Radiology: Cardiothoracic Imaging

ORIGINAL RESEARCH

Hypersensitivity Pneumonitis on Thin-Section Chest CT Scans: Diagnostic Performance of the ATS/JRS/ALAT versus ACCP Imaging Guidelines

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Purpose: To compare the diagnostic performance of the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax (ATS/JRS/ALAT) versus the American College of Chest Physicians (ACCP) imaging classifications for hypersensitivity pneumonitis (HP).

Materials and Methods: Patients in the institutional review board–approved Interstitial Lung Disease (ILD) registry referred for multidisciplinary discussion (MDD) at the authors' institution (January 1, 2006–April 1, 2021) were included in this retrospective study when ILD was diagnosed at MDD. MDD diagnoses included HP, connective tissue disease–ILD, and idiopathic pulmonary fibrosis. Retrospective review of thin-section CT images was performed in consensus by two cardiothoracic radiologists blinded to the diagnosis. Diagnostic patterns were determined for thin-section CT images using both classifications. Discordance rates were determined. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were assessed using MDD diagnosis as the reference standard.

Results: A total of 297 patients were included in the study: 200 (67%) with HP, 49 (16%) with connective tissue disease–ILD, and 48 (16%) with idiopathic pulmonary fibrosis at MDD. The discordance rate between the two classifications was 21%. Assuming low HP prevalence (10%), ATS/JRS/ALAT classification outperformed ACCP classification, with greater accuracy (92.3% vs 87.6%) and greater positive predictive value (60.7% vs 42.9%). Assuming high prevalence (50%), accuracy and negative predictive value were superior using ACCP classification (81.7% vs 79.7% and 77.7% vs 72.6%, respectively), and positive predictive value was superior using ATS/JRS/ALAT classification (93.3% vs 87.1%).

Conclusion: Accuracy of the ATS/JRS/ALAT and ACCP HP classifications was greater in settings with low and high HP prevalence, respectively. Diagnostic performance of both classifications was discordant in a minority of cases.

Supplemental material is available for this article.

Hypersensitivity pneumonitis (HP) is a form of interstitial lung disease (ILD) that results from the recurrent or ongoing exposure to inhaled pathogens in vulnerable hosts (1,2). This airborne exposure plays a central role in the triggering of non–IgE-mediated immune responses, resulting in parenchymal inflammation and pulmonary fibrosis in some patients (2). Timely diagnosis is crucial in optimizing patient prognosis by allowing prompt treatment and removal of the inciting exposure (3). Disease prevalence varies widely, approximating 12% at our ILD center and exceeding 47% of patients with new-onset ILD in India. Current nationwide registry-based estimates of fibrotic HP prevalence obtained from more than 60 ILD centers in the United States purport that about 8% of patients with ILD have HP (4–9). The heterogeneity in disease forms and overlapping presentations with other types of ILD further add to the diagnostic challenge (1,10). A diagnosis of HP should therefore be considered in any patient presenting with ILD, and a thorough review of potential exposures is necessary (11,12).

Updated classification schemes by the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax (ATS/JRS/ALAT) and the American College of Chest Physicians (ACCP) guide clinicians in their multidisciplinary approach to HP (Table S1) (12). In the most recent guidelines, previously defined categories relying on time course of the disease (ie, acute, subacute, and chronic) have been abandoned (13,14). Distinct disease categories now rely on the presence or absence of fibrosis, placing greater emphasis on the radiologic and histologic assessments. For both fibrotic HP and nonfibrotic HP, the ATS/JRS/ALAT and ACCP classifications allow the categorization of findings on thin-section chest CT scans as typical HP (tHP), compatible HP (cHP), or indeterminate HP (iHP). tHP refers to a pattern of abnormality suggestive of HP. This pattern requires a combination of small airway disease manifestations and parenchymal infiltration or fibrosis. In the ATS/JRS/ALAT classification, diffuse distribution of findings should be present in nonfibrotic HP, and diffuse mid–lung

Abbreviations

ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax, cHP = compatible HP, HP = hypersensitivity pneumonitis, iHP = indeterminate HP, ILD = interstitial lung disease, MDD = multidisciplinary discussion, NPV = negative predictive value, PPV = positive predictive value, tHP = typical HP

Summary

The discordance rate was low between the two current classification systems for diagnosing hypersensitivity pneumonitis on thin-section chest CT scans. Diagnostic performance of each classification scheme varied according to disease prevalence.

Key Points

- In a subset of patients with interstitial lung disease who underwent thin-section chest CT, the discordance rate between the American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax (ATS/JRS/ALAT) versus the American College of Chest Physicians (ACCP) classifications for hypersensitivity pneumonitis was 21%.
- The diagnostic performance of the ATS/JRS/ALAT and ACCP imaging classifications differed, and accuracy was influenced by disease prevalence.
- The ATS/JRS/ALAT classification showed greater accuracy compared with the ACCP classification assuming low disease prevalence (92.3% vs 87.6%); in contrast, the ACCP classification showed greater accuracy assuming high disease prevalence (81.7% vs 79.7%).

