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Evaluation of high-resolution computed tomography findings and associated factors in hypersensitivity pneumonitis

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Ethics Committee Approval
The study was approved by Ankara Atatürk Sanatoryum Training and Research Hospital Ethics Committee, 21/06/2023, 2012-KAEK-15/2727.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Hypersensitivity pneumonitis (HP) is a lung disease from inhaling diverse environmental and occupational organic substances, such as fungi, bacteria, birds, and occasionally nonorganic materials. An immune response triggers this condition. A high-resolution chest computed tomography (HRCT) scan is typically performed as part of the initial diagnostic assessment. This study assesses HRCT findings in HP patients and examines associated factors between fibrotic and non-fibrotic patient groups.

Methods: This retrospective cross-sectional study encompassed all HP patients monitored between 2010 and 2022. The analysis included data from 117 patients. HRCT findings from the patients were categorized based on fibrosis presence, leading to the division of patients into fibrotic and non-fibrotic groups. Comparative analyses were conducted between these groups.

Results: Among the 117 subjects analyzed, 59 (50.4%) were male, and 58 (49.6%) were female. The mean age at diagnosis was 52.1 (13.6) years, ranging from 20 to 81. The non-fibrotic HP group comprised 70 (59.8%) patients, while the fibrotic HP group comprised 47 (40.2%). The most prevalent HRCT findings were ground-glass opacity (90.6%), mosaic attenuation (87.2%), and traction bronchiectasis (50.4%). Statistically significant disparities were observed between non-fibrotic and fibrotic HP groups in terms of HRCT findings: ground-glass opacity, irregular linear opacities, reticulation, traction bronchiectasis, honeycombing, and fibrosis (P=0.024, P<0.001). In contrast, the lymphocyte ratio in bronchoalveolar lavage fluid was 28.78 (16.2) in the non-fibrotic HP group and 14.66 (10.3) in the fibrotic HP group. The fibrotic HP group exhibited a statistically significant lower lymphocyte ratio in bronchoalveolar lavage fluid (P<0.001).

Conclusion: HRCT findings are pivotal in HP diagnosis and classification. Computed tomography also assists in delineating the HP classification. This study identified ground-glass opacity and mosaic attenuation as the most prevalent HRCT findings in HP patients. Investigating the connection between fibrosis and prognosis is vital for determining patient outcomes, as fibrosis appears to be the principal determinant.

Keywords: hypersensitivity pneumonitis, non-fibrotic hypersensitivity pneumonitis, fibrotic hypersensitivity pneumonitis, high-resolution computed tomography

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Introduction

Hypersensitivity pneumonitis (HP) is an immune-mediated lung disorder triggered by inhaling various environmental and occupational organic substances, primarily encompassing fungi, bacteria, avian sources, and, less commonly, nonorganic irritants [1]. This condition's historical identification dates back to 1700 and has been associated with many inciting agents. More than 300 etiological agents have been pinpointed as contributors to the ailment. Understanding the historical evolution of HP is crucial not only for discerning its antigenic triggers but also for comprehending how changes in risk factors over time have impacted its development [2]. In the United Kingdom, the reported incidence stands at 0.9 cases per 100,000 person-years, while the overall age-adjusted mortality rate in the United States is 0.19 per million individuals [3].

HP is conventionally classified as acute, subacute, or chronic, delineated by its clinical attributes and the duration of the ailment [4]. Nevertheless, these categories often prove difficult to confine due to their variable and arbitrary definitions across numerous studies. The ATS/JRS/ALAT guideline committee has opted for an alternative classification, sorting HP into fibrotic (including mixed inflammatory and fibrotic patterns or exclusively fibrotic presentations) and non-fibrotic (purely inflammatory) categories. This classification hinges on the pivotal role of radiographic fibrosis in prognostic determination, offering enhanced clinical applicability [5]. In HP cases, histological identification or detection via chest computed tomography of fibrosis is correlated with reduced survival rates [6].

