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Is Chest Imaging Alone Adequate for Diagnosing Interstitial Lung Disease in Microscopic Polyangiitis Based on the 2022 Criteria?

Hyunsue Do[1], Yong-Beom Park[2,3], Ala Woo[4], and Sang-Won Lee[2,3]

[1]Division of Rheumatology, Department of Internal Medicine, Kangwon National University School of Medicine, Chuncheon;
[2]Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul;
[3]Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Seoul;
[4]Division of Pulmonology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, Korea.

Purpose: To investigate the concordance rate between chest imaging and lung biopsy results for interstitial lung disease (ILD) in patients with microscopic polyangiitis (MPA) and to compare their clinical utility for MPA classification.

Materials and Methods: This study included 24 patients who had both chest imaging and lung biopsy results at diagnosis and who fulfiled the 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology criteria for MPA. Concordance was defined as the concurrent confirmation of ILD on chest imaging and lung biopsy. Positive and negative predictive values were assessed in patients with and without ILD on chest imaging, respectively, and compared with histologically confirmed ILD on lung biopsy.

Results: The median age was 73.5 years, and all patients had myeloperoxidase (MPO)-antineutrophil cytoplasmic antibody. Among the 24 patients, 10 (41.7%) and 5 (20.8%) exhibited radiological and histological findings consistent with ILD, respectively. Among the 10 patients with radiological findings of ILD, only 4 exhibited histological features consistent with ILD on lung biopsy, leading to a concordance rate of 40%. Conversely, among the remaining 14 patients without radiological findings of ILD, 13 showed histological features inconsistent with ILD on lung biopsy, resulting in a concordance rate of 92.9%.

Conclusion: Lung biopsy should be considered in highly selected patients who are MPO-positive without involvement of other organs. The decision to determine the need for lung biopsy should be made by a multidisciplinary team.

Key Words: Microscopic polyangiitis, interstitial lung disease, imaging, biopsy, discordance

INTRODUCTION

Microscopic polyangiitis (MPA) is one of three subtypes of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) that causes necrotising vasculitis with few or no immune deposits in small- and occasionally medium-sized arteries.[1,2] Compared with the other two subtypes, granulomatosis with polyangiitis (GPA) and eosinophilic GPA (EGPA), MPA more often exhibits pulmonary and renal manifestations such as diffuse alveolar haemorrhage and pauci-immune glomerulonephritis (GN).[1,3] In 2022, a joint group of the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) proposed classification criteria for MPA, GPA, and EGPA (the 2022 ACR/EULAR criteria). These criteria can be applied to cases with evidence of small- and medium-vessel vasculitis, without serious medical conditions mimicking AAV. Different weighted scores are assigned to each item of the criteria and when total scores ≥5 are achieved, diagnoses of MPA and GPA can be made. Whereas, for the diagnosis of EGPA, a total score of 6 or greater is need-

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Co-corresponding authors: Sang-Won Lee, MD, PhD, Division of Rheumatology, Department of Internal Medicine, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
E-mail: sangwonlee@yuhs.ac and
Ala Woo, MD, Division of Pulmonology, Department of Internal Medicine, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea.
E-mail: ALWOO@yuhs.ac

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ed.[4-6] Compared with previous criteria or definitions,[1,2] the most distinct aspect of the new criteria is the addition of an item for lung lesions in MPA classification for the first time in the stratified scoring system: an item of fibrosis or interstitial lung disease (ILD) on chest imaging.[4]

The ILD included in the 2022 ACR/EULAR criteria for MPA is quite a different pattern from the lung lesions of the GPA surrogate markers described in the 2007 European Medicines Agency (EMA) algorithm for AAV and non-fixed migratory lung infiltration included in the 1990 ACR criteria for Churg-Strauss syndrome (EGPA).[1,4,7,8] Accordingly, from the perspective of lung lesions in patients with AAV, it is believed that ILD could largely contribute to the classification of MPA and further to the differential diagnosis among the three subtypes of AAV. However, in real clinical practice, when classifying MPA, we frequently encounter the following fundamental question regarding ILD: whether chest imaging can be a sufficient method to confirm the presence of ILD for MPA diagnosis, as well as to exclude the causes of ILD other than MPA.[9,10] In other words, should a lung biopsy be performed to confirm the presence of ILD for MPA classification and further exclude the causes of ILD other than MPA.[11,12] Furthermore, these questions are raised even in patients with myeloperoxidase (MPO)-ANCA.[4] To answer these questions, we investigated the concordance rate and reasons for the discordance between chest imaging and lung biopsy results for ILD in patients with MPO-ANCA-positive MPA who underwent both chest imaging and lung biopsy at diagnosis. In addition, we compared the clinical utility of the two modalities for MPA classification.