Keywords

CT, Thorax, Hypersensitivity Pneumonitis, Interstitial Lung Disease

predominant or relative basilar sparing should be seen in fibrotic HP. cHP refers to nonspecific patterns of abnormality that could be observed in HP, including evidence of small airway disease. iHP signifies the absence of supportive findings of HP, favoring alternative diagnoses. Diagnostic criteria relevant to these categories at thin-section CT vary considerably between the two classification schemes, potentially contributing to confusion among clinicians and inconsistencies in patient management (12).

The current study aims to assess the rate of discordance and provides a formal comparison of the diagnostic performance of the ATS/JRS/ALAT and ACCP classifications using multidisciplinary diagnosis (before the inception of the new HP diagnostic criteria) as the reference standard.

Materials and Methods

Patient Selection

This retrospective, Health Insurance Portability and Accountability Act–compliant study was conducted at the University of Chicago under an institutional review board–approved protocol (IRB protocol #14163-A). Patients referred for ILD care at our institution between January 1, 2006, and April 1, 2021, were selected when a multidisciplinary discussion (MDD) diagnosis of ILD was made and an optimal thin-section CT as described below was available for review.

Diagnoses were previously established during MDD based on a comprehensive review of occupational and environmental exposures; pertinent medical history; and laboratory tests, imaging, and histopathologic results when available. A proportion of the cases was considered in the MDD setting before any HP guidelines were released and considered using our imaging team's opinion on the most likely diagnosis based on thin-section CT. After release of the guidelines, both guidelines were considered at MDD before this study. In cases in which clinical and pathologic findings favored HP, imaging was considered concordant if a higher confidence diagnostic category (ie, typical and compatible) could be attained by either classification. All patients with an MDD HP diagnosis meeting these criteria were included, and two subcohorts of patients with a non–HP MDD diagnosis of ILD (connective tissue disease–ILD and idiopathic pulmonary fibrosis) were selected as standardized controls using random number generators. Case-control analyses were performed at a 2:1 ratio, with controls evenly split, resulting in a 4:1:1 ratio (HP to connective tissue disease–ILD to idiopathic pulmonary fibrosis). Less frequent ILD subtypes like sarcoidosis, pleuroparenchymal fibroelastosis, drug-induced fibrosis, and familial ILD were excluded due to inadequate statistical power required for meaningful adjustments in comparative analyses across diagnostic subtypes. Additional exclusion criteria included age 18 years or younger, nondiagnostic imaging quality, or absence of thin-section CT. A thin-section CT was deemed nondiagnostic by the readers when substantial motion precluded detailed parenchymal assessment and when thin-section images (≤1.5 mm) and multiplanar reconstructions were not available for review.

Imaging Review and Data Collection

A retrospective imaging review of baseline thin-section CT scans was performed by two fellowship-trained cardiothoracic radiologists (L.C. and J.H.C., with 3 and 13 years of experience in ILD, respectively). A proportion of the cases (102 of 297 [34%]) was read independently by each of the readers, and disagreements were subsequently resolved by consensus. The interobserver agreement was assessed for this subset of cases using the Cohen κ coefficient. A consensus approach was used for the remainder of the cases whereby agreement was reached during concurrent imaging interpretation by both radiologists. Reviewers were blinded to the MDD diagnosis. All thin-section CT scans included thin-section axial lung sequences less than 1.5 mm in thickness and were previously reconstructed using a high-spatial-frequency algorithm. Multiplanar reconstructions including sagittal and coronal reformats were required for better characterization of the findings. When present, inspiratory prone and expiratory supine sequences were also reviewed. Imaging findings scored on each baseline thin-section CT included distribution of disease (axial and craniocaudal predominance); indicators of parenchymal infiltration, including ground-glass opacity and mosaic attenuation; indicators of small airway obstruction, including air trapping and centrilobular nodularity; and the presence of a three-attenuation (three-density) pattern. Diagnostic patterns (ie, tHP, cHP, and iHP) were determined

Table 1: Basic Patient Demographics and Clinical Characteristics of Patients with HP and Non-HP

Variable	HP (*n* = 200)	Non-HP (*n* = 97)	*P* Value
Age (y)	65 ± 11	65 ± 13	.97
Sex			
Male	85 (42)	48 (49)	.26
Female	115 (57)	49 (51)	.26
Ever smoking	106 (53)	45 (46)	.29
Race and ethnicity			
Black	27 (14)	20 (21)	.12
Hispanic	12 (6)	5 (5)	.77
White	133 (66)	51 (53)	.02
Other	28 (14)	21 (22)	.10
Lung function percentage predicted			
FVC	64.7 ± 18.9	68.5 ± 19.6	.12
DLco	55.1 ± 23.8	60.2 ± 22.7	.11
Lung biopsy*	121 ± 61	26 ± 27	<.001
PF-specific therapy†	145 ± 62	55 ± 64	<.001
Outcomes			
Lung transplantation	10 (5)	4 (4)	.74
Death	48 (24)	8 (8)	.001