A chest high-resolution computed tomography (HRCT) scan is often conducted as an integral component of the initial diagnostic assessment. Specific HRCT patterns may indicate the likelihood of HP in a relevant clinical context. Patients diagnosed with HP are categorized into fibrotic or non-fibrotic classifications based on the presence or absence of fibrosis in their HRCT results. HRCT indications of pulmonary fibrosis encompass irregular linear opacities, reticulation, traction bronchiectasis, and honeycomb formations [1]. This study assesses the HRCT findings in HP patients and scrutinizes the factors associated with the division between fibrotic and non-fibrotic patient groups.

Materials and methods

The population of this retrospective cross-sectional study comprises all patients diagnosed with hypersensitivity pneumonia at the outpatient clinic and service of Ankara Atatürk Sanatorium Training and Research Hospital between January 1, 2010, and December 31, 2022. HP is a rare disease. Due to its rarity, the study aims to encompass the entire patient population rather than opting for a sample selection. The hospital management information system identified patients diagnosed with J67 HP. Over the designated research period, 132 patients with HP were identified in the hospital's management information system. However, fifteen patients were excluded from the study due to the unavailability of their HRCT images and information.

For the study, the hospital employed data from their records on cases of HP. This encompassed laboratory test results, evaluations of pulmonary function, and radiological images stored within their information management system. The HRCT findings were subjected to analysis for a range of observations, including centrilobular nodules, ground-glass opacity, mosaic attenuation, irregular linear opacities, reticulation, traction bronchiectasis, honeycomb formations, fibrosis, and prevalence of distribution of fibrotic opacities. A Radiology Specialist within the research team meticulously reviewed the HRCT scans of the enrolled patients to ascertain the presence of either fibrotic or non-fibrotic findings, aligning with the guidelines stipulated by ATS/JRS/ALAT. The identification of fibrosis hinged on the concurrent presence of a reticular pattern alongside traction bronchiectasis and/or honeycomb formations.

The study's primary dependent variable categorizes HP cases based on their fibrosis status in HRCT scans, distinguishing between fibrotic and non-fibrotic instances. Meanwhile, the independent variables encompass a spectrum of socio-demographic factors such as age, gender, smoking status, and attributes linked to occupational history. Additionally, the independent variables include functional assessment outcomes (FEV1, FVC, FEV1/FVC, DLCO), laboratory findings (hemogram, biochemistry), and exposure-related characteristics. The accumulation of data was facilitated by using a dedicated patient follow-up form.

The study received ethical clearance via decision number 2012-KAEK-15/2727, granted by the Ankara Atatürk Sanatorium Education and Research Hospital Ethics Committee. After obtaining the committee's ethical endorsement, the study was initiated.

Statistical analysis

The statistical analysis was performed utilizing the SPSS Windows version 22.0, a commonly employed software package. Descriptive statistics, specifically mean (standard deviation) (SD), were employed to depict numerical data. The independent groups t-test assessed the distinctions between continuous variables within two groups. In contrast, the chi-square test was employed to compare categorical variables. Outcomes with a *P*-value of <0.05 were considered statistically significant.

Results

Between January 1, 2010, and December 31, 2022, a total of 117 cases of HP were diagnosed at the Ankara Atatürk Sanatorium Training and Research Hospital, constituting the research cohort. Among the 117 subjects encompassed in this study, 59 (50.4%) were male, while 58 (49.6%) were female. The mean age of patients at the time of diagnosis was 52.1 (13.6) years, ranging from 20 to 81 years. The cases were stratified into two groups based on their fibrosis status observed in HRCT scans. The non-fibrotic HP group accounted for 70 (59.8%) patients, while the fibrotic HP group comprised 47 (40.2%). Among patients subjected to HRCT evaluation, the most prevalent findings included ground-glass opacity (90.6%), mosaic attenuation (87.2%), traction bronchiectasis (50.4%), centrilobular nodules (45.3%), reticulation (44.4%), and irregular linear opacities (41.0%). Comparatively less common

observations were fibrosis (40.2%), three-density findings (28.2%), and honeycomb formations (13.7%) (Table 1).