MATERIALS AND METHODS

Patients

We screened 283 patients with AAV included in the Severance Hospital ANCA-associated VasculitidEs (SHAVE) cohort, which is an observational cohort of Korean patients with AAV, and selected 24 patients with MPA according to the following inclusion criteria: 1) the fulfilment of the 2007 EMA algorithm, the 2012 revised Chapel Hill Consensus Conference nomenclature of vasculitides, and 2022 ACR/EULAR classification criteria for MPA; 2) the first classification of AAV at the Department of Rheumatology, Yonsei University College of Medicine, and Severance Hospital from November 2005 to June 2023; 3) the well-documented medical records for collecting clinical, laboratory, radiological, and histological data at diagnosis for the classification and differential diagnosis of AAV; 4) in particular, the presence of results of high-resolution computed tomography (HRCT) as an imaging method, as well as lung biopsy at diagnosis (with the time gap between lung imaging and lung biopsy performance being within 3 weeks); 5) the presence of ANCA results at diagnosis; 6) the follow-up duration of ≥6 months after diagnosis; 7) the absence of serious medical conditions mimicking AAV, such as malignancies, severe infectious diseases, medications inducing ANCA false positives, or symptoms mimicking AAV; 8) no exposure to glucocorticoids or immunosuppressive drugs within 4 weeks before AAV diagnosis. Of 283 patients with AAV, 232 who did not undergo HRCT or lung biopsy at diagnosis were excluded. Of the 51 AAV patients with both HRCT and lung biopsy results at diagnosis, 27 patients with GPA and EGPA were excluded. Finally, 24 patients with MPA who had both HRCT and lung biopsy results at diagnosis were included in this study and analysed (Fig. 1).

Ethical approval

This study was conducted in compliance with the World Medical Association Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Severance Hospital, Seoul, Korea (IRB No. 4-2020-1071). The requirement for additional written informed consent was waived by the IRB due to the retrospective nature of this study and the use of anonymised patient data.

Clinical data

The demographic data included age, sex, and body mass index. The results of tests for MPO-ANCA, proteinase 3 (PR3)-ANCA, perinuclear (P)-ANCA, and cytoplasmic (C)-ANCA, as well as routinely performed laboratory tests, including acute-phase reactants at diagnosis, were collected. MPO-ANCA and PR3-ANCA were measured using immunoassays, whereas P-ANCA and C-ANCA were detected using indirect immunofluorescence assays. According to the 2022 ACR/EULAR criteria for MPA, MPO-ANCA, PR3-ANCA, P-ANCA, and C-ANCA positivity or negativity are all accepted as ANCA test results.[5] Radiological and histological data of the lung lesions at diagnosis were recorded. Concordance was defined as concurrent confirmed ILD on

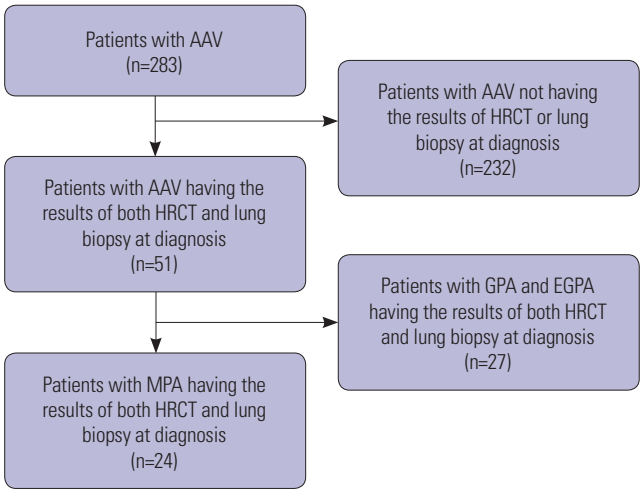

Fig. 1. Patient selection. AAV, antineutrophil cytoplasmic antibody-associated vasculitis; HRCT, high-resolution computed tomography; GPA, granulomatosis with polyangiitis; EGPA, eosinophilic granulomatosis with polyangiitis; MPA, microscopic polyangiitis.

