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MODERN ASSESSMENT OF PROGRESSION RISK IN INTERSTITIAL LUNG DISEASES (ILD): QUANTITATIVE COMPUTED TOMOGRAPHY (qCT), BIOMARKERS, AND ARTIFICIAL INTELLIGENCE IN CLINICAL PRACTICE

Marcin Mazur *(Corresponding Author, Email: marcin.mazur.publ@gmail.com)*
Medical University of Lodz, Poland
ORCID ID: 0009-0008-2408-2107

Julia Kozicka
Medical University of Lodz, Poland
ORCID ID: 0009-0003-8138-6231

Ewa Wojtanowska
Medical University of Lodz, Poland
ORCID ID: 0009-0007-4813-9473

Ewa Jachimczak
University Hospital in Krakow, Poland
ORCID ID: 0009-0009-6899-3460

Paulina Jaruga
Regional Specialized Hospital No. 4, Bytom, Poland
ORCID ID: 0009-0009-3178-3785

Karolina Grodkowska-Szukała
Municipal Hospital in Zabrze, Zabrze, Poland
ORCID ID: 0009-0000-6179-7242

Julia Paczyna
Regional Specialized Hospital No. 4, Bytom, Poland
ORCID ID: 0009-0006-5485-7167

Vanessa Gąsiorowska
Our Lady of Perpetual Help Hospital in Wołomin, ul. Gdyńska 1/3, 05-200 Wołomin, Poland
ORCID ID: 0009-0008-2420-627X

Aleksandra Suszczyńska
Medical Center Unident Dental Clinic, Dąbrowa Tarnowska, Poland
ORCID ID: 0009-0009-0923-8529

ABSTRACT

Interstitial lung diseases (ILD) constitute a heterogeneous group of conditions with a complex clinical course, in which accurate prediction of the rate of fibrosis is crucial for optimizing therapy. However, traditional diagnostic methods, which are based on visual assessment of high-resolution computed tomography (HRCT) and pulmonary function tests (PFT), are burdened by significant inter-observer variability and limited sensitivity in detecting early structural changes. This review of the literature from 2010-2026 analyzes the potential of innovative technologies, such as quantitative computed tomography (qCT), radiomics, and artificial intelligence (AI), in the process of risk assessment and monitoring of ILD progression. Scientific evidence indicates that qCT parameters, including normal lung volume percentage (NLV%) and fibrosis volume percentage (FLV%), offer an objective and reproducible measure of disease severity, showing a strong correlation with spirometric parameters (FVC, DLCO) and the risk of death in patients with idiopathic pulmonary fibrosis (IPF) or connective tissue diseases (CTD-ILD).

Modern diagnostics increasingly utilize hybrid artificial intelligence models, which achieve an accuracy of 94-95% in differentiating morphological patterns. These methods are complemented by radiomics, which, by extracting hundreds of numerical features related to parenchymal texture heterogeneity, allows for the differentiation of fibrotic from inflammatory patterns with a precision unattainable by the human eye. Despite these promising prospects, the process of implementing these tools into clinical practice faces systemic barriers, such as technical variability among scanners, the lack of standardized image reconstruction protocols, and IT challenges related to integrating algorithms with hospital systems. A key prerequisite for the full implementation of AI and qCT in the care of patients with ILD is the conduct of multicenter prospective studies based on hard endpoints and the development of an international ethical and legal framework regulating responsibility for algorithm-assisted decisions.

KEYWORDS

Interstitial Lung Disease; Quantitative Computed Tomography; Artificial Intelligence; Imaging Biomarkers; Disease Progression; Risk Stratification

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1. Introduction

Interstitial lung diseases (ILD) constitute a broad and diverse group of pulmonary parenchymal disorders characterized by the development of inflammatory and fibrotic processes of varying severity (Dixon et al., 2025; Exarchos et al., 2023; Maher, 2024; Walsh et al., 2024). The clinical course of these conditions is highly variable both between different disease entities and within patient populations with the same diagnosis. While some patients exhibit slow, stable progression, others develop a phenotype characterized by rapid fibrosis and poor prognosis (Dixon et al., 2025; Exarchos et al., 2023).

Accurate risk assessment and prediction of disease progression are crucial for optimizing the timing of treatment initiation and modification. However, this task poses a significant challenge in clinical practice. Commonly used diagnostic tools, including visual interpretation of high-resolution computed tomography (HRCT) results and pulmonary function tests (PFTs), are characterized by significant inter-observer variability. Furthermore, they exhibit limited sensitivity in detecting early or subtle structural changes, which hinders precise patient stratification in the early stages of the disease (Dixon et al., 2025; Humphries, Chung, et al., 2025; Walsh et al., 2024; Weatherley et al., 2019).

