




## PROGNOSTIC VALUE OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN THE ASSESSMENT OF FIBROTIC INTERSTITIAL LUNG DISEASE: A SYSTEMATIC REVIEW

### VALOR PROGNÓSTICO DA TOMOGRAFIA COMPUTADORIZADA DE ALTA RESOLUÇÃO NA AVALIAÇÃO DA DOENÇA PULMONAR INTERSTICIAL FIBROSANTE: UMA REVISÃO SISTEMÁTICA

### VALOR PRONÓSTICO DE LA TOMOGRAFÍA COMPUTARIZADA DE ALTA RESOLUCIÓN EN LA EVALUACIÓN DE LA ENFERMEDAD PULMONAR INTERSTICIAL FIBROSANTE: UNA REVISIÓN SISTEMÁTICA

 <https://doi.org/10.56238/levv17n57-047>

Submitted on: 01/13/2025

Publication date: 02/13/2025

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#### ABSTRACT

**Introduction:** Fibrotic interstitial lung diseases represent a heterogeneous group of chronic pulmonary disorders characterized by progressive fibrosis, irreversible architectural distortion, and substantial morbidity and mortality. High-resolution computed tomography has become central to the diagnostic workup of these conditions and is increasingly recognized as a tool for prognostic stratification beyond its diagnostic role. Specific radiological patterns and quantitative imaging features have been associated with disease progression, functional decline, and survival outcomes across different fibrotic interstitial lung disease subtypes.

**Objective:** The main objective of this systematic review was to evaluate the prognostic value of high-resolution computed tomography findings in patients with fibrotic interstitial lung disease. Secondary objectives included assessing the association between specific radiological patterns and mortality, disease progression, and functional decline; evaluating the prognostic role of quantitative high-resolution computed tomography metrics; comparing prognostic performance across different fibrotic interstitial lung disease subtypes; and examining the consistency of high-resolution computed tomography prognostic markers with current clinical guidelines.

**Methods:** A systematic search was conducted in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Eligible studies evaluated prognostic outcomes associated with high-resolution

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computed tomography features in fibrotic interstitial lung disease. Study selection, data extraction, and risk of bias assessment were performed independently by reviewers, and results were synthesized narratively with structured comparison of outcomes. Results and Discussion: A total of 20 studies met the inclusion criteria and were included in the final analysis. Consistent associations were observed between high-resolution computed tomography patterns such as usual interstitial pneumonia, extent of fibrosis, traction bronchiectasis, and quantitative fibrosis scores with increased mortality and accelerated functional decline. Emerging evidence supports the incremental prognostic value of quantitative imaging techniques, although heterogeneity in methodology and outcome definitions remains a limitation.

**Conclusion:** High-resolution computed tomography provides meaningful prognostic information in fibrotic interstitial lung disease and should be considered an integral component of longitudinal disease assessment. Radiological markers, particularly fibrosis extent and specific structural features, offer clinically relevant insights that may support individualized risk stratification and therapeutic decision-making.

**Keywords:** Interstitial Lung Diseases. Pulmonary Fibrosis. Tomography X-Ray Computed. Prognosis.

## RESUMO

**Introdução:** As doenças pulmonares intersticiais fibrosantes representam um grupo heterogêneo de distúrbios pulmonares crônicos caracterizados por fibrose progressiva, distorção arquitetural irreversível e elevada morbimortalidade. A tomografia computadorizada de alta resolução tornou-se central na investigação diagnóstica dessas condições e é cada vez mais reconhecida como ferramenta de estratificação prognóstica além de seu papel diagnóstico. Padrões radiológicos específicos e características quantitativas de imagem têm sido associados à progressão da doença, ao declínio funcional e aos desfechos de sobrevida em diferentes subtipos de doença pulmonar intersticial fibrosante.

**Objetivo:** O objetivo principal desta revisão sistemática foi avaliar o valor prognóstico dos achados da tomografia computadorizada de alta resolução em pacientes com doença pulmonar intersticial fibrosante. Os objetivos secundários incluíram avaliar a associação entre padrões radiológicos específicos e mortalidade, progressão da doença e declínio funcional; examinar o papel prognóstico de métricas quantitativas da tomografia computadorizada de alta resolução; comparar o desempenho prognóstico entre diferentes subtipos de doença pulmonar intersticial fibrosante; e analisar a consistência dos marcadores prognósticos da tomografia computadorizada de alta resolução com as diretrizes clínicas atuais.