chest imaging and lung biopsy. Additionally, multidisciplinary diagnostic approaches, in addition to chest imaging and lung biopsy, such as pulmonary function tests (PFT) and serologic markers, were reviewed, although they were not available for all patients.[11,13]

Definition of ILD on chest imaging

ILD was defined and characterised according to radiological features, such as traction bronchiectasis, ground-glass opacities accompanied by traction bronchiectasis, reticulations alongside traction bronchiectasis, and honeycombing. ILD was diagnosed by both pulmonologists and independent radiologists based on chest imaging (HRCT) results. Traction bronchiectasis is an enlarged airway located at the periphery of the lungs. Ground-glass opacity denotes a cloudy appearance of the lungs while preserving the visibility of the vessels and airways. Reticulations are described in terms of their numerous linear densities. Honeycombing is characterised by a grouping of sub-pleural cysts, each measuring 3–10 mm in diameter and possessing clearly defined walls.[14,15]

Methods for lung biopsy and histological definition of ILD

According to the clinical practice guidelines proposed by the American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Association,[16] the decision to perform lung biopsy for ILD requires a multidisciplinary discussion. In this study, the methods and sites of the lung biopsy were primarily determined by primary physician or attending physician. Lung biopsy methods include surgical lung biopsy (wedge resection and bullectomy), transbronchial lung biopsy, and computed tomography-guided lung biopsy. Histological assessments were performed by independent pathologists, and ILD diagnosis was made by pulmonologists.

RESULTS

Characteristics of MPA patients at diagnosis

In terms of the variables at diagnosis, the median age and body mass index of the 24 patients were 73.5 years and 21.5 kg/m^2. Among the 24 patients, 11 (45.8%) and 13 (54.2%) were male and female, respectively. All patients had MPO-ANCA (or P-ANCA), whereas only one had PR3-ANCA (or C-ANCA). The median erythrocyte sedimentation rate and C-reactive protein levels were 48.0 mm/h and 14.6 mg/L, respectively. The remaining laboratory test results are presented in Table 1. In terms of variables related to lung lesions, 10 of the 24 patients exhibited radiological findings consistent with ILD on chest imaging. The remaining 14 patients exhibited radiological findings other than fibrosis or ILD, including calcified nodules, centrilobular nodules, patchy consolidation, and bronchiectasis. Transbronchial, surgical, and CT-guided lung biopsies were performed in 14, 6, and 3 patients, respectively, and an endobronchial biopsy was performed in 1 patient. According

Table 1. Characteristics of MPA Patients with Both Chest Imaging and Lung Biopsy Results at Diagnosis (n=24)

	Values
Variables at diagnosis	
Demographic data	
Age (yr)	73.5 (62.5–78.0)
Male sex	11 (45.8)
Female sex	13 (54.2)
BMI (kg/m^2)	21.5 (20.2–24.5)
ANCA type and positivity	
MPO-ANCA (or P-ANCA) positivity	24 (100)
PR3-ANCA (or C-ANCA) positivity	1 (4.2)
Double ANCA positivity	1 (4.2)
Acute-phase reactants	
ESR (mm/h)	48.0 (29.3–76.0)
CRP (mg/L)	14.6 (6.8–34.1)
Laboratory results	
White blood cell (/mm^3)	7485.0 (5155.0–9547.5)
Haemoglobin (g/dL)	10.2 (9.0–11.0)
Platelet count (×1000/mm^3)	238.0 (183.0–311.8)
Blood urea nitrogen (mg/dL)	24.4 (11.8–41.8)
Serum creatinine (mg/dL)	1.3 (0.9–2.9)
Serum total protein (g/dL)	6.2 (5.3–6.9)
Serum albumin (g/dL)	3.6 (2.8–3.9)
Variables related to lung lesions at diagnosis	
Radiological evaluation	
Fibrosis or ILD on chest imaging	10 (41.7)
Other than fibrosis or ILD on chest imaging	14 (58.3)
Histological evaluation	
Methods of lung biopsy	
Transbronchial lung biopsy	14 (58.3)
Surgical lung biopsy	6 (25.0)
Wedge resection	5 (20.8)
Bullectomy	1 (4.2)
CT-guided lung biopsy	3 (12.5)
Endobronchial biopsy	1 (4.2)
Histologic diagnosis	
Presence of ILD	5 (20.8)
Usual interstitial pneumonia	3 (12.5)
Organising pneumonia	1 (4.2)
Desquamative interstitial pneumonia	1 (4.2)
Absence of ILD	19 (79.2)
Non diagnostic pathologic findings	15 (62.5)
Other than ILD	4 (16.7)