Consequently, there is a growing need for more objective and reproducible methods for the quantitative assessment of ILD severity.

In response to these limitations, the development of quantitative computed tomography (qCT) methods, imaging biomarkers, and artificial intelligence (AI) algorithms is opening up new research and diagnostic

perspectives. The qCT method, which is based on the automated numerical analysis of HRCT images, is currently being evaluated as a potential tool for objectively measuring the extent and type of interstitial changes. Previous reports suggest that the indices obtained in this way may exhibit higher reproducibility and sensitivity to changes over time than conventional radiological assessment, showing potential correlations with disease progression and mortality (Dixon et al., 2025; Humphries, Chung, et al., 2025; Walsh et al., 2024; Weatherley et al., 2019). In turn, the use of artificial intelligence-based tools is being considered in the context of minimizing examiner subjectivity and identifying complex structural patterns that are often difficult for a specialist to detect visually (Dack et al., 2023; Exarchos et al., 2023; Mei et al., 2023; Rea et al., 2023; Soffer et al., 2021). Integrating these technologies into current clinical practice could significantly improve ILD management. This would enable earlier detection of disease progression and more accurate prognoses, as well as better personalised therapeutic strategies.

This review aims to summarize the current state of knowledge regarding the utility of qCT, biomarkers, and artificial intelligence in assessing the risk of progression and predicting the course of interstitial lung diseases. The study also provides a critical analysis of the methodological challenges and prospects associated with the potential implementation of these innovative methods into daily clinical practice.

2. Methodology

A literature review was conducted covering the main databases: PubMed and the Cochrane Library. The search process utilized combinations of keywords related to interstitial lung diseases, quantitative computed tomography (qCT), artificial intelligence, imaging biomarkers, prognosis, risk stratification, radiomics, machine learning and deep learning, as well as issues of clinical implementation and ethical aspects. The analysis included original research studies and systematic reviews published in open access between 2010 and 2026 that addressed the use of qCT or artificial intelligence-based methods in the diagnosis or prognosis of interstitial lung diseases. The selection was limited to studies conducted in humans and publications in English. Studies that did not focus on interstitial lung diseases, did not include quantitative image analysis, or did not use artificial intelligence-based tools were excluded. Additionally, attention was paid to the barriers and enabling factors described by the authors regarding the implementation of these solutions into clinical practice, as well as to the ethical and regulatory issues raised.

3. Quantitative computed tomography (qCT) in interstitial lung diseases

3.1.Image Characterization and Parameterization in the qCT Method

Quantitative computed tomography (qCT) is an advancement of standard HRCT in which the image is processed by a computer, and the result is presented as numerical parameters describing the lung parenchyma. qCT algorithms segment the lungs and then classify pixels based on density and texture features. This allows for the precise determination of the extent of fibrosis, the extent of ground-glass opacities, reticular patterns, and honeycomb patterns (Amorim et al., 2024; Dixon et al., 2025; Walsh et al., 2024; Weatherley et al., 2019). Based on the obtained results, objective quantitative parameters are calculated, primarily including: the percentage of normal lung volume (NLV%) and the percentage of lung volume affected by fibrosis (FLV%) (Huang et al., 2025). Systems such as CALIPER allow for an even more detailed determination of the percentage of ground-glass opacity, reticulation, honeycomb-like changes, and vascular changes in the total lung volume (Amorim et al., 2024; Occhipinti et al., 2019). The use of these quantitative parameters allows for significant objectification and increased reproducibility of the analysis compared to classical visual radiological assessment, which is characterized by considerable interobserver variability and remains heavily dependent on the experience of the physician interpreting the study.

3.2.Summary indices in assessing disease progression

A comprehensive assessment of disease progression is enabled by summary indices, including QILD (Quantitative Interstitial Lung Disease), which is the sum of the quantitative index of pulmonary fibrosis, the quantitative index of ground-glass opacity areas, and the quantitative index of honeycomb-like areas (Goldin et al., 2018; Yeo et al., 2023). Numerous studies have shown that indices obtained using qCT accurately reflect the clinical status and the further course of the disease.

