moderate and severe NCFB), assessed by FACED and BSI scores.[33]

Perossi et al. (2022) identified a moderate correlation between R5-R20 and BSI (r=0.53), but it was stronger than the correlation found by Guan et. al (2016) (r=0.32). Also, Perossi et. al (2022) found significant correlations between IOS parameters, mainly R5 and R5-R20, and Medical Research Council (MRC) scale scores.[30,32]

In addition to clinical indices, Perossi et al. (2022) also assessed the correlation between IOS parameters and chest HRCT findings. They reported that R5 correlated with normalized bronchial wall thickness (Pi10) (r = 0.57), whereas no significant correlation was found with subjective chest HRCT scoring systems.[32]

Yamamoto et al. (2020) demonstrated that inspiratory Fres correlated with both BSI, FACED and E-FACED scores and was predictive of disease progression. Tan et al. (2022) found that IOS values like R5, R5-R20, Fres, Z5 and AX (but not R20) increased and X5 decreased with NCFB severity, assessed by BSI and FACED scores.[33,34]

Liang et al. (2022) proposed a severity grading system based on R5, R5-R20 and X5 z-scores, defining cut-offs for mildly, moderately, and severely increased parameters, while Choi et al. (2024) developed

a new scoring tool (incorporating IOS parameters, body mass index and sex) that effectively predicted moderate to severe NCFB (defined by the FACED score), with an high Area Under the Curve (AUC = 0.809) of the Receiver Operating Characteristic (ROC) curve. This study also demonstrated that only X5 ≤ −0.238 showed a significant multivariable relationship with NCFB severity (p = 0.039).[31,35]

IOS in predicting airway obstruction reversibility

Tan et al. (2022) was the only study to evaluate bronchodilator responsiveness. Pre-bronchodilator R5-R20 was identified as the strongest predictor of a positive bronchodilator response in spirometry (AUC = 0.794; 81% sensitivity, 69.8% specificity). However, the study did not report a specific cut-off value for R5–R20 to predict bronchodilator responsiveness.[33]

IOS parameters as predictors of clinical outcomes

IOS parameters were associated with clinical outcomes, including exacerbations, hospital admissions, and mortality. Guan et al. (2015) showed that Z5, R5, Fres and AX positively correlated with exacerbation frequency within a two-year period (all $p < 0.05$). Yamamoto et al. (2020) demonstrated that inspiratory Fres had the highest predictive value among reactance parameters for both hospital admissions and mortality, with AUCs of 0.672 and 0.781, respectively.[29,34]

Guan et al. (2016) showed that neither IOS nor spirometry small-airway parameters correlated with the temporal interval since symptom onset exacerbation frequency within a two-year period (all $p > 0.05$) in the subgroup with radiologically mild bronchiectasis (chest HRCT score < 6). However, R5-R20, X5, Fres and AX correlated positively with exacerbation frequency within a two-year period (all $p < 0.01$) in the mild to moderate bronchiectasis subgroup. Additionally, Tan et al. (2022) found that, although patients with previous hospital admissions had longer disease duration and more exacerbations, no significant differences were observed in IOS parameters between these patients and those without prior hospital admissions. In contrast, traditional pulmonary function parameters such as FVC and FEV_1 were significantly lower in patients with a history of hospitalisation.[30,33]

IOS parameter variability across disease stages

Guan et al. (2015) reported minimal variation in IOS parameters between baseline, exacerbations and post-exacerbation convalescence period (all $p > 0.05$), remaining stable within 5% of baseline values.[29]

Discussion

This systematic review included seven studies, each with distinct methodologies and patient populations, raising critical points for analysis and interpretation.

Excluded population

One of the main limitations identified in this review is the exclusion criteria applied in the included studies. Most studies excluded patients with allergic diseases and various systemic conditions, potentially limiting the generalizability of the findings. Additionally, the decision to exclude patients with CF or traction bronchiectasis, as they exhibit distinct pathophysiological mechanisms and may require a different clinical management, contributed to maintaining a more homogeneous population, whilst reducing applicability to a broader context. Including patients with CF bronchiectasis or traction bronchiectasis in future studies (through studies focused exclusively on these subgroups or by incorporating them into larger cohorts with stratified analyses) would enhance the relevance and applicability of the results and allow for assessment of whether findings from NCFB populations can be extrapolated to other bronchiectasis subtypes.