MPA, microscopic polyangiitis; BMI, body mass index; ANCA, antineutrophil cytoplasmic antibody; MPO, myeloperoxidase; P, perinuclear; PR3, proteinase 3; C, cytoplasmic; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; ILD, interstitial lung disease; CT, computed tomography.
Values are expressed as a median (25th–75th percentiles) or n (%).

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to the histological diagnosis, 5 patients showed pathological findings consistent with ILD; among them, 3, 1, and 1 had usual interstitial pneumonia (UIP), organising pneumonia, and desquamative interstitial pneumonia (DIP), respectively. In contrast, 19 patients exhibited pathological findings that were insufficient to diagnose ILD (Table 1).

Fulfilment of items in the 2022 ACR/EULAR classification criteria for MPA

In this study, all 24 patients fulfiled the 2022 ACR/EULAR classification criteria for MPA. We investigated whether each patient met all conditions of the 2022 ACR/EULAR criteria for MPA. Regarding ANCA positivity, patients who tested positive for both MPO-ANCA (or P-ANCA) and PR3-ANCA (or C-ANCA) did not exhibit GPA surrogate markers, particularly "lung nodules or cavitation," and did not meet the 2022 ACR/EULAR criteria for GPA.[1,5] Regarding nasal passage symptoms, none of the patients showed nasal passage symptoms or serum eosinophilia. Regarding lung and kidney involvement, 10 (41.7%) patients exhibited lung fibrosis or ILD on chest imaging, whereas 11 (45.8%) showed pauci-immune GN on kidney biopsy. However, among the 24 patients, 7 (29.2%) did not have lung fibrosis or ILD on chest imaging or pauci-immune GN on kidney biopsy. Nevertheless, 6 of these 7 patients manifested symptoms consistent with renal vasculitis, and the remaining patient exhibited mononeuritis multiplex, as defined by the 2007 EMA algorithm. Therefore, the patient was diagnosed as having MPA. Accordingly, through the presence of evidence of small-vessel vasculitis, they achieved a total score of 6 owing to MPO-ANCA (or P-ANCA) positivity and were classified as having MPA (Table 2).

Agreement or disagreement on the presence of ILD between radiological and histological results in patients with MPA

Among the 10 patients who had radiological findings consistent with ILD on chest imaging, only 4 exhibited histological features consistent with ILD on lung biopsy, indicating a concordance rate of only 40% between chest imaging and lung biopsy results in the presence of ILD. Conversely, among the remaining 14 patients who had no radiological findings consistent with ILD on chest imaging, 13 showed histological features in-

Table 2. Fulfilment of Items of the 2022 ACR/EULAR Classification Criteria for MPA