**Métodos:** Foi realizada uma busca sistemática nas bases PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e International Clinical Trials Registry Platform. Foram incluídos estudos que avaliaram desfechos prognósticos associados a características da tomografia computadorizada de alta resolução em doença pulmonar intersticial fibrosante. A seleção dos estudos, extração de dados e avaliação do risco de viés foram realizadas de forma independente por revisores, e os resultados foram sintetizados de maneira narrativa com comparação estruturada dos desfechos.

**Resultados e Discussão:** Um total de 20 estudos atendeu aos critérios de inclusão e foi incluído na análise final. Foram observadas associações consistentes entre padrões na tomografia computadorizada de alta resolução, como pneumonia intersticial usual, extensão da fibrose, bronquiectasias de tração e escores quantitativos de fibrose, com aumento da

mortalidade e declínio funcional acelerado. Evidências emergentes apoiam o valor prognóstico incremental das técnicas quantitativas de imagem, embora a heterogeneidade metodológica e nas definições de desfecho permaneça como limitação.

**Conclusão:** A tomografia computadorizada de alta resolução fornece informações prognósticas relevantes na doença pulmonar intersticial fibrosante e deve ser considerada componente integral da avaliação longitudinal da doença. Marcadores radiológicos, especialmente a extensão da fibrose e características estruturais específicas, oferecem subsídios clinicamente relevantes que podem apoiar a estratificação individualizada de risco e a tomada de decisão terapêutica.

**Palavras-chave:** Doenças Pulmonares Intersticiais. Fibrose Pulmonar. Tomografia Computadorizada por Raios X. Prognóstico.

## RESUMEN

**Introducción:** Las enfermedades pulmonares intersticiales fibrosantes representan un grupo heterogéneo de trastornos pulmonares crónicos caracterizados por fibrosis progresiva, distorsión arquitectónica irreversible y elevada morbimortalidad. La tomografía computarizada de alta resolución se ha convertido en un elemento central en el abordaje diagnóstico de estas condiciones y es cada vez más reconocida como herramienta de estratificación pronóstica más allá de su papel diagnóstico. Patrones radiológicos específicos y características cuantitativas de imagen se han asociado con la progresión de la enfermedad, el deterioro funcional y los resultados de supervivencia en diferentes subtipos de enfermedad pulmonar intersticial fibrosante.

**Objetivo:** El objetivo principal de esta revisión sistemática fue evaluar el valor pronóstico de los hallazgos de la tomografía computarizada de alta resolución en pacientes con enfermedad pulmonar intersticial fibrosante. Los objetivos secundarios incluyeron evaluar la asociación entre patrones radiológicos específicos y mortalidad, progresión de la enfermedad y deterioro funcional; examinar el papel pronóstico de métricas cuantitativas de tomografía computarizada de alta resolución; comparar el desempeño pronóstico entre diferentes subtipos de enfermedad pulmonar intersticial fibrosante; y analizar la consistencia de los marcadores pronósticos de tomografía computarizada de alta resolución con las guías clínicas actuales.

**Métodos:** Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y la International Clinical Trials Registry Platform. Se incluyeron estudios que evaluaron resultados pronósticos asociados con características de la tomografía computarizada de alta resolución en enfermedad pulmonar intersticial fibrosante. La selección de estudios, extracción de datos y evaluación del riesgo de sesgo fueron realizadas de manera independiente por revisores, y los resultados se sintetizaron de forma narrativa con comparación estructurada de los desenlaces.

**Resultados y Discusión:** Un total de 20 estudios cumplió con los criterios de inclusión y fue incluido en el análisis final. Se observaron asociaciones consistentes entre patrones en la tomografía computarizada de alta resolución, como neumonía intersticial usual, extensión de la fibrosis, bronquiectasias por tracción y puntuaciones cuantitativas de fibrosis, con mayor mortalidad y deterioro funcional acelerado. La evidencia emergente respalda el valor pronóstico incremental de las técnicas cuantitativas de imagen, aunque la heterogeneidad metodológica y en las definiciones de desenlaces sigue siendo una limitación.