Note.—Data are presented as numbers of patients with percentages in parentheses or means ± SDs. DLco = diffusion lung capacity for carbon monoxide, FVC = forced vital capacity, HP = hypersensitivity pneumonitis, PF = pulmonary fibrosis.
* Lung biopsy: surgical, video-assisted thoracoscopic, or transbronchial.
† Pulmonary fibrosis–specific antifibrotic or immunomodulatory therapy.

for each thin-section CT using both the ATS/JRS/ALAT and ACCP classifications.

Statistical Analysis

Data were summarized using descriptive statistics. Basic patient demographics, clinical characteristics, and the proportion of patients having undergone lung biopsy were assessed. Clinical characteristics included smoking history, forced vital capacity, diffusion lung capacity for carbon monoxide, antifibrotic or immunomodulatory therapy, and patient outcomes. The proportion of patients diagnosed with HP, connective tissue disease–ILD, and idiopathic pulmonary fibrosis based on MDD was determined. The discordance rate in assigned diagnostic patterns on thin-section CT scans between the ATS/JRS/ALAT and ACCP classification schemes was assessed. The proportion of patients without available expiratory imaging on thin-section CT scans was specified. Using MDD diagnoses as the reference standard, diagnostic performance metrics of each of the two classifications were analyzed, including sensitivity and specificity as well as calculated positive predictive value (PPV), negative predictive value (NPV), and accuracy assuming low (10%) and high (50%) prevalence of HP environments. Statistical significance was set at $P < .05$. Thresholds for low and high prevalence were adopted to reflect the widely variable prevalence reported in the literature worldwide. All statistical analyses were performed using Stata/MP 17.0, revision 23 (Stata).

Results

Patient Characteristics

A total of 297 patients were included in the study. Basic patient demographics and clinical characteristics are detailed in Tables 1 and S2. Patients had MDD diagnoses of HP (*n* = 200 [67%]), connective tissue disease–ILD (*n* = 49 [16%]), and idiopathic pulmonary fibrosis (*n* = 48 [16%]). The mean age of each group was 65 years ± 11 (SD), 58 years ± 14, and 72 years ± 7, respectively, and the ratio of men to women was 85:115, 12:37, and 36:12, respectively. Race and ethnicity classification relied on self-identification and was reported as documented in the ILD registry. The majority of patients in this ILD cohort were White (*n* = 184 [62%]) and had smoked tobacco (*n* = 151 [51%]). A total of 147 of 297 (49%) patients had lung biopsies supportive of the MDD diagnosis. Notably, of the 200 patients diagnosed with HP, 121 (60%) patients had concordant pathologic results, including 58 (29%) having undergone surgical lung biopsy.

Diagnostic Categories

Key findings on thin-section CT scans are detailed in Table 2. The greatest proportion of thin-section CT scans was categorized as iHP, using the ATS/JRS/ALAT classification, at 45% (133 of 297). tHP represented the predominant category, using the ACCP classification, in 48% (144 of 297) of patients. A total of 85% (253 of 297) of studies used to evaluate patients

Table 2: Summary of Imaging Findings on Thin-Section Chest CT Scans Relevant to Each of the MDD Diagnoses

	MDD Diagnoses				
Imaging Findings	HP (*n* = 200)	CTD-ILD (*n* = 49)	IPF (*n* = 48)	All (*n* = 297)	*P* Value
Craniocaudal distribution					<.001
Upper lung predominant	22 (11)	0	0	22 (7)	
Mid–lung predominant	7 (4)	1 (2)	0	8 (3)	
Lower lung predominant	67 (34)	40 (82)	34 (71)	141 (47)	
Random	104 (52)	8 (16)	14 (29)	126 (42)	
Axial distribution					<.001
Central or peribronchovascular	7 (4)	9 (18)	0	16 (5)	
Peripheral	61 (30)	17 (35)	35 (73)	113 (38)	
Peripheral with subpleural sparing	6 (3)	9 (18)	3 (6)	18 (6)	
Random	126 (63)	14 (29)	10 (21)	150 (51)	
GGO	147 (74)	34 (69)	21 (44)	202 (68)	.08
Reticulation	177 (88)	42 (86)	47 (98)	266 (90)	.79
Diffuse CLN	41 (20)	4 (8)	1 (2)	46 (15)	.005
Mosaicism or air trapping	158 (79)	20 (41)	22 (46)	200 (67)	.002
Three-attenuation pattern	87 (44)	4 (8)	2 (4)	93 (31)	<.001

Note.—Data are presented as numbers, with percentages in parentheses. CLN = (ill-defined ground-glass) centrilobular nodules, CTD-ILD = connective tissue disease–interstitial lung disease, GGO = ground-glass opacity, HP = hypersensitivity pneumonia, IPF = idiopathic pulmonary fibrosis, MDD = multidisciplinary discussion.