Patient number	MPO-ANCA (or P-ANCA) positivity (+6)	Fibrosis or ILD on chest imaging (+3)	Pauci-immune GN on biopsy (+3)	Nasal passage symptoms* (-3)	PR3-ANCA (or C-ANCA) positivity (-1)	Serum eosinophil count ≥1000/mm^3 (-4)	Total score
#1	Yes	Yes	Yes	No	No	No	12
#2	Yes	Yes	Yes	No	No	No	12
#3	Yes	Yes	Yes	No	No	No	12
#4	Yes	Yes	Yes	No	No	No	12
#5	Yes	No	Yes	No	No	No	9
#6	Yes	No	Yes	No	Yes	No	8
#7	Yes	No	Yes	No	No	No	9
#8	Yes	No	Yes	No	No	No	9
#9	Yes	No	Yes	No	No	No	9
#10	Yes	No	No	No	No	No	6
#11	Yes	Yes	No	No	No	No	9
#12	Yes	No	No	No	No	No	6
#13	Yes	Yes	No	No	No	No	9
#14	Yes	Yes	No	No	No	No	9
#15	Yes	Yes	No	No	No	No	9
#16	Yes	No	Yes	No	No	No	9
#17	Yes	No	Yes	No	No	No	9
#18	Yes	Yes	No	No	No	No	9
#19	Yes	Yes	No	No	No	No	9
#20	Yes	No	No	No	No	No	6
#21	Yes	No	No	No	No	No	6
#22	Yes	No	No	No	No	No	6
#23	Yes	No	No	No	No	No	6
#24	Yes	No	No	No	No	No	6

ACR, American College of Rheumatology; EULAR, European Alliance of Associations for Rheumatology; MPA, microscopic polyangiitis; MPO, myeloperoxidase; ANCA, antineutrophil cytoplasmic antibody; P, perinuclear; ILD, interstitial lung disease; GN, glomerulonephritis; PR3, proteinase 3; C, cytoplasmic.
*Nasal passage symptoms: nasal bloody discharge, ulcers, crusting, congestion, or blockage, or nasal septal defect/perforation.

consistent with ILD on lung biopsy, indicating a concordance rate of up to 92.9% between chest imaging and lung biopsy results in the absence of ILD (Table 3). In summary, the negative predictive value of non-ILD observed on chest imaging for histologically confirmed ILD was as high as 92.9%, whereas the positive predictive value for radiologically confirmed ILD was only 40%.

Among the ILD patterns observed on imaging, there were 6 cases of UIP, 2 cases of reticulation (non-UIP), 1 case of organising pneumonia (characterised by consolidation), and 1 case of DIP with emphysema.

A total of 7 patients showed discordance between chest imaging and lung biopsy findings. Among these cases, 3 showed a UIP pattern on imaging but were non-diagnostic findings on histology, and 1 case showed a UIP pattern on chest imaging but was not consistent with ILD on lung biopsy (Table 3).

DISCUSSION

In real clinical settings, when patients with ILD and ANCA positivity without specific concomitant diseases are referred, it is a cautious approach to classify them as having MPA by simply applying the 2022 ACR/EULAR criteria. As ILD may occur due to various aetiologies other than MPA, chest imaging alone has limitations in identifying the correlation between ILD and MPA. Furthermore, chest imaging itself has limitations in differentiating ILD from non-ILD in the MPA classification. However, lung biopsy results showing fibrinoid and necrotising vasculitis in small-sized vessels without granulomatous alterations or eosinophilic infiltration suggestive of MPA may make a crucial contribution to the MPA classification. Accordingly, performing lung biopsy in patients with ILD and MPO-ANCA positivity may improve the diagnostic accuracy of MPA; however, there are limitations in performing lung biopsy in all patients due to concerns about the systemic complications of invasive procedures. Therefore, we face a dilemma regarding whether lung biopsy should be performed in patients with MPO-ANCA-positive ILD on chest imaging. To answer these questions, we investigated the concordance rate and reasons for the discordance between chest imaging and lung biopsy results for ILD in patients with MPO-ANCA-positive MPA who underwent both chest imaging and lung biopsy at diagnosis.

Several findings were obtained from this study. In terms of

Table 3. Agreement on the Presence of ILD between Radiological and Histological Results in Patients with MPA