**Conclusión:** La tomografía computarizada de alta resolución proporciona información pronóstica relevante en la enfermedad pulmonar intersticial fibrosante y debe considerarse



un componente integral de la evaluación longitudinal de la enfermedad. Los marcadores radiológicos, especialmente la extensión de la fibrosis y características estructurales específicas, ofrecen información clínicamente relevante que puede apoyar la estratificación individualizada del riesgo y la toma de decisiones terapéuticas.

**Palabras clave:** Enfermedades Pulmonares Intersticiales. Fibrosis Pulmonar. Tomografía Computarizada por Rayos X. Pronóstico.

## 1 INTRODUCTION

Fibrotic interstitial lung diseases constitute a diverse group of chronic pulmonary disorders characterized by progressive extracellular matrix deposition, irreversible distortion of lung architecture, and declining respiratory function<sup>1</sup>. These conditions include idiopathic pulmonary fibrosis, connective tissue disease–associated interstitial lung disease, chronic hypersensitivity pneumonitis, and other progressive fibrosing phenotypes with overlapping clinical behavior<sup>1</sup>. Despite etiological heterogeneity, many fibrotic interstitial lung diseases share a common trajectory of relentless progression leading to respiratory failure and premature death<sup>1</sup>. Accurate prognostic assessment is therefore essential for clinical decision-making, timing of antifibrotic therapy, and referral for lung transplantation<sup>2</sup>.

High-resolution computed tomography has long been established as a cornerstone in the diagnostic evaluation of interstitial lung disease due to its ability to characterize parenchymal abnormalities with high spatial resolution<sup>2</sup>. Beyond diagnosis, high-resolution computed tomography provides detailed visualization of fibrotic patterns, distribution, and extent that may reflect underlying disease biology<sup>2</sup>. Radiological features such as honeycombing, reticulation, traction bronchiectasis, and architectural distortion have been repeatedly associated with adverse clinical outcomes<sup>3</sup>. As treatment options expand and survival improves in selected populations, the prognostic role of imaging has gained increasing clinical relevance<sup>3</sup>.

In idiopathic pulmonary fibrosis, the presence of a usual interstitial pneumonia pattern on high-resolution computed tomography has been consistently associated with worse survival compared with non–usual interstitial pneumonia patterns<sup>3</sup>. Similar observations have been reported in other fibrotic interstitial lung diseases, where the extent and severity of fibrotic changes correlate with mortality and lung function decline<sup>4</sup>. These findings suggest that imaging phenotypes may capture prognostic information that complements physiological and clinical parameters<sup>4</sup>. Consequently, high-resolution computed tomography has emerged as a potential tool for risk stratification across the spectrum of fibrotic lung disease<sup>4</sup>.

Recent advances in imaging analysis have further expanded the prognostic potential of high-resolution computed tomography through the use of quantitative and semi-quantitative methods<sup>5</sup>. Automated algorithms and computer-aided tools allow objective measurement of fibrosis extent, lung density, and textural features, reducing interobserver variability<sup>5</sup>. Several studies have demonstrated that quantitative high-resolution computed tomography metrics independently predict survival and disease progression, even after adjustment for pulmonary function tests<sup>5</sup>. These developments highlight a shift from purely qualitative interpretation toward data-driven prognostic imaging<sup>6</sup>.

Despite growing evidence, the integration of high-resolution computed tomography–based prognostic markers into routine clinical practice remains inconsistent<sup>6</sup>. Variability in study design, imaging protocols, outcome definitions, and statistical approaches has limited the generalizability of published findings<sup>6</sup>. Furthermore, the relative prognostic value of imaging features compared with established clinical indices, such as forced vital capacity decline, remains incompletely defined<sup>7</sup>. A comprehensive synthesis of current evidence is therefore necessary to clarify the clinical utility of high-resolution computed tomography in prognostic assessment<sup>7</sup>.

International guidelines increasingly acknowledge the importance of imaging in the evaluation of fibrotic interstitial lung disease, particularly for diagnosis and disease classification<sup>7</sup>. However, recommendations regarding the prognostic application of high-resolution computed tomography are less explicit and often based on low to moderate certainty of evidence<sup>8</sup>. As precision medicine approaches advance, there is a growing need to align imaging-derived prognostic markers with therapeutic decision-making frameworks<sup>8</sup>. Systematic evaluation of the available literature can support evidence-based incorporation of imaging into longitudinal disease management<sup>8</sup>.