Table 3: Distribution of Diagnostic Patterns Using Both ATS/JRS/ALAT and ACCP Classifications

Diagnostic Pattern	tHP	cHP	iHP
ATS/JRS/ALAT	93	71	133
ACCP	144	26	127

Note.—Data are numbers of cases classified in each pattern and under each of the two classifications. Concordance rate = 0.79. Discordance rate = 0.21. ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax, cHP = compatible hypersensitivity pneumonitis, iHP = indeterminate hypersensitivity pneumonitis, tHP = typical hypersensitivity pneumonitis.

in our cohort included expiratory phase imaging. Of 200 patients with HP, 177 (88%) presented with fibrotic HP and 23 (12%) presented with nonfibrotic HP based on thin-section CT. Diagnostic patterns were concordant in 79% (234 of 297) and discordant between the two classification schemes in 21% (63 of 297) of thin-section CT scans (Table 3). The majority of discordances occurred between the tHP and cHP groups (Figs 1, 2; Table 4). Of 133 cases categorized as iHP per the ATS/JRS/ALAT classification, six (5%) were discordant and classified as cHP per the ACCP classification (Fig 3). All other iHP thin-section CT scans were concordant between the two classification schemes.

Interobserver Agreement

When using ATS/JRS/ALAT guideline criteria for HP, the overall agreement on thin-section CT imaging reads between both expert radiologists was 97% (κ = 0.95 ± 0.07 [95% CI: 0.94, 1.00]; $P < .001$). When using ACCP guideline criteria for HP, the overall agreement on thin-section CT imaging reads between both expert radiologists was 96% (κ = 0.93 ± 0.08 [95% CI: 0.88, 0.97]; $P < .001$).

Diagnostic Performance

When considering tHP alone, the ACCP classification demonstrated greater sensitivity (74%) when compared with the ATS/JRS/ALAT classification (64%). However, the ATS/JRS/ALAT classification demonstrated greater specificity (95%) when compared with the ACCP classification (89%). When combining the tHP and cHP groups, among which the majority of discordances occurred, into a single diagnostic group (tHP + cHP), differences in sensitivity and specificity were less evident with comparable performance of the two classifications (Table 4).

The influence of disease prevalence variability on diagnostic performance was also evaluated, specifically focusing on the comparison of NPV and PPV between the ATS/JRS/ALAT and ACCP classifications. The analysis revealed that at a hypothetical lower prevalence of HP (10%), the ATS/JRS/ALAT classification demonstrated superior performance over the ACCP classification, with a higher accuracy (92.3% vs 87.6%) and a better PPV (60.7% vs 42.9%). The NPVs of both classifications were similarly high (96.1% vs 97.0%). This result suggests that both classifications are effective in reliably excluding HP in low-prevalence scenarios. At a higher prevalence of HP (50%), the PPV was still more favorable for the ATS/JRS/ALAT classification (93.3% vs 87.1%), though the ACCP classification showed better accuracy (81.7% vs 79.7%) and NPV (77.7% vs 72.6%) (Table 5).