Variability in IOS systems

Another important factor to consider is the heterogeneity of IOS equipments used in the studies. Differences in device calibration, technical specifications, measurement standards and the training of respiratory physiologists in performing and interpreting the test may contribute to variability in IOS parameter outcomes, challenging cross-study comparisons. This inconsistency highlights the need for standardized protocols and consensus on reference values to enhance comparability and reproducibility.

Main findings and interpretation

The use of IOS in detecting early-stage or mild NCFB has been consistently demonstrated by the studies, even in patients with preserved spirometry, which is relevant as early detection may allow for timely intervention. However, it is crucial to note that IOS parameters like R5 z-score, while showing high specificity, demonstrated low sensitivity according to Liang et al. (2022), and an overlap in oscillometric parameters between healthy subjects and disease patients, indicating that IOS alone might not be sufficient for diagnostic purposes, and rather be utilized as a complementary tool to traditional PFTs and other methods.[31] The discordance in the sensitivity and specificity reported among studies may be attributed to differences in study populations, the severity of bronchiectasis, or the criteria used to define abnormal IOS values. Overall, the literature suggests that while IOS has

discriminatory potential, especially in assessing small-airway dysfunction, it may be more appropriate for a more thorough characterization of pulmonary function than for establishing a definitive diagnosis of NCFB.

Several studies have explored the correlation between IOS parameters and the severity of bronchiectasis, utilizing different severity indices, such as BSI and FACED. IOS parameters, except R20, have shown varying degrees of correlation with disease severity markers, such as chest HRCT scores and BSI. Nevertheless, the strength of these correlations varied, with some studies (e.g., Perossi et al., 2022) reporting stronger associations than others (e.g., Guan et al., 2016).[30,32] This discrepancy might be explained by differences in patient inclusion criteria, particularly the presence of patients with severe disease in the first study versus their exclusion in the second.

Moreover, Perossi et al. (2022) supports the use of quantitative chest HRCT analysis over subjective scoring when evaluating structural-functional relationships with IOS.[32] Another important consideration is that some IOS small-airway parameters (e.g., R5-R20) showed moderate correlations with severity indices, but these became non-significant when the analysis was restricted to patients with milder radiological involvement (chest HRCT score < 6). This suggests that IOS may be less reflective of disease severity when NCFB presents with mild structural changes.[30]

Nevertheless, the strength and significance of these correlations can vary depending on the specific IOS parameter and the severity index being considered. Additionally, IOS's ability to reflect disease severity may vary depending on the dominant NCFB morphology (e.g., cystic versus cylindrical), which remains insufficiently explored.

Regarding the influence of factors such as *Pseudomonas aeruginosa* chronic bronchial infection, although this situation is associated with a worse prognosis, studies have reported inconsistent findings. While Tan et al. (2022) and Guan et al. (2016) showed that no significant differences were found in IOS parameters between the *Pseudomonas aeruginosa* positive and negative subgroups, Guan et al. (2015) found that IOS parameters were significantly higher in the *Pseudomonas aeruginosa* positive subgroup.[29,30,33]

Tan et al. (2022) identified R5-R20 as the most reliable predictor of bronchodilator responsiveness, suggesting its potential utility in identifying NCFB patients with small-airway disease responsive to bronchodilators, who are more likely to benefit from bronchodilator therapy even without an

established obstructive ventilatory defect in spirometry.[33] Nonetheless, the lack of corroborative studies limits the generalizability of this finding, highlighting the need for further validation.

The relationship between IOS parameters and clinical outcomes such as exacerbations, hospitalizations, and mortality remains inconsistent. While some studies, including Guan et al. (2015) and Yamamoto et al. (2020), found significant correlations between IOS parameters and these outcomes (with inspiratory Fres being identified as the most predictive parameter), others, such as Guan et al. (2016) and Tan et al. (2022), did not.[29,30,33,34] For instance, Guan et al. (2016) reported no correlation between IOS small-airway parameters and exacerbation frequency over the previous two years in the radiologically mild bronchiectasis subgroup (chest HRCT score < 6), suggesting that IOS measured during a stable phase may not adequately capture the cumulative impact of past exacerbations. Likewise, Guan et al. (2015) observed that IOS parameters remained stable across both baseline (stable disease phase), acute exacerbations and post-exacerbation convalescence period. One possible explanation for this unexpected finding is the presence of significant underlying airway dysfunction already during clinical stability, due to persistent features such as mucus plugging and airway remodeling, as suggested by Guan et al. (2015). As a result, the increase in peripheral airway obstruction during exacerbations may not be sufficiently distinct from baseline to produce statistically significant changes in IOS measures. Additionally, IOS may not be sufficiently sensitive to certain acute pathophysiological alterations during exacerbations, such as changes in sputum rheology or airway microenvironment. Finally, methodological limitations, particularly the small number of patients assessed during exacerbations (n = 16), may have limited the ability to detect relevant changes in IOS parameters.

