

Original Article

Evaluating the Diagnostic Performance of High-Resolution Computed Tomography in Detecting Idiopathic Pulmonary Fibrosis in Suspected Cases

Asbat Naseer¹, Tahira Batool², Muhammad Naveed Babur³

¹ Faculty of Allied Health Sciences, The Superior University, Lahore, Pakistan

² Faculty of Allied Health Sciences, The Superior University, Lahore, Pakistan

³ Professor, Faculty of Allied Health Sciences, The Superior University, Lahore, Pakistan

✉ Correspondence: Tahira Batool, tahira.batool@superior.edu.pk

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ABSTRACT

Background: High-resolution computed tomography (HRCT) is central to the evaluation of suspected idiopathic pulmonary fibrosis (IPF), particularly through recognition of usual interstitial pneumonia (UIP) patterns. Diagnostic interpretation must nevertheless integrate clinical exclusion of alternative causes and, where appropriate, multidisciplinary assessment. **Objective:** To evaluate HRCT features associated with a final radiologist classification of IPF in suspected cases. **Methods:** A cross-sectional study included 68 adults referred for HRCT because of suspected IPF. Ground-glass opacity, honeycombing, reticulation, their distributions, and final radiological diagnosis were recorded. **Results:** Sixty-two patients (91.2%) received a final HRCT classification of IPF and six (8.8%) another pulmonary diagnosis. Honeycombing was present in 38/68 (55.9%), reticulation in 41/68 (60.3%), and ground-glass opacity in 35/68 (51.5%). All 38 patients with honeycombing were within the final HRCT-IPF group, while 24 additional HRCT-IPF cases had no honeycombing. Against this internal radiological classification, honeycombing showed sensitivity of 61.3% (95% CI 48.8–72.4%), specificity of 100% (95% CI 61.0–100%), positive predictive value of 100% (95% CI 90.8–100%), and negative predictive value of 20.0% (95% CI 9.5–37.3%). **Conclusion:** Honeycombing, reticulation, and ground-glass opacity were associated with the final radiological classification, but the study does not provide independent diagnostic-accuracy validation because the HRCT features and final diagnosis derive from the same imaging assessment. **Keywords:** Idiopathic Pulmonary Fibrosis; HRCT; Usual Interstitial Pneumonia; Honeycombing; Reticulation; Ground-Glass Opacity.

INTRODUCTION

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive fibrosing interstitial pneumonia characterized by persistent epithelial injury, aberrant repair, extracellular-matrix deposition, architectural distortion, and progressive deterioration in pulmonary function. The disease is associated with substantial morbidity and mortality, and accurate distinction of IPF from other fibrotic interstitial lung diseases is clinically important because prognosis, therapeutic strategies, and follow-up pathways differ across disease entities (1–3).

Contemporary IPF diagnosis does not rely on a single imaging sign. It requires integration of the clinical history, exclusion of identifiable causes of interstitial lung disease, and assessment of thoracic imaging within an appropriate diagnostic context. Multidisciplinary evaluation may be particularly valuable when imaging, clinical, or pathological findings are discordant or do not establish a high-confidence diagnosis (4–6).

HRCT has a central role in this process because characteristic imaging patterns may permit a confident diagnosis of UIP in an appropriate clinical setting and can reduce the need for invasive lung biopsy. The revised diagnostic frameworks distinguish UIP, probable UIP, indeterminate-for-UIP patterns, and imaging appearances suggestive of an alternative diagnosis, thereby moving interpretation beyond the presence or absence of an individual radiological sign (4,5,7,8).

A typical UIP pattern on HRCT is characterized by basal and subpleural predominance of fibrosis, heterogeneous reticulation, architectural distortion, and honeycombing, frequently accompanied by peripheral traction bronchiectasis or bronchiolectasis. Conversely, findings such as marked upper- or mid-lung predominance, prominent peribronchovascular distribution, extensive ground-glass opacity, profuse nodules, consolidation, cysts, or substantial mosaic attenuation may reduce confidence in UIP and suggest alternative causes of fibrotic lung disease (4–6,8).