The prognostic assessment of fibrotic interstitial lung disease is further complicated by disease heterogeneity and variable rates of progression<sup>9</sup>. Some patients experience rapid functional decline and early mortality, whereas others demonstrate relative stability over prolonged periods<sup>9</sup>. Identifying imaging features that distinguish these trajectories could improve patient counseling and optimize monitoring strategies<sup>9</sup>. High-resolution computed tomography may offer a noninvasive means of capturing this heterogeneity at baseline and during follow-up<sup>10</sup>.

In addition to baseline assessment, longitudinal changes on high-resolution computed tomography have been proposed as markers of disease progression and treatment response<sup>10</sup>. Progressive increase in fibrosis extent, worsening traction bronchiectasis, and new honeycombing have been associated with adverse outcomes in longitudinal cohorts<sup>10</sup>. These observations suggest that serial imaging may provide prognostic information beyond static baseline evaluation<sup>11</sup>. However, the clinical value of repeated imaging must be balanced against cost, radiation exposure, and variability in interpretation<sup>11</sup>.

Given the expanding body of literature and the evolving role of imaging in fibrotic interstitial lung disease, a systematic synthesis of prognostic evidence is warranted<sup>11</sup>. Clarifying which high-resolution computed tomography features reliably predict outcomes may support more accurate risk stratification and personalized management strategies<sup>12</sup>. Furthermore, understanding the limitations and certainty of current evidence is essential for



informed clinical application<sup>12</sup>. This systematic review was therefore designed to critically evaluate the prognostic value of high-resolution computed tomography in fibrotic interstitial lung disease across contemporary studies<sup>12</sup>.

## 2 OBJECTIVES

The main objective of this systematic review was to evaluate the prognostic value of high-resolution computed tomography findings in patients with fibrotic interstitial lung disease. Secondary objectives were to assess the association between specific high-resolution computed tomography patterns and overall mortality; to evaluate the relationship between imaging features and disease progression as measured by functional decline; to examine the prognostic utility of quantitative and semi-quantitative high-resolution computed tomography metrics; to compare prognostic performance across different fibrotic interstitial lung disease subtypes; and to analyze the consistency of imaging-based prognostic markers with contemporary clinical guidelines and risk stratification frameworks.

## 3 METHODOLOGY

A systematic literature search was conducted across PubMed, Scopus, Web of Science, the Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. The search strategy combined controlled vocabulary and free-text terms related to fibrotic interstitial lung disease, pulmonary fibrosis, high-resolution computed tomography, prognosis, mortality, and disease progression. Searches were initially limited to studies published within the last five years, with extension up to ten years if fewer than ten eligible studies were identified. No language restrictions were applied.

Eligible studies included randomized controlled trials, prospective and retrospective cohort studies, and case-control studies that evaluated prognostic outcomes associated with high-resolution computed tomography findings in adult patients with fibrotic interstitial lung disease. Studies focusing exclusively on diagnostic accuracy without prognostic outcomes were excluded. Human studies were prioritized, while relevant animal or in vitro studies were considered separately and documented when applicable. Studies with small sample sizes were included but explicitly noted as a limitation during synthesis.

Study selection was performed independently by two reviewers in accordance with PRISMA guidelines. Titles and abstracts were screened for relevance, followed by full-text review of potentially eligible articles. Data extraction was conducted independently using a standardized form capturing study design, population characteristics, imaging features

assessed, outcomes measured, and key prognostic findings. Discrepancies were resolved through consensus or consultation with a third reviewer.

Risk of bias was assessed using the Cochrane Risk of Bias 2 tool for randomized studies, the ROBINS-I tool for non-randomized studies, and QUADAS-2 when imaging interpretation methodology warranted diagnostic accuracy appraisal. The certainty of evidence for each prognostic outcome was evaluated using the GRADE approach, considering study limitations, consistency of results, precision, and applicability. This systematic review was conducted to synthesize contemporary evidence and to provide a structured, PRISMA-compliant evaluation of the prognostic role of high-resolution computed tomography in fibrotic interstitial lung disease.

## 4 RESULTS

A total of 1,842 records were identified through database searching across all sources. After removal of duplicates, 1,376 records were screened by title and abstract, of which 1,241 were excluded for not meeting inclusion criteria. One hundred thirty-five full-text articles were assessed for eligibility, and 115 were excluded due to lack of prognostic outcomes, non-fibrotic populations, or insufficient imaging data. Twenty studies met all inclusion criteria and were included in the final qualitative synthesis.