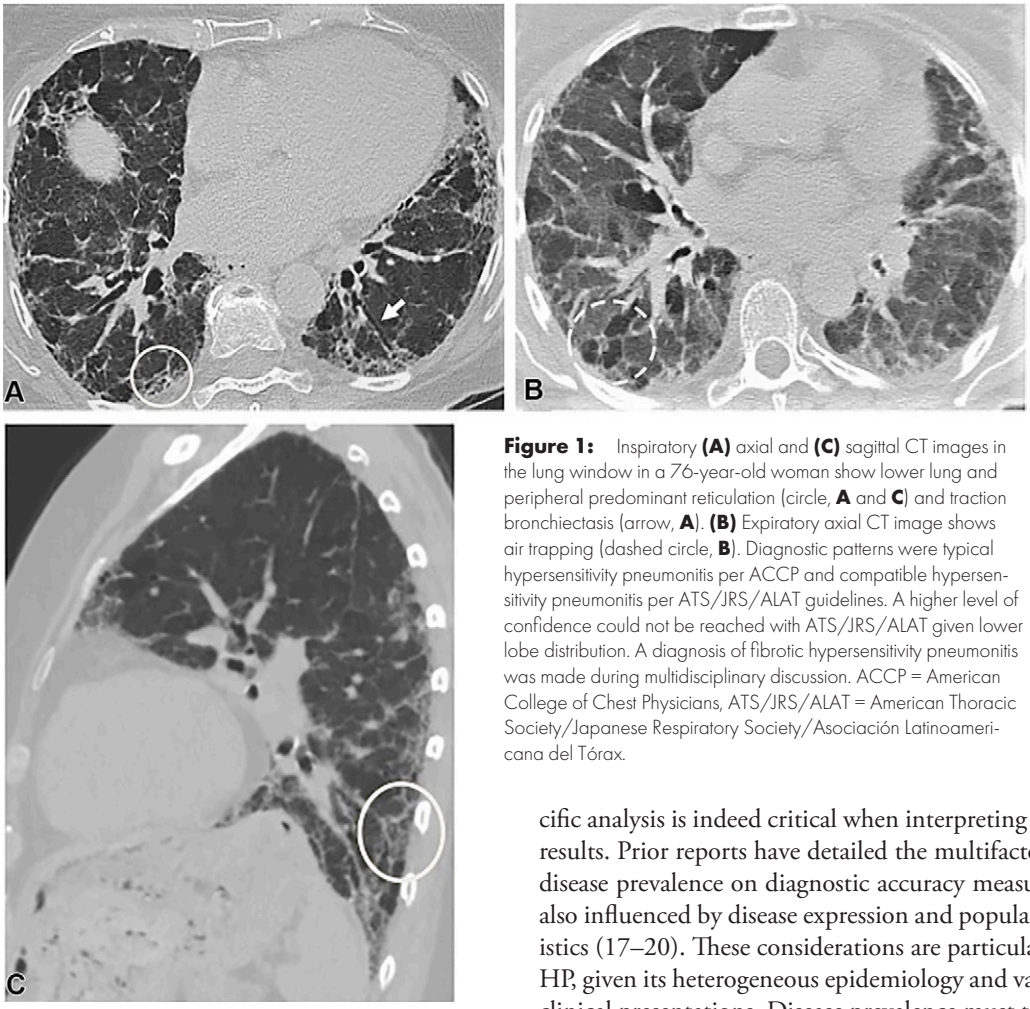

Figure 1: Inspiratory **(A)** axial and **(C)** sagittal CT images in the lung window in a 76-year-old woman show lower lung and peripheral predominant reticulation (circle, **A** and **C**) and traction bronchiectasis (arrow, **A**). **(B)** Expiratory axial CT image shows air trapping (dashed circle, **B**). Diagnostic patterns were typical hypersensitivity pneumonitis per ACCP and compatible hypersensitivity pneumonitis per ATS/JRS/ALAT guidelines. A higher level of confidence could not be reached with ATS/JRS/ALAT given lower lobe distribution. A diagnosis of fibrotic hypersensitivity pneumonitis was made during multidisciplinary discussion. ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society/Japanese Respiratory Society/Asociación Latinoamericana del Tórax.

Discussion

The diagnosis of HP is made challenging in part by the variable prevalence, various possible forms and clinical presentations of the disease, and the inexhaustible list of potential inciting exposures (3,15,16). The diagnostic approach relies greatly on MDD guided by the updated ATS/JRS/ALAT and ACCP society guidelines. Both HP guidelines are in their first iteration and will likely be revised further as evidence emerges and our understanding of HP improves. To our knowledge, the present study offers the first formal comparison of the diagnostic performance of both classification schemes in a subset of patients presenting with ILD. In this subset, both classification systems performed better in low-prevalence than high-prevalence settings, although performance varied differently under different prevalence conditions. There was greater specificity and PPV of the ATS/JRS/ALAT classification in diagnosing tHP regardless of disease prevalence. There was greater sensitivity of the ACCP classification and greater NPV assuming high prevalence. The ATS/JRS/ALAT and ACCP classifications showed greater accuracy in low- and high-prevalence settings, respectively. Our findings underscore the importance of considering disease prevalence in interpreting diagnostic accuracy, rather than making generalized statistical assumptions. Context-specific analysis is indeed critical when interpreting diagnostic test results. Prior reports have detailed the multifactorial impact of disease prevalence on diagnostic accuracy measures, which are also influenced by disease expression and population characteristics (17–20). These considerations are particularly relevant to HP, given its heterogeneous epidemiology and variable possible clinical presentations. Disease prevalence must therefore be accounted for in the selection of the best diagnostic approach. Reliance on a higher performing, more robust classification scheme could theoretically optimize diagnosis and management, allowing greater accuracy and improved prognosis.