The stability of IOS parameters during exacerbations and post-exacerbation convalescence periods supports the growing clinical focus on long-term lung function trajectories rather than short-term fluctuations. As this concept gains recognition for its relevance in monitoring and guiding treatment decisions in chronic respiratory diseases, serial IOS measurements during stable phases may help to define an individual's lung function trajectory.[36]

These findings suggest that IOS may be better suited for patient chronic monitoring in the stable phase of NCFB, as it can reflect disease severity at a given moment, but does not consistently capture acute changes, long-term disease progression or the cumulative impact of past clinical events, highlighting its uncertain role in predicting long-term outcomes.

The variability in results across studies may be attributed to differences in study design, such as the inclusion of patients with varying degrees of disease severity, differences in follow-up duration, and heterogeneity in the baseline health status of included patients.

Comparison with other reviews

While previous reviews on IOS have primarily focused on asthma and COPD, there is limited literature specifically addressing IOS in NCFB. To our knowledge, no systematic review to date has explored the use of IOS in the assessment of patients with NCFB. This systematic review contributes to the field by synthesizing data from multiple studies that specifically address NCFB, highlighting both the potential and limitations of IOS as a diagnostic and monitoring tool in this population, thereby filling a gap in the existing literature.

Limitations and strengths of the included studies

Several studies had limitations related to small sample sizes and single-center designs, which may have introduced selection bias. Additionally, as all the studies are cross-sectional, the lack of longitudinal data limits generalization and the ability to draw prognostic conclusions. Furthermore, the exclusion of patients with more severe NCFB in some studies restricts the applicability of the findings to the broader NCFB patient population.

Nonetheless, the studies have notable strengths, including the use of rigorous statistical methods and the integration of clinical, radiological, and oscillometric data, which enhances the reliability of their conclusions.

Clinical implications and contributions

Despite the inherent limitations of IOS, including variability between devices and the lack of standardized cut-off values, this review highlights its potential to identify small-airway dysfunction in NCFB patients, particularly those with mild or early-stage disease. Integrating IOS into routine clinical practice could facilitate earlier diagnosis and improved monitoring of disease progression, especially when traditional spirometry fails to detect subtle changes, or when its use is not possible, such as in individuals with physical frailty or limited cooperation. However, given the inconsistencies in diagnostic accuracy and clinical outcome predictions, IOS should be used as a complementary tool rather than in isolation, integrated within a comprehensive diagnostic approach that includes clinical, radiological, and spirometric assessments. Also, IOS might have a role in long-term monitoring, although it may not adequately detect acute changes.

To enhance its practical application, providing training for healthcare professionals on executing IOS and interpreting its results, especially in distinguishing between central and peripheral airway involvement, is crucial. Nonetheless, its clinical implementation remains challenged by variability in study designs, device specifications, and measurement standards, highlighting the need for standardized guidelines and further research to consolidate its role in routine clinical practice.

Future directions

Further multicenter, longitudinal studies are needed to validate IOS in NCFB and explore its clinical applications, with a focus on standardizing measurements and establishing cut-off values to enhance consistency across different devices and generalizability. Additionally, research comparing IOS with other diagnostic methods, such as spirometry and chest HRCT, across different disease stages is essential to determine its predictive value in monitoring disease progression and exacerbation risk. Studies assessing the real-world impact of integrating IOS into routine practice would also provide valuable insights into its practical utility, thereby guiding personalized management strategies.

Conclusion

This systematic review highlights the potential of IOS in detecting small-airway abnormalities and monitoring disease progression in NCFB, particularly in early stages. However, variability in study populations, methodologies, and IOS devices calls for cautious interpretation. Standardized protocols and further research are essential to establish IOS as a reliable tool in bronchiectasis management, optimizing its integration into clinical practice.

Appendix

Table I. Quality assessment of the selected studies, based on the Newcastle-Ottawa Scale adapted for cross-sectional studies.[27] (Very Good Studies: 9–10 stars; Good Studies: 7–8 stars; Satisfactory Studies: 5–6 stars; Unsatisfactory Studies: 0–4 stars).