The Fleischner Society likewise emphasizes that a radiological pattern must be interpreted in the context of the clinical probability of IPF and appropriate exclusion of alternative causes. Because several fibrotic interstitial lung diseases can reproduce components of the UIP pattern, multidisciplinary synthesis of radiological, pulmonary, rheumatological, exposure-related, and pathological information can increase diagnostic confidence when the presentation is uncertain (5,9,10).

Diagnostic categories have continued to evolve as the relationship between HRCT patterns, histopathology, and clinical diagnosis has become better characterized. Updated ATS/ERS/JRS/ALAT guidance retains the central importance of HRCT pattern classification while refining the position of probable UIP and invasive diagnostic procedures. Contemporary reviews similarly emphasize that diagnostic categories represent different probabilities of underlying UIP rather than completely discrete radiological diseases (6,11–13).

Honeycombing remains one of the most characteristic imaging findings associated with a definite UIP pattern when its morphology and spatial distribution are appropriate. Nevertheless, absence of honeycomb cysts does not exclude IPF. A probable UIP pattern may show basal and subpleural reticulation with peripheral traction bronchiectasis or bronchiolectasis without established honeycombing, and real-world application of contemporary diagnostic criteria has therefore increased the number of patients who may reach a high-confidence diagnosis without classic honeycomb change (4–8,13,14).

Reticulation is another important manifestation of fibrotic interstitial lung disease, but its diagnostic significance depends strongly on distribution and accompanying abnormalities rather than simple presence. Basal and peripheral reticulation combined with traction bronchiectasis and architectural distortion increases compatibility with UIP, whereas alternative distributions and associated findings may favor other interstitial pneumonias. CT pattern and extent also provide clinically relevant information beyond simple morphological detection (8,15,16).

Ground-glass opacity can occur in IPF, particularly when limited in extent or superimposed upon a predominantly fibrotic pattern. It is less specific than honeycombing or characteristic traction-related fibrosis, and extensive or predominant ground-glass change may suggest another diagnosis. Its interpretation therefore requires assessment of the relative extent of fibrosis, reticulation, traction bronchiectasis, honeycombing, mosaic attenuation, consolidation, and the overall anatomical distribution of abnormalities (4–6,8,12,15).

The present study evaluated HRCT findings among adults referred with clinical suspicion of IPF and examined the association of individual HRCT features with the final radiological classification.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted over six months beginning in February 2025 at AYK Hospital, Lahore.

Sixty-eight adults referred for HRCT because of suspected IPF were included using purposive sampling. Participants aged ≥ 18 years who were referred for HRCT with clinical suspicion of IPF and who provided consent were eligible for inclusion. Patients were excluded if they had a previously established interstitial

lung disease other than IPF, a condition considered to mimic IPF, pregnancy, incomplete clinical records, or technically inadequate imaging.

HRCT examinations were reviewed for characteristic interstitial abnormalities. Recorded findings included ground-glass opacity, honeycombing, reticulation, and the anatomical distribution of these abnormalities. Ground-glass opacity was categorized descriptively as patchy, peripheral, or diffuse, while reticulation distribution was categorized as upper-zone, lower-zone, or diffuse.

A final radiologist interpretation classified cases as IPF or another pulmonary condition. The study also recorded a fibrosis-severity score as a continuous study variable.

Ethical approval was obtained from the Institutional Review Board of Superior University, Lahore, Pakistan. Participants provided consent for inclusion in the study.

Data were analyzed using SPSS. Categorical variables were summarized as frequencies and percentages, while continuous variables were summarized using mean $\pm$ SD. Associations between individual HRCT features and the final radiological classification were evaluated using score-test statistics.