The higher sensitivity of the ACCP classification reflects the more lenient criteria, allowing high confidence diagnoses with greater ease. The greatest proportion of thin-section CT scans was indeed categorized as tHP in our subset using the ACCP guidelines. In this subset, the majority of discordances observed resulted from a more restrictive categorization of cHP using the ATS/JRS/ALAT classification compared with a categorization of tHP using the ACCP classification. In contrast to the ATS/JRS/ALAT classification, distribution of abnormality is not emphasized in the ACCP classification, and the identification of concurrent airway and parenchymal abnormality on thin-section CT is not needed for a high confidence diagnosis (12,13). For example, a tHP diagnosis can be made per the ACCP guidelines on the basis of diffuse centrilobular nodularity and in the absence of features suggesting alternative diagnoses (13). A simpler, less involved classification scheme could be beneficial in guiding radiologists in general practice who may not be specialized in ILD diagnosis. The use of the ACCP classification is notably more appealing in a high-prevalence setting, allowing greater diagnostic accuracy as well as greater

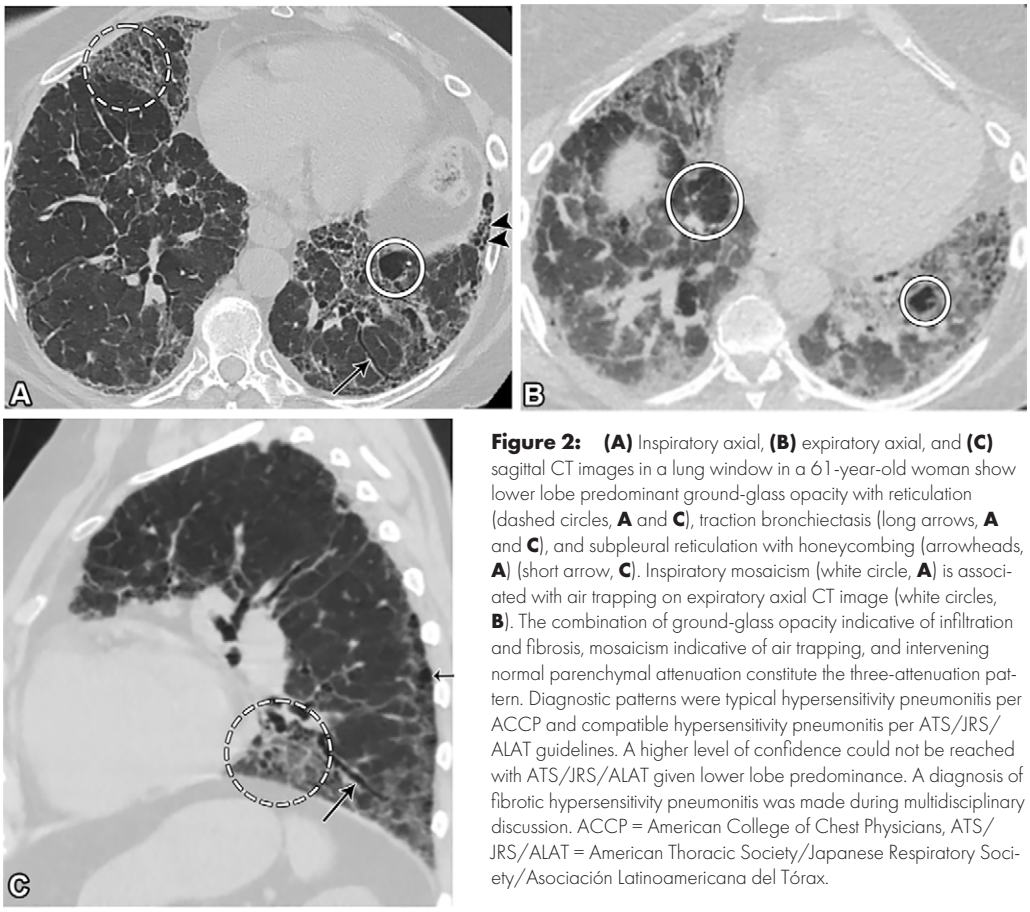

Figure 2: **(A)** Inspiratory axial, **(B)** expiratory axial, and **(C)** sagittal CT images in a lung window in a 61-year-old woman show lower lobe predominant ground-glass opacity with reticulation (dashed circles, **A** and **C**), traction bronchiectasis (long arrows, **A** and **C**), and subpleural reticulation with honeycombing (arrowheads, **A**) (short arrow, **C**). Inspiratory mosaicism (white circle, **A**) is associated with air trapping on expiratory axial CT image (white circles, **B**). The combination of ground-glass opacity indicative of infiltration and fibrosis, mosaicism indicative of air trapping, and intervening normal parenchymal attenuation constitute the three-attenuation pattern. Diagnostic patterns were typical hypersensitivity pneumonitis per ACCP and compatible hypersensitivity pneumonitis per ATS/JRS/ALAT guidelines. A higher level of confidence could not be reached with ATS/JRS/ALAT given lower lobe predominance. A diagnosis of fibrotic hypersensitivity pneumonitis was made during multidisciplinary discussion. ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society/Japanese Respiratory Society/Asociación Latinoamericana del Tórax.