Study	Selection (max. 5 stars)	Comparability (max. 2 stars)	Outcome (max. 3 stars)	Total Score
Choi et al. (2024)	★★★	★★	★★★	8 Good Study
Tan et al. (2022)	★★★★	★★	★★★	9 Very Good Study
Guan et al. (2015)	★★★★	★★	★★★	9 Very Good Study
Guan et al. (2016)	★★★★★	★★	★★★	10 Very Good Study
Yamamoto et al. (2020)	★★★★★	★★	★★★	10 Very Good Study
Perossi et al. (2022)	★★	★★	★★★	7 Good Study
Liang et al. (2022)	★★★★★	★★	★★★	10 Very Good Study

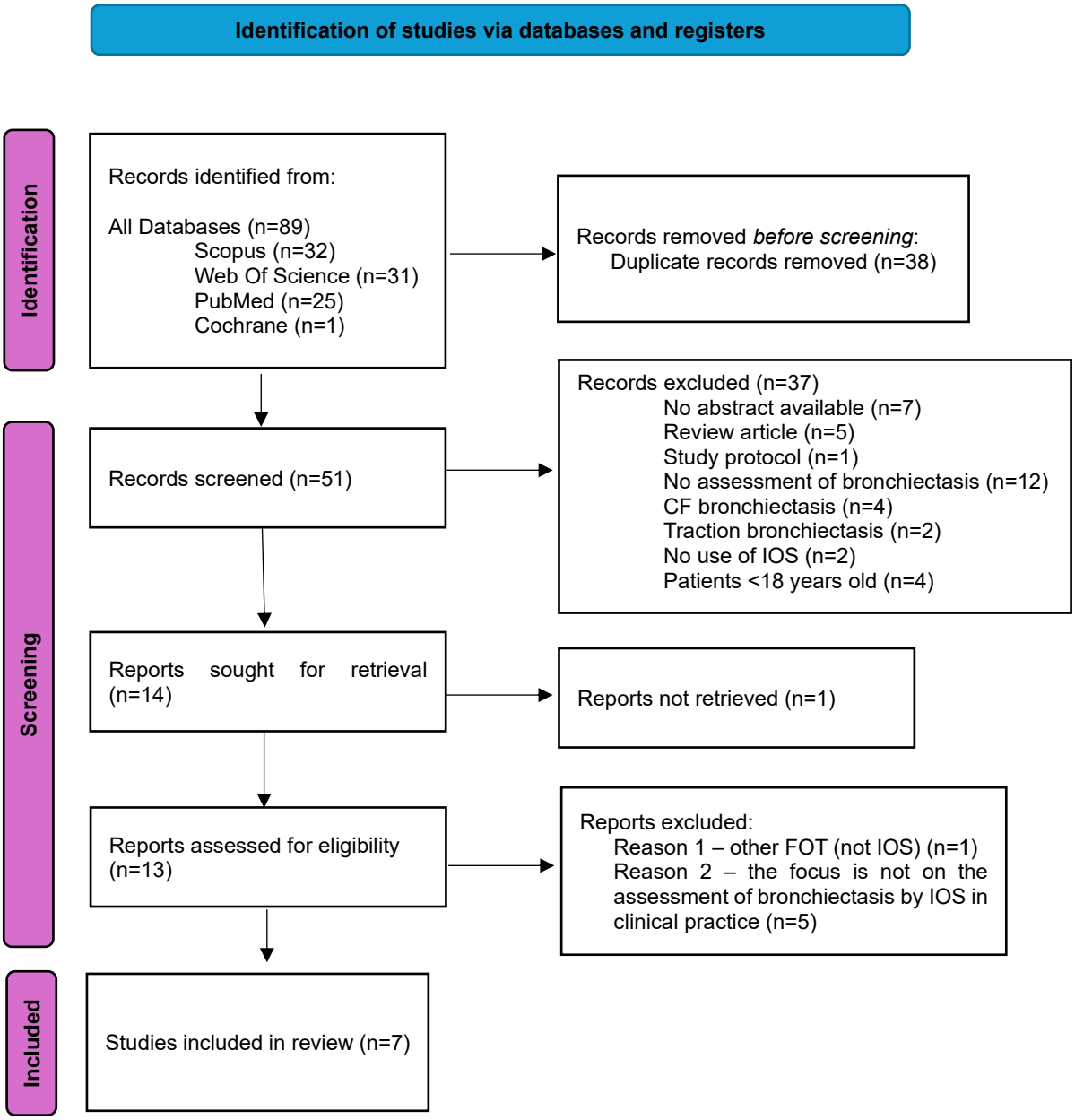

Figure 1. PRISMA 2020 flow diagram of the literature search process.[26] CF: Cystic Fibrosis. IOS: Impulse Oscillometry System. FOT: Forced Oscillation Technique.