For honeycombing, a 2 $\times$ 2 table was reconstructed directly from the observed counts. Sensitivity, specificity, positive predictive value, negative predictive value, 95% Wilson confidence intervals, and Fisher exact p value were calculated against the final HRCT-based classification. Receiver operating characteristic area under the curve (ROC AUC) was also reported for honeycombing. These measures represent internal concordance with the final radiological interpretation rather than diagnostic accuracy against an independent clinical or pathological reference standard.

RESULTS

Sixty-eight patients were included. Mean age was 58.53 $\pm$ 12.02 years, with an observed range of 40–80 years. Thirty-five participants were male (51.5%) and 33 were female (48.5%). The final HRCT interpretation classified 62 patients (91.2%) as IPF and six (8.8%) as another pulmonary condition.

HRCT Findings

Reticulation was the most frequent recorded HRCT feature and was present in 41 patients (60.3%). Honeycombing was identified in 38 patients (55.9%), while ground-glass opacity was present in 35 (51.5%).

Among patients with ground-glass opacity, 15 demonstrated a patchy distribution, 11 had a peripheral distribution, and nine had diffuse ground-glass opacity. Reticulation was categorized as upper-zone in 18 patients, lower-zone in 12, and diffuse in 11.

Table 1. Participant and HRCT Characteristics

Variable	n (%) / Mean $\pm$ SD
Total sample	68
Age, years	58.53 $\pm$ 12.02
Male	35 (51.5)
Female	33 (48.5)
Final HRCT classification: IPF	62 (91.2)
Other final radiological classification	6 (8.8)
Ground-glass opacity	35 (51.5)
└ Patchy	15 (22.1)
└ Peripheral	11 (16.2)
└ Diffuse	9 (13.2)
Honeycombing	38 (55.9)
Reticulation	41 (60.3)
└ Upper-zone	18 (26.5)
└ Lower-zone	12 (17.6)
└ Diffuse	11 (16.2)
Fibrosis severity score	2.85 $\pm$ 1.41

Honeycombing and Final HRCT Classification

All 38 patients with honeycombing were classified as IPF in the final HRCT interpretation. Among the 30 patients without honeycombing, 24 were nevertheless classified as IPF and six were assigned another radiological diagnosis.

Internal Classification Characteristics of Honeycombing

Against the final radiologist HRCT classification, honeycombing had sensitivity of 61.3% and specificity of 100%. Positive predictive value was 100%, whereas negative predictive value was 20.0%.

Table 2. Honeycombing Versus Final HRCT-Based Classification

	Final HRCT IPF	Other Classification	Total
Honeycombing present	38	0	38
Honeycombing absent	24	6	30
Total	62	6	68

Fisher exact $p=0.005$.

Table 3. Honeycombing as a Marker of Final HRCT IPF Classification

Measure	Estimate	95% CI
Sensitivity	61.3%	48.8–72.4
Specificity	100%	61.0–100
Positive predictive value	100%	90.8–100
Negative predictive value	20.0%	9.5–37.3
ROC AUC	0.806	0.687–0.926

The high positive predictive value reflects the absence of honeycombing among all six patients classified radiologically as having another diagnosis. Conversely, the substantially lower negative predictive value reflects the presence of 24 honeycombing-negative patients who were nevertheless classified radiologically as IPF.

Associations of HRCT Features With Final Classification

Score-test analysis demonstrated statistically significant associations between honeycombing, ground-glass opacity, reticulation, and the final radiological classification.

Table 4. Score-Test Associations With Final HRCT Classification

HRCT Feature	Score χ^2	df	p Value
Honeycombing	8.335	1	0.004
Ground-glass opacity	5.327	1	0.021
Reticulation	6.616	1	0.010

These statistics demonstrate associations within the radiological dataset. Regression coefficients and odds ratios were not part of the reported analysis, and the final radiological classification was derived from the same HRCT assessment as the evaluated imaging features.