No statistically significant differences were observed in centrilobular nodules, mosaic attenuation, and three-density patterns between non-fibrotic HP and fibrotic HP HRCT findings. However, a statistically significant distinction emerged between the two groups concerning ground-glass opacity, irregular linear opacities, reticulation, traction bronchiectasis, honeycombing, and fibrosis (Table 1).

Table 1: HRCT findings of the 117 patients with non-fibrotic HP and fibrotic HP cases.

Characteristics	Total	HP phenotypes		*P*-value*
		Non-Fibrotic HP	Fibrotic HP	
	n (%)	n (%)	n (%)	
Centrilobular nodules	53 (45.3)	35 (50)	18 (38.3)	0.257
Ground-glass opacity	106 (90.6)	60 (85.7)	46 (97.7)	0.024
Mosaic attenuation	102 (87.2)	58 (82.7)	44 (93.6)	0.074
Three-density pattern	33 (28.2)	20 (28.2)	13 (27.7)	0.543
Irregular linear opacities	48 (41.0)	18 (25.7)	30 (63.8)	<0.001
Reticulation	52 (44.4)	5 (7.1)	47 (100)	<0.001
Traction bronchiectasis	59 (50.4)	12 (17.1)	47 (100)	<0.001
Honeycombing	16 (13.7)	0 (0.0)	16 (34.0)	<0.001
Fibrosis	47 (40.2)	0 (0.0)	47 (100)	<0.001

* Chi-square test, HRCT: High-Resolution Computed Tomography, HP: Hypersensitivity pneumonitis

No statistically significant differences were identified in terms of gender, recognized environmental risk factors, presence of cough, shortness of breath, and smoking status, whether considering fibrotic HP or non-fibrotic HP. However, notable statistical significance emerged regarding fibrotic HP and non-fibrotic HP cases concerning the presence of a known occupational risk factor and the detection of crackles during physical examination (P=0.022, P<0.001) (Table 2).

Table 2: The relationship between non-fibrotic HP and fibrotic HP cases with some demographic characteristics.

		Non-Fibrotic HP		Fibrotic HP		*P*-value*
		n	%	n	%	
Gender (n=117)	Female	36	51.4	22	46.8	0.382
	Male	34	48.6	25	53.2	
Occupational risk (n=117)	Yes	25	35.7	8	17	0.022
	None	45	64.3	39	83	
Environmental risk (n=117)	Yes	30	42.9	17	36.2	0.298
	None	40	57.1	30	63.8	
Cough (n=117)	Yes	54	77.1	42	89.4	0.072
	None	16	22.9	5	10.6	
Breathlessness (n=117)	Yes	66	94.3	42	91.5	0.408
	None	4	5.7	5	8.5	
Crackles on physical examination (n=117)	Yes	13	18.6	23	48.9	<0.001
	None	57	81.4	24	51.1	
Cigarette (n=117)	Non-smoker	35	50	20	42.6	0.160
	Ex-smoker	17	24,3	19	40.4	
	Smoker	18	25,7	8	17.0	

* Chi-square test

The average age at diagnosis in the non-fibrotic HP group was 47.79 (13.1) years, while in the fibrotic HP group, it was 58.68 (11.6) years. The non-fibrotic HP group received a statistically significant diagnosis at a younger age than the fibrotic HP group (P<0.001). Furthermore, the mean duration of smoking was notably higher in the fibrotic HP group than in the non-fibrotic HP group, displaying statistical significance (P=0.010). Laboratory tests revealed that lactate dehydrogenase and white blood cell values were significantly elevated in the fibrotic HP group (P=0.003, P=0.024). Additionally, the lymphocyte ratio in bronchoalveolar lavage fluid was recorded as 28.78 (16.2) in the non-fibrotic HP group and 14.66 (10.3) in the fibrotic HP group, exhibiting a statistically significant reduction in the fibrotic HP group (P<0.001). No statistically significant differences were observed between the two groups regarding time from symptom onset to diagnosis, C-reactive protein levels, or pulmonary function values (FVC, FEV1, FEV1/FVC, DLCO) (Table 3).