Table II. Summary of the characteristics of the selected studies. NTM: non-tuberculous mycobacteria. BSI: Bronchiectasis Severity Index. MRC: Medical Research Council. IOS: Impulse Oscillometry System. HRCT: High-Resolution Computed Tomography. R5, R10, R15, R20, R25, R35: resistance at 5Hz, 10Hz, 15Hz, 20Hz, 25Hz and 35Hz, respectively. R5-R20: peripheral airway resistance. Fres: resonant frequency. AX: reactance area. ALX: low-frequency reactance area. X5: reactance at 5Hz. Z5: airway impedance at 5Hz. Rc: central resistance. Rp: peripheral resistance.

Authors, Year	Title	Population (sample size (N) and mean age)	Evaluation of the severity of bronchiectasis	IOS system	Comparison	Outcomes (IOS parameters)
Choi et al., 2024	Usefulness of Impulse Oscillometry in Predicting the Severity of Bronchiectasis	N=145 bronchiectasis patients: 101 mild (mean age 67.9) and 44 moderate/severe (mean age 76.2)	FACED score	MasterLab IOS System (Erich Jaeger, Würzburg, Germany)	Spirometry	R5, R20, R5-R20, Fres, AX, X5
Tan et al., 2022	The Role of Impulse Oscillometry in Evaluating Disease Severity and Predicting the Airway Reversibility	N=74 bronchiectasis patients (mean age 60.4); N=121 healthy controls (mean age 57)	FACED, BSI, modified Reiff, Bhalla and BRICS scores	SentrySuite® IOS system (CareFusion Co, California, US)	Plethysmography, Spirometry, Sputum culture	Rc, Rp, Z5, R5, R10, R15, R20, R5-R20, R25, R35, Fres, X5
Guan et al., 2015	Impulse Oscillometry in Adults with Bronchiectasis	N=100 bronchiectasis patients (mean age 43.9); N=28 healthy controls (mean age 39.9)	BSI	JAEGER MS-IOS system (CareFusion, Hochberg, Germany)	Spirometry, chest HRCT score, Sputum culture	Z5, R5, R20, Fres , AX, X5,
Guan et al., 2016	Impulse Oscillometry and Spirometry Small-Airway Parameters in Mild to Moderate Bronchiectasis	N=94 mild/moderate bronchiectasis patients; N=26 healthy controls (range 18-75 years)	BSI	JAEGER MS-IOS system (CareFusion, Hochberg, Germany)	Spirometry, chest HRCT score, Sputum culture	R5-R20, Fres, AX, X5
Yamamoto et al., 2020	Evaluation of Disease Severity in Bronchiectasis Using Impulse Oscillometry	N=206 bronchiectasis patients (mean age 70.6): 98 in the NTM subgroup and 108 in the non-NTM subgroup	BSI, FACED and E-FACED scores	IOS Mostgraph-01, Chest M.I. Co., Ltd., Tokyo, Japan	Spirometry, chest HRCT score, Sputum culture	R5, R20, R5-R20, ALX, Fres, X5
Perossi et al., 2022	Correlation among clinical, functional and morphological indexes in non-cystic fibrosis bronchiectasis	N=38 bronchiectasis patients (mean age 51.8)	BSI, MRC scale and modified Reiff scores	Jaeger IOS (Jaeger, Wurzburg, Germany), software Launch SentrySuite TM version 2.11	Spirometry, chest HRCT, Quantitative CT analysis using Yacta program, version 2.0	R5, R20, R5-R20
Liang et al., 2022	Clinical application of oscillometry in respiratory diseases: an impulse oscillometry registry	N=109 bronchiectasis patients (mean age 52.9); N=567 healthy controls (mean age 38.3)	Severity grading cut-offs of FEV_1	MasterScreen IOS (CareFusion, Hochberg, Germany)	Spirometry	R5, R20, R5-R20, Fres, AX, X5

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