DISCUSSION

The present study demonstrated that reticulation, honeycombing, and ground-glass opacity were common HRCT abnormalities among patients referred with suspected IPF. A final HRCT interpretation classified 91.2% of the cohort as IPF. Honeycombing demonstrated the strongest internal concordance with this classification: every patient with honeycombing was categorized as IPF, producing 100% specificity and positive predictive value against the internal HRCT classification. Sensitivity was substantially lower at 61.3% because 24 of the 62 radiologically classified IPF cases did not demonstrate honeycombing.

The very high proportion of patients ultimately classified radiologically as IPF is consistent with the highly selected nature of a cohort already referred because of clinical suspicion of this disease. Contemporary diagnostic frameworks emphasize that the probability of IPF is determined by the combination of clinical context and imaging phenotype rather than by population screening characteristics, and diagnostic confidence can change substantially after integration of exposure history, autoimmune evaluation, imaging, and multidisciplinary assessment (4,5,9,14).

The finding that honeycombing was strongly associated with the final IPF classification but lacked high sensitivity is consistent with modern UIP classification. Honeycombing in an appropriate basal and subpleural distribution remains highly characteristic of a definite UIP pattern, but probable UIP can be defined by peripheral and basal reticulation with traction bronchiectasis or bronchiolectasis in the absence of honeycombing. Consequently, lack of honeycomb cysts cannot independently exclude IPF (4–8,13,14).

Interpretation of these abnormalities also depends on reader assessment. Studies evaluating application of contemporary UIP criteria have demonstrated that agreement in categorizing CT patterns is not perfect even among radiologists, while a recent meta-analysis of HRCT interpretation across interstitial lung diseases confirmed clinically relevant interobserver variability. This variability is important when individual qualitative imaging signs are treated as discrete diagnostic variables (17,18).

Radiological-pathological studies further demonstrate why individual signs cannot be treated as completely independent disease markers. Honeycomb-like cystic remodeling correlates with advanced

structural fibrosis, but pathological UIP can be present in cases without a classic definite-UIP appearance on CT. CT manifestations of pathological UIP vary in extent and combination, and thin-section CT differentiation of UIP from other interstitial pneumonias depends on the overall pattern rather than one abnormality alone (19–22).

The negative predictive value of honeycombing was only 20.0% in the present cohort. This value directly reflects the large number of honeycombing-negative cases that were still assigned an IPF classification and the very high prevalence of final radiological IPF within this selected sample. Predictive values are intrinsically dependent on the population in which a diagnostic marker is evaluated, making them particularly sensitive to case selection and disease prevalence. Diagnostic-accuracy standards therefore emphasize transparent description of participant selection and the relationship between the index test and reference standard (23,24).

Reticulation occurred in approximately 60% of participants and was the most frequently recorded abnormality. In fibrotic interstitial lung disease, reticulation is an important morphological manifestation of fibrosis, but interpretation depends on its spatial distribution, associated traction bronchiectasis, architectural distortion, honeycombing, and other accompanying features. Basal and peripheral predominance is compatible with the UIP spectrum, while alternative distributions may change the differential diagnosis. CT pattern and fibrotic morphology may also carry prognostic information in established IPF (8,15,16,21,22).

Ground-glass opacity was identified in approximately half of the cohort. Ground-glass change may coexist with UIP/IPF but is considerably less specific than a characteristic fibrotic UIP pattern. Limited ground-glass opacity may occur alongside reticulation or traction-related fibrosis, whereas extensive or predominant ground-glass change can suggest alternative inflammatory, infiltrative, or fibrotic disorders. The diagnostic implication therefore depends on the relative extent of ground-glass opacity and its relationship to reticulation, honeycombing, traction bronchiectasis, mosaic attenuation, consolidation, and anatomical distribution (4–6,8,12,15).

The ROC AUC of 0.806 for honeycombing is mathematically compatible with the observed combination of approximately 61% sensitivity and 100% specificity for this binary feature. However, the AUC must be interpreted as discrimination against the study's internal radiological classification rather than as independent validation of HRCT for diagnosing IPF. Diagnostic-accuracy methodology requires clear separation and appropriate definition of the index test and reference standard; when components of the index assessment contribute directly to the reference classification, estimates may be affected by incorporation bias (23,24).