Table 4: Comparison of Sensitivity and Specificity between Guidelines in Higher Confidence Diagnostic Patterns

Diagnostic Pattern	Guideline	Sensitivity (%)	Specificity (%)
tHP + cHP	ATS/JRS/ALAT	75 (150/200)	86 (83/97)
	ACCP	77 (154/200)	84 (81/97)
tHP	ATS/JRS/ALAT	64 (89/139)	95 (83/87)
	ACCP	74 (134/180)	89 (81/91)

Note.—Data are presented as percentages, with numbers in parentheses. ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax, cHP = compatible hypersensitivity pneumonitis, tHP = typical hypersensitivity pneumonitis.

confidence in the exclusion of HP given the higher NPV. In contrast, the greater accuracy of the ATS/JRS/ALAT classification is advantageous in low-prevalence environments.

In classifying each thin-section CT per the ATS/JRS/ALAT and ACCP classifications, the large majority of discordances in our subset occurred between tHP and cHP. While impacting accuracy and PPV, discordant classifications between these higher confidence diagnostic groups may not necessarily alter management. When combining tHP and cHP in our analysis, both classification schemes showed similar sensitivity and specificity. Discordances between low (iHP) and high (tHP and cHP) confidence groups are conceivably more likely to translate into a substantially different management approach.

This study had several limitations. It was a single-center retrospective study with a relatively small patient cohort, limiting the generalizability of the results to a broader patient population. Included patients were known to carry a diagnosis of ILD, which may have introduced a selection bias and could have affected the observed performance metrics. Patient comorbidities, which could have influenced the clinical presentation and impacted the accuracy of classification schemes, were not explored. Additionally, the direct impact on patient management and outcomes was not assessed. However, as we have outlined, the epidemiologic impact resulting from prospective application of these guidelines would frequently be influenced by the HP prevalence in the clinician's geographic location. Furthermore, the geographic heterogeneity of environmental exposures may translate into variable radiologic manifestations. Findings from the current cohort may not be consistent across other geographic settings. Additionally, pathologic proof was not available for all patients, as lung biopsies are less frequently performed in clinical practice in an attempt to mitigate potential associated risks. Nevertheless, a substantial proportion of patients with HP in our