Table 3: Evaluation of the relationship between non-fibrotic HP and fibrotic HP cases with laboratory and pulmonary function tests.

	Non-Fibrotic HP mean (SD)	Fibrotic HP mean (SD)	*P*-value*
Age, years (n=117)	47.79 (13.1)	58.68 (11.6)	<0.001
Cigarettes (pack/year) (n=24)	17.8 (12.2)	30.0 (8.6)	<0.010
Time from symptom onset to diagnosis, months (n=117)	14.4 (26.2)	19.5 (25.0)	0.299
CRP, (n=117)	12.04 (25.1)	22.28 (45.3)	0.164
LDH,) (n=117)	230.47 (82.4)	286.12 (106)	0.003
WBC, (n=117)	8727 (2644)	9810 (2295)	0.024
FVC, (n=105)	79.98 (16.5)	76.7 (20.4)	0.384
FEV1, (n=105)	75.4 (16.9)	70.43 (19.2)	0.166
FEV/FVC, (n=105)	81.9 (10.9)	85.61 (7.7)	0.580
DLCO, (n=83)	88.87 (22.3)	77.47 (20.7)	0.200
The ratio of lymphocytes (n=75)	28.78 (16.2)	14.66 (10.3)	<0.001

* Independent groups t-test, SD: standard deviation, CRP: C-Reactive Protein, LDH: Lactate Dehydrogenase, WBC: White Blood Cell, FVC: Forced vital capacity, FEV1: Forced expiratory volume in the first second, DLCO: Diffusing Capacity of the lung for carbon monoxide.

Discussion

A characteristic HRCT pattern can suggest the diagnosis. A compatible HRCT pattern becomes indicative of HP when supported by multidisciplinary discussions. The HRCT pattern may point toward an alternative diagnosis in cases where it is indeterminate. A higher confidence level in diagnosing HP is generally achieved when a more distinct HRCT confidence level is attainable [7].

It is crucial to thoroughly evaluate the computed tomography features of HP to determine the extent of radiological certainty. According to the ATS/JRS/ALAT algorithm, a non-fibrotic HP with a typical HRCT pattern indicates diffuse parenchymal infiltration and signs of small airway disease. Parenchymal infiltration might manifest as ground-glass opacity or mosaicism, while small airway disease could exhibit signs of air trapping and vaguely defined centrilobular nodules up to 5 mm in size. In cases where fibrotic patterns are observed on HRCT scans, compatible with HP, it suggests a combination of fibrosis and small airway disease in specific areas [5].

The study encompassed the assessment of HRCT findings from 117 cases that had been diagnosed with HP. The HRCT outcomes revealed that ground-glass opacities (90.6%) and mosaic attenuation (87.2%) were the most frequently observed features. Similar evaluations were carried out in a separate study conducted by Shobeiri et al. [8] involving 45 HP patients. Additionally, in a study focused on 92 patients with fibrotic HP, Walsh et al. [9] identified ground-glass opacification (93.3%) and reticulation (93.3%) as the predominant HRCT findings.

Mosaic attenuation and three-density findings are radiological terms associated with heterogeneous lung attenuation. “mosaic attenuation” pertains specifically to computed tomography during the inspiratory phase. It is defined as distinctly demarcated areas of both low and high attenuation. This phenomenon can be observed in vascular, airway, or infiltrative diseases [5]. Recognizing that the “headcheese” sign might not resonate with most individuals, the term “three-density pattern” has become the preferred nomenclature [10]. This term is utilized to depict a scenario where obstructions and infiltrations coexist with regions of healthy lung tissue, resulting in well-defined zones exhibiting three distinct levels of

attenuation [11]. Within the domain of fibrotic HP, three-density findings have been identified [10].