Patient number	ILD on chest imaging	Radiology pattern	Methods for lung biopsy	Histologically confirmed ILD	Agreement*
#1	Yes	Non-UIP (reticulation only)	Transbronchial lung biopsy	No	Discordance
#2	Yes	UIP	Transbronchial lung biopsy	No	Discordance
#3	Yes	OP (consolidation)	Transbronchial lung biopsy	Yes	
#4	Yes	UIP	Transbronchial lung biopsy	No	Discordance
#5	No		Transbronchial lung biopsy	No	
#6	No		Transbronchial lung biopsy	No	
#7	No		Transbronchial lung biopsy	No	
#8	No		CT-guided lung biopsy	No	
#9	No		Transbronchial lung biopsy	No	
#10	No		Transbronchial lung biopsy	No	
#11	Yes	UIP	Wedge resection	Yes	
#12	No		Wedge resection	Yes	Discordance
#13	Yes	UIP	Wedge resection	Yes	
#14	Yes	UIP	Transbronchial lung biopsy	No	Discordance
#15	Yes	DIP+emphysema	Wedge resection	Yes	
#16	No		Wedge resection	No	
#17	No		Transbronchial lung biopsy	No	
#18	Yes	UIP	Bullectomy	No	Discordance
#19	Yes	non-UIP (reticulation only)	CT-guided lung biopsy	No	Discordance
#20	No		Transbronchial lung biopsy	No	
#21	No		CT-guided lung biopsy	No	
#22	No		Transbronchial lung biopsy	No	
#23	No		Endobronchial biopsy	No	
#24	No		Transbronchial lung biopsy	No	

MPA, microscopic polyangiitis; ILD, interstitial lung disease; GN, glomerulonephritis; CT, computed tomography; UIP, usual interstitial pneumonia; DIP, desquamative interstitial pneumonia; OP, organising pneumonia.
*Agreement means the concordance or discordance on the presence of ILD between chest imaging and lung biopsy results.

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radiological findings, 10 of the 24 patients exhibited ILD on chest imaging, whereas in terms of histological findings, 5 of the 24 patients showed pathological findings consistent with ILD. Second, 4 of the 10 patients with ILD on chest imaging exhibited histological features consistent with those of ILD on lung biopsy, resulting in a discordance rate of 60% in the presence of ILD. Third, only 1 of the 14 patients without ILD on chest imaging showed histological features consistent with ILD on lung biopsy, resulting in a concordance rate of up to 92.9% in the absence of ILD. Accordingly, the negative predictive value of non-ILD observed on chest imaging for histologically confirmed ILD was 92.9%, whereas the positive predictive value for radiologically confirmed ILD was only 40%. Therefore, we suggest that when ILD is observed on chest imaging, the classification of MPA should be made based on the extrapulmonary clinical manifestations of MPA, and when the diagnosis is difficult, lung biopsy can be considered. However, we suggest that when ILD is not observed on chest imaging and lung lesions do not require lung biopsy for differential diagnosis, lung biopsy for the diagnosis of MPA alone may not be recommended.

Among the 10 patients who exhibited ILD on chest imaging, 5, 3, 1, and 1 underwent transbronchial lung biopsy, wedge resection, bullectomy, and CT-guided lung biopsy, respectively. Six of the 10 cases showed discordance between radiological (consistent with ILD) and histological (inconsistent with ILD) findings. We deduced that this discordance might be due to differences in lung biopsy methods. In clinical practice, the choice of method or site of lung biopsy is often based on clinical conditions. Although surgical lung biopsy is currently considered the best method of lung biopsy for ILD evaluation, transbronchial lung biopsy is also considered as an alternative method and is widely used.[16-18] In this study, among the 4 patients with radiological ILD on chest imaging and histologically confirmed ILD on lung biopsy (Patients #3, 11, 13, and 15), 3 who underwent wedge resection were diagnosed with UIP which can be detected only by surgical lung biopsy, and the remaining patient, who underwent transbronchial lung biopsy, was diagnosed with organising pneumonia, which can be confirmed by both surgical and transbronchial lung biopsy. Conversely, among the 6 patients with radiological ILD on chest imaging and without histologically confirmed ILD (Patients #1, 2, 4, 14, 18, and 19), 4, 1, and 1 underwent transbronchial lung biopsy, bullectomy, and CT-guided lung biopsy, respectively. Four patients who underwent transbronchial lung biopsy exhibited usual or non-specific interstitial pneumonia patterns on chest imaging. Since these lung lesions were peripherally located in the lungs, a surgical lung biopsy might have been needed to confirm the histological diagnosis of ILD.