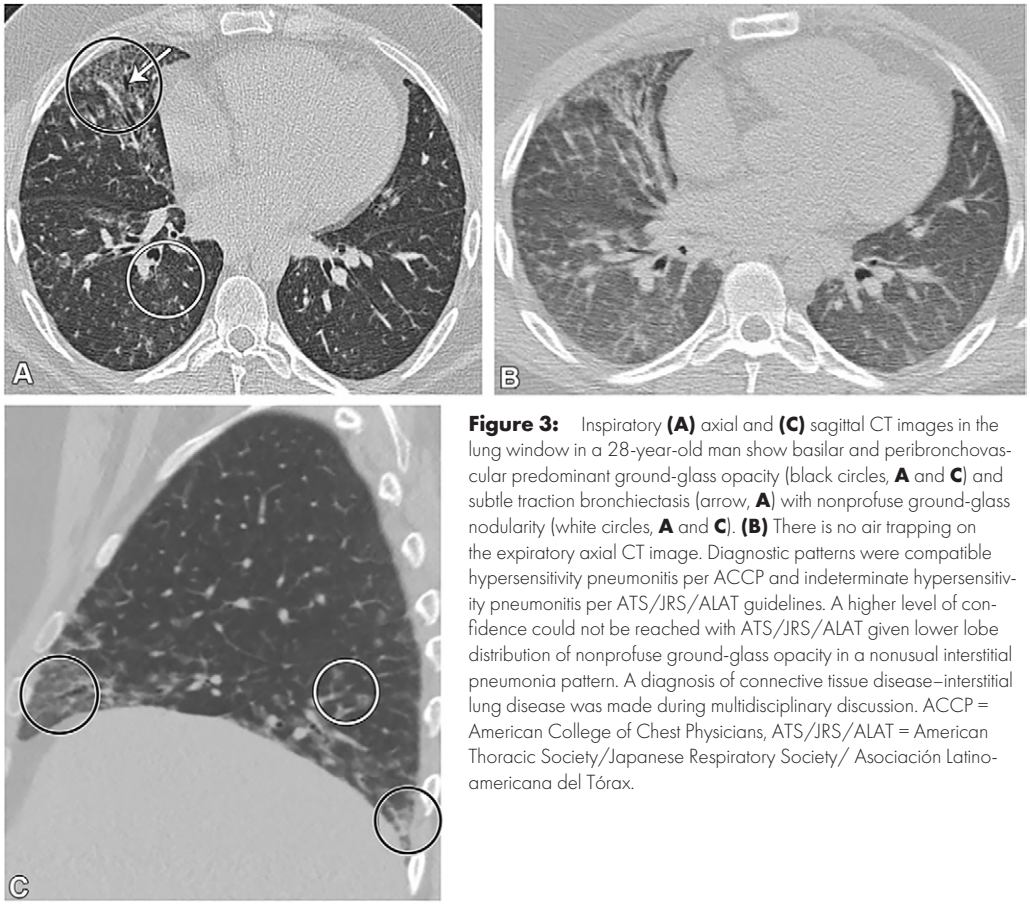

Figure 3: Inspiratory **(A)** axial and **(C)** sagittal CT images in the lung window in a 28-year-old man show basilar and peribronchovascular predominant ground-glass opacity (black circles, **A** and **C**) and subtle traction bronchiectasis (arrow, **A**) with nonprofuse ground-glass nodularity (white circles, **A** and **C**). **(B)** There is no air trapping on the expiratory axial CT image. Diagnostic patterns were compatible hypersensitivity pneumonitis per ACCP and indeterminate hypersensitivity pneumonitis per ATS/JRS/ALAT guidelines. A higher level of confidence could not be reached with ATS/JRS/ALAT given lower lobe distribution of nonprofuse ground-glass opacity in a nonusual interstitial pneumonia pattern. A diagnosis of connective tissue disease–interstitial lung disease was made during multidisciplinary discussion. ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society/Japanese Respiratory Society/ Asociación Latinoamericana del Tórax.

Table 5: Comparison of Diagnostic Performance between Guidelines When Accounting for Prevalence of Hypersensitivity Pneumonitis

Prevalence	Guideline	Accuracy (%)	NPV (%)	PPV (%)
Low (10%)	ATS/JRS/ALAT	92.3	96.1 (85.9/89.4)	60.7 (64.0/105.4)
	ACCP	87.6	97.0 (80.1/82.6)	42.9 (74.4/173.4)
High (50%)	ATS/JRS/ALAT	79.7	72.6 (47.7/65.7)	93.3 (32.0/34.3)
	ACCP	81.7	77.7 (44.5/57.3)	87.1 (37.2/42.7)

Note.—Data are presented as percentages or percentages with numerators/denominators in parentheses. ACCP = American College of Chest Physicians, ATS/JRS/ALAT = American Thoracic Society, Japanese Respiratory Society, and Asociación Latinoamericana del Tórax, NPV = negative predictive value, PPV = positive predictive value.

study sample (29%) had surgical lung biopsies supportive of the diagnosis. In the remainder of the patients, when lung biopsy could be avoided, MDD relied on imaging and clinical data. At MDD, beyond the identification of an antigen, attention was given to establish a temporal relationship between an identified inhalational exposure and the development of symptoms. When an inciting exposure is identified, a typical pattern of HP on thin-section CT scans allows a diagnosis of HP per the ACCP guidelines and a moderate confidence diagnosis per the ATS/JRS/ALAT guidelines even in the absence of pathologic results or bronchoalveolar lavage lymphocytosis. It is also worth noting that the lack of expiratory imaging in a minority of patients (44 of 297 [15%]) limited the assessment for air trapping. In these patients, a higher confidence diagnosis of HP could be made only when inspiratory views depicted other imaging features supportive of small airway disease, such as centrilobular nodules or clear mosaic attenuation. The radiologic approach to the HP diagnosis constituted the primary focus of the current study. Histologic diagnostic criteria detailed in both classifications were not addressed, as they were beyond the scope of this study. Finally, differences in years of experience of readers could theoretically lead to bias in a consensus approach. However, in the subset of independently assessed cases, the interobserver agreement between the two readers of this study was high.

In conclusion, the diagnostic performance of the ATS/JRS/ALAT and ACCP classifications for HP on thin-section CT scans differed, and accuracy was impacted by disease prevalence. There was greater specificity and PPV of the ATS/JRS/ALAT classification. There was greater sensitivity of the ACCP classification and greater NPV assuming high prevalence. There was greater accuracy using the ATS/JRS/ALAT and ACCP classifications in low- and high-prevalence environments, respectively. It is therefore critical that the use of these guidelines be considered relative to HP prevalence as well as the radiologist's level of comfort. Further studies are needed to evaluate the potential impact of different classification systems on management decisions and prognosis.

Author contribution: Guarantor of integrity of entire study, **L.C.;** study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; approval of final version of submitted manuscript, all authors; agrees to ensure any questions related to the work are appropriately resolved, all authors; literature research, **L.C., A.A., M.S., J.H.C.;** clinical studies, **L.C., A.A., M.S., R.J., A.N.H., I.U., J.H.C.;** statistical analysis, **L.C., A.A., J.H.C.;** and manuscript editing, **L.C., A.A., M.S., C.T.L., R.J., J.H.C.**

Data sharing: Data generated or analyzed during the study are available from the corresponding author by request.

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