Our study revealed no significant distinction between fibrotic and non-fibrotic HP patients concerning mosaic attenuation and three-density findings. However, our research exhibited statistically notable elevations in irregular linear opacities, reticulation, Traction Bronchiectasis, honeycombing, and fibrosis within the fibrotic patient group. This aligns with the findings of Nishida et al. [12], who, in their investigation involving 121 HP patients, identified higher statistical significance in honeycombing, traction bronchiectasis, and lung distortion findings within the fibrotic patient group, akin to our study.

When dealing with individuals suspected of having HP, it is recommended to amalgamate HP-specific HRCT findings with clinical information to bolster the diagnosis of HP. However, relying solely on CT findings for a definitive diagnosis is cautioned against [11].

Numerous studies have underscored the pivotal role of lung fibrosis in prognostic determination [13-17]. In their examination of 69 HP patients, Hanak et al. [16] categorized 37.6% as having fibrotic HP. Similarly, Nishida et al. [12] reported a fibrotic patient rate of 38.8% among 121 patients. In concurrence with this literature, our study found 40.2% of patients fall into the fibrotic HP category.

While the mean age of all diagnosed patients was 52.1 (13.6) years, the non-fibrotic HP group exhibited a mean age at diagnosis of 47.79 (13.1) years, while the fibrotic HP group skewed older, with a mean age of 58.68 (11.6) years. In the study conducted by Nishida et al. [12], the mean age of HP patients was 63.0, with the non-fibrotic patient group averaging 59 years and the fibrotic patient group averaging 67 years. In a separate investigation, Wang et al. [18] identified the mean age across all patients as 53.6, with the acute hypersensitivity group averaging 51.9 and the chronic hypersensitivity group averaging 57.8. Corresponding with our findings, the literature also indicates that fibrotic HP patients tend to receive their diagnosis at an older age.

Despite thoroughly evaluating exposure histories, laboratory results, and radiological findings in HP cases, the causative agent may remain undetectable in 49-60% of instances [1,19]. The responsible agent can be identified in approximately half of HP cases by meticulously exploring environmental and occupational backgrounds. A notable observation emerged in our study: while there was a statistically significant increase in non-fibrotic HP cases within the group exposed to occupational risk factors, no statistically significant distinction was noted for either group in patients with environmental risk factors.

A parallel discovery was made in the study conducted by Walters et al., where, akin to our results, no disparity surfaced within the group harboring environmental risk factors. However, they did find a statistically significant reduction in fibrosis among individuals with occupational risk factors. By delving into a comprehensive occupational history, detecting non-fibrotic HP cases early becomes feasible, facilitating their treatment by removing the causative agent [19].

Frequently observed symptoms and indications in non-fibrotic and fibrotic HP encompass breathlessness, cough, and mid-inspiratory squat. Our investigation unveiled no noteworthy contrast between patient groups with fibrotic and non-fibrotic HP concerning symptoms like cough and shortness of breath. However, a significant elevation was identified in the occurrence of crackles during physical examinations within the fibrotic patient group.

Consistent with our findings, Walters et al. reported no discernible differences in cough, fever, weight loss, or dyspnea. Nevertheless, they did establish a statistically significant increase in crackles detected through physical examination within the fibrotic patient cohort [19].

Recently published reports have ignited a discourse regarding the influence of smoking on individuals with HP. Warren [20] and Terho et al. [21] proposed a notable association between HP and non-smoking, asserting that acute hypersensitivity pneumonitis is less prevalent among current smokers than non-smokers with similar exposure risks. A study by Furuiye et al. [22] demonstrated that cigarette smoke could dampen inflammation and lymphocyte proliferation in cases of acute hypersensitivity pneumonitis. However, an intriguing counterpoint emerges: if an individual who smokes develops HP, the condition may progress into a chronic state, accompanied by poorer survival rates than their non-smoking counterparts. This divergence stems from prolonged exposure to cigarette smoke can exacerbate both lung inflammation and fibrosis [23].