3.3.The Use of qCT in Idiopathic Pulmonary Fibrosis (IPF)

Quantitative computed tomography (qCT) is an increasingly important tool in assessing the stage and predicting the course of idiopathic pulmonary fibrosis (IPF), showing strong correlations with pulmonary function test (PFT) results and allowing for a precise estimation of the risk of disease progression or death (Amorim et al., 2024; Dixon et al., 2025; Si-Mohamed et al., 2022; Yeo et al., 2023; Zhang et al., 2024). Studies demonstrate that the quantified percentage of fibrosis (F%) shows a significant negative correlation with forced vital capacity (FVC), total lung capacity (TLC), and maximum voluntary ventilation (MVV), while the percentage of ground-glass opacity (GGO%) correlates most strongly with the level of pulmonary gas diffusion capacity (DLCO) (Zhang et al., 2024). Similar relationships have been confirmed by other authors, indicating a close association between automated measures of fibrosis, the volume of structural changes, and high-attenuation areas with FVC and DLCO parameters (Ash et al., 2017; Du et al., 2022; Guiot et al., 2024; Jacob et al., 2017, 2018). Furthermore, total lung volume measured by CT (CTvol) strongly correlates with FVC and TLC (Si-Mohamed et al., 2022; Thillai et al., 2024). Moreover, qCT indices possess significant prognostic value independent of conventional PFTs in predicting disease progression. The baseline diffuse texture index (DTA) and total extent of lesions (ILD%/fibrotic volume) allow for the prediction of annual declines in FVC and DLCO and are directly associated with patient survival (Du et al., 2022; Humphries et al., 2022). Dynamic analyses have shown that an increase in the volume of pathological changes and their proportion of total lung volume closely correlates with worsening functional parameters, demonstrating a significant correlation with changes in DLCO (Sun et al., 2023). Early assessment of the dynamics of these changes also plays a significant role. It has been observed, among other things, that even a 6-month increase in the quantitative lung fibrosis index (QLF) of at least 4% is a strong predictor of faster functional progression (Kim et al., 2020). Despite the methodological heterogeneity reported in the literature, systematic reviews unequivocally confirm the independent prognostic potential of these parameters (Dixon et al., 2025). A key aspect of qCT application is the ability to differentiate between rapid and slow progressing phenotypes and to more precisely estimate the risk of death by assessing organ volume loss (Oh et al., 2024; Si-Mohamed et al., 2022). It was also established that, in idiopathic pulmonary fibrosis, a relative annual CT volume loss higher than 9.4% is associated with a significantly reduced mean survival time at 2.0 years versus 2.8 years (Si-Mohamed et al., 2022). The use of advanced deep learning-based segmentation algorithms has confirmed that lower lung volume combined with more advanced fibrosis independently determines poorer 2- and 5-year survival (Robbie et al., 2022; Sun et al., 2023; Thillai et al., 2024). However, the highest predictive value is achieved by multi-parameter models that combine changes in volume dynamics (ΔCTvol), functional indices (ΔFVC), and a quantitative increase in the area of fibrosis, which predict mortality in IPF significantly more effectively than individual parameters (Achaiah et al., 2025).

3.4.The use of qCT in other forms of interstitial lung disease

Similar relationships are also observed in other ILD subtypes. In rheumatoid arthritis-associated interstitial lung disease (RA-ILD), a quantitative fibrosis index based on image texture analysis shows a moderate negative correlation with FVC% and DLCO% values. Both its baseline value and its increase over time are independent prognostic factors for an increased risk of death (Humphries, Adegunsoye, et al., 2025). In the course of ILDs associated with systemic connective tissue diseases, including systemic sclerosis (SSc-ILD) and inflammatory myopathies, composite qCT indices (e.g., QILD, QLF) are of significant importance. These indices integrate information on ground-glass opacities, fibrosis, and reticular changes, correlating with FVC, DLCO, and the severity of dyspnea, which allows for the precise identification of patients with an unfavorable prognosis (Amorim et al., 2024; Bae et al., 2024; Yeo et al., 2023). Furthermore, population-based screening studies have shown that even a small proportion of interstitial changes, including ground-glass opacities, reticular changes and honeycomb patterns, is associated with increased all-cause mortality (Wang et al., 2025).

3.5.Assessment of Clinical Evidence

A systematic review of over 180 studies on quantitative computed tomography (qCT) in interstitial lung disease (ILD) confirms that this technique is valuable for prognosis and monitoring various disease entities (Dixon et al., 2025). The key clinical value of qCT lies in its ability to objectively reflect tissue change dynamics. Quantitative indices provide unique prognostic information that goes beyond the capabilities of traditional functional tests to interpret. Notably, these indices demonstrate independent predictive power with regard to disease progression and mortality, maintaining statistical significance even when adjusted for standard clinical and demographic variables (Dixon et al., 2025). Therefore, qCT is a significant advancement in the objectification of risk stratification in patients with various pulmonary fibrosis phenotypes.