In this study, the concordance rate between the radiological and histological findings of ILD was only 40% in patients with ILD on chest imaging. Therefore, we raised the following question: Is a lung biopsy really necessary for the classification of MPA in patients with ILD on chest imaging? Idiopathic pulmonary fibrosis is the most common idiopathic ILD to date.[19] Hypersensitivity pneumonitis and sarcoidosis are also considered as frequent causes of ILD, with ethnic or geographic differences.[20] Therefore, idiopathic pulmonary fibrosis should be understood as a comprehensive disease group with a broader spectrum than MPA in clinical settings.[21,22] In this study, patient #15 showed ILD on chest imaging, and histological ILD was confirmed through surgical lung biopsy.

According to the 2022 ACR/EULAR criteria for MPA, the patient achieved a total score of 9 and could thus be classified as having MPA. However, there is a patient who was a current heavy smoker (>30 pack-years) and exhibited a histological diagnosis of DIP, which is associated with environmental exposure, especially smoking.[23] In this case, we could not conclude that ILD was definitively associated with the clinical course of MPA; it is more likely attributable to smoking. Since this patient did not fulfil other criteria for MPA, if ILD had not been recognised as a clinical symptom of MPA, the patient could not have been reclassified as having MPA.

The advantage of this study is that it is the first to investigate the concordance rate between chest imaging and lung biopsy results for ILD in patients with MPO-ANCA-positive MPA who underwent both chest imaging and lung biopsy at diagnosis and to compare its clinical utility with lung biopsy.

This study has several limitations. The most critical limitation is the absence of results from PFT performed close to the HRCT scan day. This is because PFT can provide important clues for determining the presence of the disease, not only the radiological abnormalities.[21] Additionally, the number of study subjects was not large enough to generalise and apply the results of this study to MPO-ANCA-positive patients suspected of having MPA in clinical practice. Second, owing to the small number of patients with ILD and the retrospective design, it was not possible to perform a subgroup analysis of the contribution to MPA classification according to ILD patterns, such as UIP and non-UIP. The lung biopsy may not have been performed using the same method or for the same purposes, which is a limitation of retrospective analysis that may have resulted in the low reliability of the study results. Case #18 showed radiologic and histologic discordance even with the surgical lung biopsy result; the reason was that the purpose of the biopsy was not for diagnosis, but for the treatment of pneumothorax. These suggest that if the sample was acquired from a non-target lesion, surgical lung samples could not diagnose or exclude the ILD, and the histologic report should always be interpreted with clinical and radiologic context. It is believed that a prospective future study with more patients will provide more reliable information on the clinical significance of ILD on chest imaging, not only in classifying MPA but also in making a differential diagnosis in patients suspected of having MPA.

This study demonstrated that in patients with MPO-ANCA positivity and no extrapulmonary involvement, the evaluation

of ILD should be carefully evaluated under multidisciplinary discussion: interpretation of radiology results, decision of lung biopsy method, and interpretation of histologic reports. Especially in case of the absence of radiologic evidence of ILD, a multidisciplinary approach is recommended to determine the need for additional diagnostic assessment and to inform decisions regarding the indication and optimal modality for lung biopsy. The high concordance rate of ILD observed on chest imaging and surgical lung biopsy suggests that chest imaging could substitute for surgical lung biopsy in the diagnosis of ILD.

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AUTHOR CONTRIBUTIONS

Conceptualization: Hyunsue Do and Ala Woo. Data curation: Ala Woo, Hyunsue Do, and Sang-Won Lee. Formal analysis: Hyunsue Do and Ala Woo. Funding acquisition: Sang-Won Lee. Investigation: Yong-Beom Park. Methodology: Ala Woo, Hyunsue Do, and Sang-Won Lee. Project administration: Ala Woo and Sang-Won Lee. Resources: Sang-Won Lee. Software: Hyunsue Do. Supervision: Yong-Beom Park, Ala Woo, and Sang-Won Lee. Validation: Ala Woo and Sang-Won Lee. Visualization: Hyunsue Do and Ala Woo. Writing—original draft: Ala Woo, Hyunsue Do, and Sang-Won Lee. Writing—review & editing: Ala Woo, Hyunsue Do, and Sang-Won Lee. Approval of final manuscript: all authors.

ORCID iDs

Hyunsue Do https://orcid.org/0000-0002-9550-1048
Yong-Beom Park https://orcid.org/0000-0003-4695-8620
Ala Woo https://orcid.org/0000-0002-8818-6115
Sang-Won Lee https://orcid.org/0000-0002-8038-3341

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