This issue represents the most important methodological limitation of the present study. Honeycombing, reticulation, and ground-glass opacity were evaluated on the same HRCT examination from which the final radiologist diagnosis was derived. The final classification is therefore not independent of the features whose diagnostic characteristics are being estimated. In contemporary IPF diagnosis, the reference process may involve multidisciplinary synthesis of clinical history, relevant environmental and occupational exposures, autoimmune evaluation, pulmonary assessment, HRCT pattern and, in selected uncertain cases, histopathological evidence (4–6,9,10). Accordingly, the sensitivity and specificity reported here should be interpreted as measures of internal feature-classification concordance rather than generalizable diagnostic accuracy.

The small number of participants assigned to the non-IPF category introduces additional uncertainty. Specificity was calculated from only six individuals, all of whom lacked honeycombing, producing an estimate of 100% but a wide 95% confidence interval of 61.0–100%. The precision of estimates involving this comparison group is therefore limited, and the point estimate should not be interpreted as evidence that honeycombing has perfect specificity across broader populations of patients with suspected fibrotic interstitial lung disease (23,24).

The six alternative radiological diagnoses were also not individually characterized. This limits assessment of how the recorded HRCT findings behaved across clinically important differential diagnoses such as nonspecific interstitial pneumonia, fibrotic hypersensitivity pneumonitis, connective-tissue-disease-associated interstitial lung disease, sarcoidosis, infection, and other fibrotic or inflammatory disorders. Contemporary IPF diagnostic frameworks emphasize active exclusion of such alternative causes because overlapping radiological manifestations can occur across several interstitial lung diseases (4–6,8,12).

Image-acquisition technique is another relevant consideration in interpretation of fibrotic interstitial lung disease. Modern HRCT assessment relies on high-quality thin-section imaging at full inspiration,

while prone acquisition may help distinguish dependent opacity from genuine subpleural abnormality and expiratory imaging can provide additional information when air trapping or small-airway disease is suspected. Reconstruction technique and image quality can also influence visualization of reticulation, traction bronchiectasis, and honeycombing (8,15). The present analysis therefore reflects the imaging dataset as obtained and does not permit evaluation of how protocol variation may have affected feature detection.

Reader characteristics and interobserver agreement were not incorporated into the reported analysis. This is relevant because classification of UIP patterns and recognition of individual features such as honeycombing can vary according to reader experience and interpretive criteria. Evidence from both individual studies and pooled analyses indicates that agreement in HRCT interpretation of interstitial lung disease is meaningful but incomplete, reinforcing the importance of standardized pattern definitions and multidisciplinary interpretation in uncertain cases (17,18).

Despite these limitations, the study provides a focused description of commonly encountered HRCT features in a clinically suspected IPF cohort and demonstrates how strongly honeycombing, reticulation, and ground-glass opacity were associated with the final radiological classification in this sample. Its principal contribution is therefore the characterization of HRCT abnormalities and their internal concordance with the radiologist's final interpretation. The findings also illustrate an important clinical principle: honeycombing substantially increases confidence in a UIP-type interpretation when appropriately distributed, whereas absence of honeycombing alone does not exclude a radiological diagnosis within the IPF/UIP spectrum.

CONCLUSION

Honeycombing, reticulation, and ground-glass opacity were common among adults referred for HRCT with suspected IPF. Honeycombing was highly concordant with the final HRCT-based IPF classification when present but demonstrated limited sensitivity because a substantial proportion of radiologically classified IPF cases lacked honeycombing.

The findings reinforce the importance of pattern-based HRCT assessment rather than reliance on an individual imaging sign. However, the study does not independently validate the diagnostic accuracy of HRCT for IPF because the evaluated imaging features and the final diagnostic classification arose from the same radiological examination.

Clinical exclusion of alternative causes and multidisciplinary interpretation remain important components of definitive IPF diagnosis, particularly where HRCT findings do not establish a high-confidence UIP pattern.

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