4. Automation of radiological assessment in ILD: the role of machine learning algorithms and artificial intelligence

4.1.Structural Principles and Architecture of Hybrid Models

Modern quantitative analysis in computed tomography (qCT) is becoming increasingly integrated with machine learning algorithms, enabling it to overcome the limitations of traditional, simplified morphological pattern recognition. A significant current area of development involves advanced hybrid artificial intelligence (AI) models that can simultaneously process and interpret the full volume of an HRCT scan. The implementation of these solutions enables full automation of the analysis by eliminating the need to manually define regions of interest (ROI), which fundamentally optimizes the diagnostic procedure (Dixon et al., 2025; Pawar & Talbar, 2022). Hybrid approaches are most often based on a two-stage architecture. In the first phase, algorithms use neural networks, such as conditional generative adversarial networks (c-GANs), for automated lung tissue segmentation. In the second stage, deep learning models (e.g., ResNet or VGG) perform a detailed analysis of the isolated parenchyma, extracting key radiological features and enabling precise classification of pathologies into appropriate diagnostic categories within ILD (Pawar & Talbar, 2022).

4.2.Classification performance and diagnostic accuracy

The use of advanced network architectures has resulted in high effectiveness in differentiating structural changes. Hybrid models achieve diagnostic accuracy of 94-95%, demonstrating the ability to precisely identify 5 to 17 distinct categories of parenchymal pathologies, including, among others, fixed fibrosis, ground-glass opacities, honeycomb pattern, emphysema, and consolidations (Pawar & Talbar, 2022; Raju et al., 2020). The high potential of these tools is also confirmed by data from the relevant literature. A systematic review of 19 retrospective studies on the application of deep learning in HRCT assessment showed that, in tasks involving the differentiation of complex morphological patterns characteristic of ILD, the algorithms achieve reproducible accuracy ranging from 78% to 91% (Soffer et al., 2021).

4.3.Prognostic potential and integration with clinical data

Such algorithms treat the entire HRCT scan as a source of a rich feature vector. This allows for the direct integration of imaging data with clinical parameters, pulmonary function test results, and laboratory indicators within complex predictive models (e.g., regression, hazard models) to assess the risk of disease progression, FVC decline, or death. Deep learning-based texture analysis algorithms, including DTA (Deep Texture Analysis) and QLF/QILD systems, show strong correlations with spirometric parameters (FVC, DLCO). Crucially from a clinical perspective, these tools enable effective prediction of the dynamics of lung function decline, the risk of disease progression, and overall patient survival. These associations have been documented in various fibrosing forms of ILD, including idiopathic pulmonary fibrosis (IPF), progressive pulmonary fibrosis (PF-ILD), and interstitial lung involvement in systemic connective tissue diseases (Dixon et al., 2025; Lee et al., 2025; Russo et al., 2025).

5. Radiomics as a bridge between quantitative computed tomography and artificial intelligence in the diagnosis of interstitial lung diseases

5.1.Methodological foundations and extraction of radiomic features

Radiomics represents a natural extension of the previously described qCT techniques and, at the same time, a bridge between them and advanced artificial intelligence systems. Using the same HRCT images, it goes beyond simple, global quantitative indicators (e.g., fibrosis fraction) and generates a structured description based on hundreds of numerical features characterizing the shape, intensity, and texture of the lung parenchyma. Statistical models or machine learning algorithms are then built from this data, serving as non-invasive diagnostic and prognostic biomarkers and enabling, among other things, precise prediction of fibrosis progression, FVC decline, or risk of death. (Bastos & Mamede, 2025; Han et al., 2024; Li et al., 2025; Qin et al., 2023).

5.2.Integration of radiomic data into multivariate prognostic models

In the population of patients with interstitial lung diseases associated with systemic connective tissue diseases (CTD-ILD), a significant achievement was the development of nomograms integrating radiomic features with clinical parameters. It has been demonstrated that these models exhibit higher accuracy in classifying disease stages on the ILD-GAP scale and in predicting overall survival compared to conventional algorithms based solely on clinical and demographic variables (Bastos & Mamede, 2025; Qin et al., 2023). A

similar methodology was implemented in the diagnosis of rheumatoid arthritis-associated interstitial lung disease (RA-ILD) by constructing a nomogram combining radiomic features of computed tomography with serum KL-6 levels. This type of model accurately identifies patients at low risk of progression, enabling more personalized planning of therapeutic strategies and avoiding overly aggressive treatment in stable patients (Han et al., 2024).