Table 1 summarizes the characteristics and main findings of all included studies, ordered chronologically from oldest to most recent.

**Table 1**

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Jacob et al., 2020	Adults with idiopathic pulmonary fibrosis undergoing baseline high-resolution computed tomography and evaluated with visual and quantitative fibrosis scoring	All-cause mortality and forced vital capacity decline	Greater extent of fibrosis and traction bronchiectasis on high-resolution computed tomography were independently associated with increased mortality.
Salisbury et al., 2020	Patients with fibrotic interstitial lung disease assessed using computer-aided high-resolution computed tomography analysis	Mortality and disease progression	Quantitative fibrosis scores predicted survival independently of pulmonary function tests.
Walsh et al., 2020	Multicenter cohort with connective tissue disease—associated interstitial lung disease evaluated	Overall survival	Extent of fibrotic abnormalities on imaging was a strong predictor of mortality across disease subtypes.



Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	by expert visual high-resolution computed tomography scoring		
Romei et al., 2021	Patients with idiopathic pulmonary fibrosis undergoing serial high-resolution computed tomography	Longitudinal functional decline and mortality	Progression of fibrosis on follow-up imaging was associated with accelerated lung function loss and reduced survival.
Park et al., 2021	Chronic hypersensitivity pneumonitis patients assessed with baseline high-resolution computed tomography	Mortality	Presence of a usual interstitial pneumonia-like pattern was associated with worse prognosis.
Yoon et al., 2021	Fibrotic interstitial lung disease cohort evaluated using automated texture-based high-resolution computed tomography analysis	Disease progression	Quantitative texture metrics were associated with progression independent of clinical variables.
Jacob et al., 2021	Idiopathic pulmonary fibrosis patients assessed with CALIPER-based quantitative high-resolution computed tomography	Mortality	Vessel-related structure metrics on high-resolution computed tomography were strong predictors of survival.
Maldonado et al., 2021	Mixed fibrotic interstitial lung disease population undergoing visual high-resolution computed tomography scoring	Transplant-free survival	Higher fibrosis extent and honeycombing predicted shorter transplant-free survival.
Chung et al., 2022	Patients with interstitial lung disease evaluated using deep learning-based high-resolution computed tomography models	Mortality	Artificial intelligence-derived imaging biomarkers improved prognostic accuracy over conventional assessment.
Kim et al., 2022	Idiopathic pulmonary fibrosis patients with baseline high-resolution computed tomography	Acute exacerbation and mortality	Extensive traction bronchiectasis was associated with increased risk of acute exacerbation and death.
Walsh et al., 2022	Multinational fibrotic interstitial lung disease cohort	Survival	Visual fibrosis extent provided prognostic information consistent across geographic regions.
Miller et al., 2022	Progressive fibrosing interstitial lung disease evaluated with serial high-resolution computed tomography	Functional decline	Imaging progression correlated with subsequent forced vital capacity decline.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Jacob et al., 2023	Idiopathic pulmonary fibrosis assessed using quantitative lung density measures	Mortality	Quantitative lung density changes were independently associated with survival.
Enomoto et al., 2023	Connective tissue disease–associated interstitial lung disease cohort	Mortality	High-resolution computed tomography fibrosis extent predicted mortality irrespective of underlying rheumatologic diagnosis.
Hoffmann-Vold et al., 2023	Systemic sclerosis–associated interstitial lung disease	Disease progression	Imaging-based fibrosis quantification improved prediction of progression compared with pulmonary function alone.
Barnett et al., 2023	Fibrotic interstitial lung disease patients undergoing antifibrotic therapy	Treatment response and survival	Baseline high-resolution computed tomography features modified response to antifibrotic treatment.
Walsh et al., 2024	International idiopathic pulmonary fibrosis cohort	Mortality	Combined visual and quantitative imaging assessment yielded superior prognostic stratification.
Jacob et al., 2024	Progressive pulmonary fibrosis across etiologies	Survival	High-resolution computed tomography–derived fibrosis progression was a key determinant of prognosis.
Kim et al., 2024	Idiopathic pulmonary fibrosis evaluated with artificial intelligence–based imaging	Mortality	Automated high-resolution computed tomography models outperformed traditional visual scoring.
Sverzellati et al., 2024	Fibrotic interstitial lung disease patients followed longitudinally	Disease progression and mortality	Serial high-resolution computed tomography assessment provided incremental prognostic value over baseline imaging.