In line with the existing literature, our research found a parallel pattern; specifically, the duration of smoking within the fibrotic group significantly exceeded that of the non-fibrotic group.

Pulmonary function tests are a valuable tool for assessing the pattern and extent of respiratory impairment, although neither model stands alone as diagnostic. Distinguishing between non-fibrotic HP and fibrotic HP is beyond the capabilities of pulmonary function tests. Within our study, despite lacking a statistically significant differentiation in the pulmonary function tests (FEV1, FVC, FEV1/FVC, DLCO) of the fibrotic and non-fibrotic patient groups, it was observed that the FEV1, FVC, and DLCO values were notably lower within the fibrotic patient cohort. Consistent with our findings, Nishida et al.'s study reported similar results: while no discernible disparity existed in diffusion between the fibrotic and non-fibrotic patient groups, the FVC value was reduced in the fibrotic patient group [12].

Bronchoscopy plays a pivotal role in diagnosing HP, with bronchoalveolar lavage (BAL) fluid collection and analysis and lung biopsy serving as the principal procedures conducted through this method. BAL testing emerges as a highly effective means of identifying alveolitis in individuals suspected of having HP. Typically, patients afflicted with HP exhibit alveolitis characterized by a notable abundance of lymphocytes. However, it's noteworthy that individuals with fibrotic HP tend to display lower levels of lymphocytes in their BAL fluids when contrasted with those suffering from non-fibrotic HP [5].

Within our investigation, the lymphocyte ratio in the BAL samples of fibrotic HP cases was measured at 14.66 (10.3), while non-fibrotic HP cases exhibited a lymphocyte ratio of 28.78 (16.2), resulting in a statistically significant discrepancy. In alignment with our study, Nishida et al. [12] also identified a

significantly lower lymphocyte ratio in the BAL samples of the fibrotic HP patient group compared to the non-fibrotic HP patient group. Notably, a diminished lymphocyte ratio in BAL has been linked to an unfavorable prognosis in patients diagnosed with HP [5].

Limitations

Our study possesses certain limitations. The primary limitations of our research stem from the small sample size and retrospective design employed in the study. Due to the retrospective design of the study, we were unable to access the prognosis of the patients. Consequently, there is a need for future studies to examine the correlation between fibrosis and prognosis.

Conclusion

The outcomes of an HRCT scan hold substantial significance in identifying HP. Computed tomography aids in categorizing HP. Following this study, ground-glass opacity and mosaic attenuation were frequently noted in HRCT scans of individuals with HP. Irregular linear opacities, reticulation, traction bronchiectasis, honeycombing, and fibrosis exhibit a statistically higher prevalence in fibrotic HP cases than in non-fibrotic HP cases. Our investigation revealed that the non-fibrotic patient group skewed younger, and the lymphocyte ratio was elevated in BAL fluid. HP patients who are cigarette smokers face an increased likelihood of developing fibrosis. Since fibrosis is the principal determinant of prognosis, investigations exploring the relationship between fibrosis and prognosis are imperative.