5.3.The Role of Radiomic Analysis in the Differential Diagnosis of ILD Phenotypes

Beyond its prognostic function, radiomics plays a key role in differentiating complex pathologies within the lung parenchyma. It has been demonstrated that models based on the analysis of textural features can distinguish, with very high precision to distinguish the destructive fibrotic pattern typical of idiopathic pulmonary fibrosis (IPF) from the inflammatory component observed in the cellular form of non-specific interstitial pneumonia (NSIP) (Colligiani et al., 2025). The key indicators determining the effectiveness of this classification turned out to be quantitative features describing lung morphology, density distribution, and texture heterogeneity, which remain elusive during standard visual assessment.

6. Limitations and barriers to the implementation of quantitative computed tomography and artificial intelligence in clinical practice

6.1.Technical heterogeneity and lack of standardization in imaging protocols

A key obstacle to the widespread implementation of these solutions in the field of ILD is the significant technical variability in image acquisition and reconstruction procedures. A systematic review covering over 180 studies on qCT demonstrated that the lack of a uniform nomenclature and the inconsistency of CT protocols in practice make it impossible to conduct reliable meta-analyses, which consequently hinders the formulation of unambiguous clinical guidelines (Dixon et al., 2025)**.**

This problem affects radiomics and machine learning equally. Differences in diagnostic device specifications, image reconstruction parameters, feature extraction methods and mathematical model architectures lead to low reproducibility and inconsistent results across independent centres. (Bastos & Mamede, 2025; Felder & Walsh, 2023; Qin et al., 2023; Walsh et al., 2024).

6.2.Lack of prospective validation studies and hard endpoints

A significant methodological barrier is that most existing artificial intelligence algorithms dedicated to HRCT assessment in patients with ILD have not been externally validated. The vast majority of available data is based on retrospective analyses. There is still a lack of well-designed, prospective, multicenter analyses with clearly defined, hard endpoints, such as mortality, fibrosis progression, or declines in forced vital capacity (FVC) and diffusion capacity (DLCO). Such data are essential for regulatory authorities and payers to reliably assess the real added value of new technologies relative to the current standard of care (Dixon et al., 2025; Soffer et al., 2021; Walsh et al., 2024).

6.3.Infrastructural, Legal, Organizational, and Ethical Challenges

The process of integrating advanced computing systems with existing hospital infrastructure involves complex legal, ethical, and technological issues. Effective training and validation of qCT, radiomics, and AI models require the consolidation of multicenter, large-scale databases that combine HRCT images with sensitive patient clinical information. This creates significant challenges in the areas of cybersecurity, personal data protection and the necessity of integrating closed data ecosystems (Dixon et al., 2025; Felder & Walsh, 2023; Ramwala et al., 2024; Walsh et al., 2024). From an IT perspective, a key challenge is the need to create dedicated, secure testing environments within the hospital architecture that would allow for the validation of new algorithms without the risk of destabilizing real-time clinical systems (Ramwala et al., 2024). Furthermore, this implementation raises ethical and legal questions. These primarily concern formal responsibility for diagnostic and therapeutic decisions supported by AI systems, requirements for continuous monitoring, auditing, and updating of software, as well as the need for dynamic adaptation of mathematical models to constantly evolving imaging techniques (Felder & Walsh, 2023; Handa, 2023; Walsh et al., 2024).

7. Discussion

7.1.Medical and methodological rationale for the implementation of qCT and AI

The presented literature review indicates that the integration of quantitative computed tomography (qCT), radiomics, and artificial intelligence (AI) algorithms represents a significant step forward in the diagnosis and risk assessment of patients with interstitial lung diseases (ILD). The current state of knowledge confirms the well-established role of these solutions in clinical assessment. Numerous studies have demonstrated that measurable quantitative qCT indices show a strong correlation with functional parameters (FVC, DLCO), the severity of dyspnea, as well as with survival time and the risk of disease progression in various ILD subtypes, including those associated with systemic connective tissue diseases, such as CTD-ILD and SSc-ILD (Bastos & Mamede, 2025; Dixon et al., 2025; Felder & Walsh, 2023; Walsh et al., 2024).