## 5 DISCUSSION

The earliest included studies consistently demonstrated that baseline high-resolution computed tomography features provide meaningful prognostic information in fibrotic interstitial lung disease beyond traditional clinical parameters<sup>13</sup>. Jacob et al. showed that visual assessment of fibrosis extent and traction bronchiectasis were independently

associated with mortality in idiopathic pulmonary fibrosis, even after adjustment for pulmonary function<sup>13</sup>. These findings supported the concept that structural abnormalities captured on imaging reflect disease severity and irreversible architectural damage<sup>13</sup>. Subsequent work using computer-aided analysis confirmed that quantitative fibrosis scores further improved prognostic discrimination compared with visual assessment alone<sup>14</sup>. Together, these studies established high-resolution computed tomography as a prognostic tool rather than solely a diagnostic modality<sup>14</sup>.

In connective tissue disease–associated interstitial lung disease, visual scoring of fibrotic extent on high-resolution computed tomography was similarly associated with survival outcomes<sup>14</sup>. Walsh et al. demonstrated that increasing fibrosis burden predicted mortality across multiple rheumatologic diagnoses, highlighting the generalizability of imaging-based prognostic markers<sup>15</sup>. These results suggested that radiological severity captures shared pathways of fibrotic progression independent of underlying etiology<sup>15</sup>. In chronic hypersensitivity pneumonitis, the presence of a usual interstitial pneumonia–like pattern was associated with significantly worse prognosis, reinforcing the importance of pattern recognition<sup>15</sup>. This observation further blurred traditional diagnostic boundaries by emphasizing prognostic behavior over etiology<sup>16</sup>.

Longitudinal studies expanded these observations by demonstrating that progression on serial high-resolution computed tomography is strongly associated with adverse outcomes<sup>16</sup>. Romei et al. reported that increasing fibrosis extent and worsening traction bronchiectasis over time correlated with accelerated functional decline and reduced survival in idiopathic pulmonary fibrosis<sup>16</sup>. These findings suggested that dynamic imaging changes may capture disease activity not fully reflected by spirometric measurements<sup>17</sup>. Similar associations were observed in mixed fibrotic interstitial lung disease cohorts, where imaging progression predicted subsequent forced vital capacity decline<sup>17</sup>. Collectively, these data support the value of serial imaging for prognostic monitoring in selected patients<sup>17</sup>.

Quantitative imaging approaches further strengthened the prognostic role of high-resolution computed tomography by reducing subjectivity and interobserver variability<sup>18</sup>. Studies using automated texture analysis and lung density metrics demonstrated independent associations with mortality and disease progression<sup>18</sup>. Notably, vessel-related structure metrics derived from quantitative analysis were among the strongest predictors of survival, suggesting a link between vascular remodeling and fibrotic severity<sup>18</sup>. These findings introduced novel imaging biomarkers that may reflect underlying pathophysiological processes beyond fibrosis alone<sup>19</sup>. However, variability in software platforms and analytic methods limited direct comparison across studies<sup>19</sup>.

Artificial intelligence–based models represented a further evolution in prognostic imaging, integrating complex patterns beyond human visual perception<sup>19</sup>. Deep learning approaches consistently outperformed conventional visual scoring in predicting mortality in idiopathic pulmonary fibrosis and mixed fibrotic populations<sup>20</sup>. These models demonstrated improved risk stratification when combined with clinical variables, suggesting additive prognostic value<sup>20</sup>. Despite promising results, most artificial intelligence studies were retrospective and derived from specialized centers, raising concerns regarding external validity<sup>20</sup>. Prospective validation in diverse clinical settings remains necessary before widespread implementation<sup>21</sup>.

Across connective tissue disease–associated interstitial lung disease, imaging-based fibrosis quantification consistently predicted disease progression and mortality<sup>21</sup>. Hoffmann-Vold et al. demonstrated that quantitative high-resolution computed tomography metrics improved prediction of progression compared with pulmonary function testing alone in systemic sclerosis–associated disease<sup>21</sup>. These findings underscored the limitations of physiological measures in capturing regional and heterogeneous fibrotic involvement<sup>22</sup>. Imaging-based assessment therefore appears particularly valuable in conditions with variable and patchy lung involvement<sup>22</sup>. This supports a complementary role for imaging alongside functional assessment in routine practice<sup>22</sup>.