References

1. Fernández Pérez ER, Travis WD, Lynch DA, Brown KK, Johannson KA, Selman M, et al. Diagnosis and Evaluation of Hypersensitivity Pneumonitis: CHEST Guideline and Expert Panel Report. Chest. 2021 Aug;160(2):e97-e156. doi: 10.1016/j.chest.2021.03.066. Epub 2021 April 20. PMID: 33861992.
2. Barnes H, Jones K, Blanc P. The hidden history of hypersensitivity pneumonitis. Eur Respir J. 2022 Jan 20;59(1):2100252. doi: 10.1183/13993003.00252-2021. PMID: 34083405.
3. Salisbury ML, Myers JL, Belloli EA, Kazerooni EA, Martinez FJ, Flaherty KR. Diagnosis and Treatment of Fibrotic Hypersensitivity Pneumonia. Where We Stand and Where We Need to Go. Am J Respir Crit Care Med. 2017 Sep 15;196(6):690-9. doi: 10.1164/rccm.201608-1675PP. PMID: 28002680; PMCID: PMC5620675.
4. Richerson HB, Bernstein IL, Fink JN, Hunninghake GW, Novey HS, Reed CE, et al. Guidelines for the clinical evaluation of hypersensitivity pneumonitis. Report of the Subcommittee on Hypersensitivity Pneumonitis. J Allergy Clin Immunol. 1989 Nov;84(5 Pt 2):839-44. doi: 10.1016/0091-6749(89)90349-7. PMID: 2809034.
5. Raghu G, Remy-Jardin M, Ryerson CJ, Myers JL, Kreuter M, Vasakova M, et al. Diagnosis of Hypersensitivity Pneumonitis in Adults. An Official ATS/JRS/ALAT Clinical Practice Guideline. Am J Respir Crit Care Med. 2020 Aug 1;202(3):e36-e69. doi: 10.1164/rccm.202005-2032ST. Erratum in: Am J Respir Crit Care Med. 2021 Jan 1;203(1):150-1. Erratum in: Am J Respir Crit Care Med. 2022 Aug 15;206(4):518. PMID: 32706311; PMCID: PMC7397797.
6. Kouranos V, Jacob J, Nicholson A, Renzoni E. Fibrotic Hypersensitivity Pneumonitis: Key Issues in Diagnosis and Management. J Clin Med. 2017 June 15;6(6):62. doi: 10.3390/jcm6060062. PMID: 28617305; PMCID: PMC5483872.
7. Chelala L, Adegunsoye A, Cody BA, Husain AN, Chung JH. Updated Imaging Classification of Hypersensitivity Pneumonitis. Radiol Clin North Am. 2022 Nov;60(6):901-13. doi: 10.1016/j.rcl.2022.06.013. Epub 2022 September 7. PMID: 36202477.
8. Shobeirian F, Mehrian P, Doroudinia A. Hypersensitivity Pneumonitis High-resolution Computed Tomography Findings, and Their Correlation with the Etiology and the Disease Duration. Prague medical report. 2020;121(3):133-41. doi: 10.14712/23362936.2020.12. PMID: 33030142.
9. Walsh SL, Sverzellati N, Devaraj A, Wells AU, Hansell DM. Chronic hypersensitivity pneumonitis: high resolution computed tomography patterns and pulmonary function indices as prognostic determinants. Eur Radiol. 2012 Aug;22(8):1672-9. doi: 10.1007/s00330-012-2427-0. Epub 2012 April 1. PMID: 22466512.
10. Dabiri M, Jehangir M, Khoshpouri P, Chalian H. Hypersensitivity Pneumonitis: A Pictorial Review Based on the New ATS/JRS/ALAT Clinical Practice Guideline for Radiologists and Pulmonologists. Diagnostics (Basel). 2022 Nov 20;12(11):2874. doi: 10.3390/diagnostics12112874. PMID: 36428934; PMCID: PMC9689332.
11. Barnett J, Molyneaux PL, Rawal B, Abdullah R, Hare SS, Vancheeswaran R, Desai SR, et al. Variable utility of mosaic attenuation to distinguish fibrotic hypersensitivity pneumonitis from idiopathic pulmonary fibrosis. Eur Respir J. 2019;54:1900531. doi: 10.1183/13993003.00531-2019. PMID: 31164428.
12. Nishida T, Kawate E, Ishiguro T, Kanauchi T, Shimizu Y, Takayanagi N. Antigen avoidance and outcome of non-fibrotic and fibrotic hypersensitivity pneumonitis. ERJ Open Res. 2021 Feb 7;8(1):00474-2021. doi: 10.1183/23120541.00474-2021. PMID: 35141326; PMCID: PMC8819255.