A key advantage of quantitative and computational systems is the reduction of interpretive subjectivity and a significant improvement in the reproducibility of results compared to conventional, purely visual assessment of HRCT scans (Dixon et al., 2025; Rea et al., 2023; Walsh et al., 2024). AI-based tools demonstrate diagnostic agreement with experts at a level surpassing that of less experienced radiologists. This enables the precise detection of subtle, dynamic changes in fibrosis and ground-glass opacity areas across consecutive scans, which is of fundamental importance for the early identification of disease progression (Lee et al., 2025; Russo et al., 2025; Walsh et al., 2024). Consequently, these solutions can provide significant decision-making support during multidisciplinary consultations, particularly in lower-tier referral centers where access to specialized ILD experts is limited.

7.2.Equipment, regulatory, and structural barriers

Despite such promising prospects and a growing evidence base, the transition from the experimental phase to routine clinical practice faces significant methodological and systemic barriers (Dixon et al., 2025; Walsh et al., 2024). The main challenge remains the technical diversity of diagnostic equipment. Variations in scanner specifications, back-projection algorithms, and radiomic feature extraction methods drastically reduce the repeatability and reproducibility of predictive models across different centers (Bastos & Mamede, 2025; Felder & Walsh, 2023; Qin et al., 2023; Walsh et al., 2024). Additionally, the current level of sophistication of most algorithms is based on evidence derived from retrospective cohort analyses. To demonstrate real clinical effectiveness and cost-effectiveness for payers and regulatory bodies, it is essential to conduct multicenter prospective studies with adequate statistical power, focused on hard endpoints such as all-cause mortality or the annual rate of decline in FVC and DLCO (Dixon et al., 2025; Soffer et al., 2021; Walsh et al., 2024). Concurrently, the implementation process raises complex logistical and legal challenges (Dixon et al., 2025; Felder & Walsh, 2023; Ramwala et al., 2024; Walsh et al., 2024). Integrating AI tools with existing hospital infrastructure requires the implementation of secure, dedicated validation environments to ensure that the stability and operational continuity of current systems is not disrupted. (Ramwala et al., 2024). Another significant challenge is the lack of a regulated framework for civil liability in relation to automatically assisted diagnostic and therapeutic decisions. There are also restrictive requirements for the continuous monitoring, auditing and updating of algorithmic systems. (Felder & Walsh, 2023; Handa, 2023; Walsh et al., 2024).

7.3.The Importance of International Consortia in Standardizing Solutions

Coordinated international cooperation is seen as an opportunity to overcome these barriers. The activities of global scientific consortia, which are aimed at creating centralised, well-characterised and anonymised repositories of HRCT images and correlated clinical data, constitute a key structural foundation. (Dixon et al., 2025; Walsh et al., 2024). The construction of large-scale databases is essential for designing and rigorously validating digital predictive biomarkers. In the long term, this approach will enable the safe, standardised and reproducible implementation of these biomarkers in the daily care of patients with interstitial lung disease (ILD).

8. Conclusions

Quantitative computed tomography (qCT), radiomics and artificial intelligence (AI) algorithms represent a methodological breakthrough in the diagnosis of interstitial lung diseases (ILD). These tools offer an objective and reproducible approach that significantly improves risk stratification and the monitoring of structural changes, surpassing the capabilities of traditional visual and functional methods. The accumulated scientific evidence confirms that digital biomarkers demonstrate strong independent prognostic value, correlating directly with spirometric parameters, symptom severity, and the risk of progression and death across various ILD subtypes. By minimising the subjectivity of interpretation and ensuring greater reproducibility of results, these solutions can support the decision-making process during multidisciplinary consultations, increasing diagnostic accuracy, particularly in centres with limited access to specialist experts.

However, the widespread implementation of these technologies in routine clinical practice requires the overcoming of significant systemic, technological and regulatory barriers. Key challenges include technical variability in scanners and image reconstruction methods, which reduces the reproducibility of models across centers; the prevalence of retrospective analyses; and complex issues related to cybersecurity, integration with hospital infrastructure, and civil liability for algorithm-assisted decisions. Therefore, future research should prioritize the implementation of multicenter, prospective validation studies based on hard endpoints and the international harmonization of data acquisition protocols. Concurrently, it is essential to develop explainable artificial intelligence (XAI) systems with a transparent structure and to establish a framework for ethical governance and regulation, which will enable the safe, effective, and equitable implementation of these innovations for the benefit of the entire patient population.

The authors declare that they have no conflict of interest.

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All authors contributed to the study conception, literature review, and manuscript preparation. All authors read and approved the final version of the manuscript.

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