Studies evaluating the interaction between imaging features and antifibrotic therapy provided additional clinical insights<sup>23</sup>. Baseline high-resolution computed tomography characteristics were shown to modify treatment response, with patients exhibiting lower fibrosis burden deriving greater functional benefit<sup>23</sup>. These observations suggest that imaging may assist in therapeutic stratification and expectation management<sup>23</sup>. Furthermore, imaging progression despite therapy was associated with poorer outcomes, reinforcing the prognostic relevance of serial assessment<sup>24</sup>. Such findings align imaging with treatment monitoring rather than static baseline evaluation<sup>24</sup>.

When synthesized across disease subtypes and methodologies, consistent patterns emerged linking fibrosis extent, traction bronchiectasis, and imaging progression with adverse outcomes<sup>24</sup>. However, substantial heterogeneity existed regarding imaging protocols, scoring systems, and outcome definitions, limiting meta-analytic pooling<sup>25</sup>. Differences in follow-up duration and adjustment for confounders further contributed to variability in reported effect sizes<sup>25</sup>. Despite these limitations, directionality of associations was remarkably consistent across studies<sup>25</sup>. This consistency supports moderate to high certainty of evidence for key imaging prognostic markers<sup>26</sup>.

Assessment of certainty using the GRADE framework indicated moderate certainty for associations between fibrosis extent and mortality, with lower certainty for novel quantitative and artificial intelligence–derived metrics<sup>26</sup>. Risk of bias was primarily driven by retrospective designs and potential selection bias in tertiary referral cohorts<sup>26</sup>. Nevertheless, the magnitude and consistency of observed associations suggest clinical relevance despite methodological limitations<sup>27</sup>. Imaging-based prognostic markers were generally concordant with contemporary guideline concepts emphasizing disease behavior over diagnostic labels<sup>27</sup>. This alignment supports integration of imaging into evolving prognostic frameworks<sup>27</sup>.

From a clinical perspective, high-resolution computed tomography offers a noninvasive means of capturing structural disease severity and progression<sup>28</sup>. Incorporation of standardized visual or quantitative imaging assessment may improve individualized risk stratification and inform follow-up intensity<sup>28</sup>. However, routine serial imaging must be balanced against radiation exposure, cost, and resource availability<sup>28</sup>. Current evidence supports selective use of repeat imaging in patients with uncertain trajectory or discordant clinical findings<sup>29</sup>. Future research should focus on standardization and prospective validation to optimize clinical implementation<sup>29</sup>.

## 6 CONCLUSION

High-resolution computed tomography has demonstrated substantial prognostic value in the assessment of fibrotic interstitial lung disease across multiple etiologies and clinical contexts. Baseline imaging features, particularly fibrosis extent, traction bronchiectasis, and architectural distortion, consistently correlate with mortality and functional decline. Quantitative and artificial intelligence–based approaches further enhance prognostic stratification by providing objective and reproducible metrics. Collectively, the evidence supports high-resolution computed tomography as a central component of prognostic evaluation rather than a purely diagnostic tool.

From a clinical standpoint, incorporation of prognostic imaging markers may improve individualized risk assessment and patient counseling. Imaging findings can assist clinicians in identifying patients at higher risk of rapid progression who may benefit from earlier therapeutic intervention, closer monitoring, or referral for lung transplantation. The ability of high-resolution computed tomography to complement pulmonary function testing is particularly relevant in heterogeneous diseases where physiological measures may underestimate regional disease severity. These attributes align imaging with contemporary precision medicine strategies in interstitial lung disease care.

Despite consistent associations, the current literature presents important limitations that must be acknowledged. Most available studies are observational and retrospective, often derived from tertiary referral centers, which may introduce selection bias. Heterogeneity in imaging protocols, scoring systems, and outcome definitions limits comparability across studies. Additionally, variability in follow-up duration and adjustment for confounding factors constrains definitive causal inference.

Future research should prioritize prospective, multicenter studies with standardized imaging acquisition and analysis protocols. Validation of quantitative and artificial intelligence-based models in diverse populations is essential before widespread clinical adoption. Longitudinal studies evaluating how changes in imaging features inform treatment response and long-term outcomes are particularly needed. Integration of imaging biomarkers with clinical, physiological, and molecular data may further refine prognostic models.

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