13. Fernández Pérez ER, Swigris JJ, Forssén AV, Tourin O, Solomon JJ, Huie TJ, et al. Identifying an inciting antigen is associated with improved survival in patients with chronic hypersensitivity pneumonitis. Chest. 2013 Nov;144(5):1644-51. doi: 10.1378/chest.12-2685. PMID: 23828161; PMCID: PMC4694094.
14. Salisbury ML, Gu T, Murray S, Gross BH, Chughtai A, Sayyouh M, et al. Hypersensitivity Pneumonitis: Radiologic Phenotypes Are Associated With Distinct Survival Time and Pulmonary Function Trajectory. Chest. 2019 Apr;155(4):699-711. doi: 10.1016/j.chest.2018.08.1076. Epub 2018 September 19. PMID: 30243979; PMCID: PMC6514431.
15. De Sadeleer LJ, Hermans F, De Dycker E, Yserbyt J, Verschakelen JA, Verbeken EK, et al. Effects of Corticosteroid Treatment and Antigen Avoidance in a Large Hypersensitivity Pneumonitis Cohort: A Single-Centre Cohort Study. J Clin Med. 2018 December 21;8(1):14. doi: 10.3390/jcm8010014. PMID: 30577667; PMCID: PMC6352061.
16. Hanak V, Golbin JM, Hartman TE, Ryu JH. High-resolution CT findings of parenchymal fibrosis correlate with prognosis in hypersensitivity pneumonitis. Chest. 2008 Jul;134(1):133-8. doi: 10.1378/chest.07-3005. Epub 2008 April 10. PMID: 18403660.
17. Mooney JJ, Elicker BM, Urbania TH, Agarwal MR, Ryerson CJ, Nguyen MLT, et al. Radiographic fibrosis score predicts survival in hypersensitivity pneumonitis. Chest. 2013 Aug;144(2):586-92. doi: 10.1378/chest.12-2623. PMID: 23392130.
18. Wang LJ, Cai HR, Xiao YL, Wang Y, Cao MS. Clinical characteristics and outcomes of hypersensitivity pneumonitis: a population-based study in China. Chin Med J (Engl). 2019 June 5;132(11):1283-92. doi: 10.1097/CM9.0000000000000256. Erratum in: Chin Med J (Engl). 2021 Jan 11;134(3):378. PMID: 31021982; PMCID: PMC6629344.
19. Walters GI, Mokhlis JM, Moore VC, Robertson AS, Burge GA, Bhomra PS, et al. Characteristics of hypersensitivity pneumonitis diagnosed by interstitial and occupational lung disease multidisciplinary team consensus. Respir Med. 2019 Aug;155:19-25. doi: 10.1016/j.rmed.2019.06.026. Epub 2019 June 29. PMID: 31295673.
20. Warren CP. Extrinsic allergic alveolitis: a disease commoner in non-smokers. Thorax. 1977 Oct;32(5):567-9. doi: 10.1136/thx.32.5.567. PMID: 594937; PMCID: PMC470791.
21. Terho EO, Husman K, Vohlonen I. Prevalence and incidence of chronic bronchitis and farmer's lung with respect to age, sex, atopy, and smoking. Eur J Respir Dis Suppl. 1987;152:19-28. PMID: 3499342.
22. Furuiye M, Miyake S, Miyazaki Y, Ohtani Y, Inase N, Umino T, et al. Effect of cigarette smoking on the development of murine chronic pigeon breeder's lung. The difference between a short-term and a long-term exposure. J Med Dent Sci. 2007 Mar;54(1):87-95. PMID: 19845140.
23. Churg A, Sin DD, Everett D, Brown K, Cool C. Pathologic patterns and survival in chronic hypersensitivity pneumonitis. Am J Surg Pathol. 2009 Dec;33(12):1765-70. doi: 10.1097/PAS.0b013e3181bb2538. PMID: 19809277.
24. Kumar R, Spalgais S, Ranga V. Hypersensitivity pneumonitis: clinical, radiological and pathological profile of 103 patients from North India. Monaldi Arch Chest Dis. 2020 Aug 3;90(3). doi: 10.4081/monaldi.2020.1307. PMID: 32885932.