Clinical utility of ^{18}F-FDG PET/CT in patients with microscopic polyangiitis and interstitial lung disease: a retrospective cohort study

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Abstract

Objective

We investigated the diagnostic and prognostic value of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for interstitial lung disease (ILD) in patients with microscopic polyangiitis (MPA).

Methods

In this single-centre observational study, 61 patients with MPA who underwent high-resolution computed tomography (HRCT) and ^{18}F-FDG PET/CT were included. ILD diagnosis was based on HRCT. ^{18}F-FDG uptake in the lung parenchyma was assessed as a binary variable (present/absent). Diagnostic performance was evaluated by sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The prognostic value was determined by Δ (1-year-baseline; positive=improvement) in forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) using multivariable linear regression models.

Results

^{18}F-FDG uptake showed high specificity and PPV (both 1.00) but limited sensitivity (0.63) and NPV (0.26) for ILD detection. Patients with ^{18}F-FDG uptake demonstrated significantly greater Δ in FVC (β=8.26 [2.87–13.64], p=0.004) and DLCO (β=7.38 [0.06–14.69], p=0.048) compared with those without uptake. The prognostic value of ^{18}F-FDG uptake was greater than that of the ILD pattern determined by HRCT (usual interstitial pneumonia [UIP] vs. non-UIP). While non-UIP patterns were associated with favourable Δ in FVC (β=8.02 [0.66–15.38], p=0.034), they were not associated with significant changes in DLCO (β=0.66 [-8.83–10.16], p=0.885).

Conclusion

^{18}F-FDG PET/CT demonstrated high specificity but limited sensitivity for detecting ILD in MPA, limiting its use as a screening tool. However, given its prognostic value, ^{18}F-FDG PET/CT could be considered as a complementary imaging modality may aid prognostic stratification in MPA-associated ILD.

Key words

^{18}F-fluorodeoxyglucose positron emission tomography, interstitial lung disease, microscopic polyangiitis, prognosis

Clinical and Experimental Rheumatology 2026; **44**: 758-766.

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Received on September 9, 2025; accepted in revised form on November 3, 2025.

Funding: this study was funded by a faculty research grant of Yonsei University College of Medicine, Seoul, Republic of Korea (6-2023-0155), Eisai Korea Inc. Seoul, Republic of Korea (4-2024-0700), Yuhan Corporation, Seoul, Republic of Korea, as part of their "2024 Investigator Initiated Translation Research Program" (4-2025-0044) and Samsung Bioepis Co., Ltd., Incheon, Republic of Korea (4-2025-1066). The funder was not involved in the study design, collection, analysis, interpretation of data, the writing of this article, or the decision to submit it for publication.

Competing interests: none declared.

Introduction

Microscopic polyangiitis (MPA) is a subtype of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, characterised by necrotising inflammation of small- to medium-sized vessels, which can affect multiple organs (1, 2). Among these, the lungs are commonly involved, with approximately 50–65% of patients experiencing pulmonary manifestations (3, 4). Specifically, interstitial lung disease (ILD) is the most frequent type of lung involvement in MPA, occurring in 25-50% of affected individuals (3, 5, 6). Importantly, the presence of ILD in MPA significantly worsens long-term prognosis, with affected patients having a 2- to 4-fold higher risk of mortality compared to those without ILD (5, 7, 8). Therefore, careful evaluation and management of ILD are crucial in patients with MPA.

^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) is a non-invasive and sensitive imaging modality that detects inflammation by capturing increased glucose metabolism in activated inflammatory cells, such as neutrophils, lymphocytes, and macrophages. While ^{18}F-FDG PET/CT is widely used to assess disease activity in large-vessel vasculitis (9, 10), its utility in ANCA-associated vasculitis has been less extensively studied. In a small case series involving 10 patients with granulomatosis with polyangiitis, 4 with MPA, and 2 with eosinophilic granulomatosis with polyangiitis, ^{18}F-FDG PET/CT accurately localised organ involvement in patients with granulomatosis with polyangiitis, except for the nervous system, eyes, and skin (11). However, due to the limited number of MPA cases, conclusions regarding its clinical utility in MPA could not be drawn, highlighting the need for further investigation (11). In particular, the role of ^{18}F-FDG PET/CT in evaluating ILD in patients with MPA remains unclear.

Although high-resolution computed tomography (HRCT) is the gold standard imaging modality for ILD (12), several studies suggest that ^{18}F-FDG PET/CT may play a complementary role by providing information on ongoing inflammation and potential prognosis (13-15). Indeed, ^{18}F-FDG uptake in lung parenchyma has been reported in patients with idiopathic pulmonary fibrosis (IPF), suggesting a potential diagnostic role of ^{18}F-FDG PET/CT in IPF (16, 17). Regarding systemic sclerosis-associated ILD, studies have reported that ^{18}F-FDG uptake in lung parenchyma was higher in patients with ILD than in those without ILD (18, 19). Moreover, a study assessing ^{18}F-FDG PET/CT in patients with systemic sclerosis-associated ILD demonstrated its ability to differentiate ILD-affected regions from unaffected lung tissue, suggesting its potential diagnostic value (20). These findings support its potential diagnostic value in systemic sclerosis-associated ILD 18-20).

Furthermore, studies have shown that ^{18}F-FDG uptake, as assessed by standardised uptake value $(SUV)_{max}$ and SUV_{mean}, correlated with disease severity, and high target-to-backgroud ratio (TBR) was associated with mortality in patients with IPF, suggesting the role of ^{18}F-FDG PET/CT in evaluating ILD severity and predicting prognosis (21, 22). In patients with systemic sclerosis-associated ILD, high SUVmax, SUVmin, and TBR have shown to be associated with higher risk of mortality, suggesting the prognostic role of ^{18}F-FDG PET/CT also in patients with systemic sclerosis-associated ILD (23).

Given the limited clinical data on the use of ^{18}F-FDG PET/CT in MPA and growing evidence supporting its role in ILD evaluation, this study aimed to investigate the clinical utility of ^{18}F-FDG PET/CT in assessing ILD in patients with MPA. Specifically, we evaluated the diagnostic performance of ^{18}F-FDG PET/CT in detecting ILD in MPA and explored its potential prognostic significance.

Methods

Study population

Participants were selected from the Severance Hospital ANCA-associated Vasculitides (SHAVE) cohort, a prospective, single-centre cohort comprising Korean patients diagnosed with ANCA-associated vasculitis. Detailed information on the SHAVE cohort has been published previously (24). From this cohort, patients who met the 2022 American College of Rheumatology/ European Alliance of Associations for Rheumatology classification criteria for MPA (25) were initially screened (n=186). Among these, those who had undergone both HRCT and ^{18}F-FDG PET/CT between 2015 and 2024 were selected (n=62). All ^{18}F-FDG PET/CT scans were performed as part of routine clinical care for diagnostic evaluation, such as malignancy exclusion, and fever focus evaluation. One patient was excluded due to a concurrent pneumonia diagnosis at the time of PET/CT, leaving 61 patients with MPA included in the final analysis (Fig. 1).

The clinical data collected included age at MPA diagnosis, sex, smoking history, ANCA profile, organ involvement distribution, forced vital capacity (FVC) and diffusing capacity of the lung for carbon monoxide (DLCO) at ILD diagnosis, FVC and DLCO 1 year post-ILD diagnosis, cumulative glucocorticoid (GC) dose during the first year after ILD diagnosis, and the use of immunosuppressive agent (cyclophosphamide, mycophenolate mofetil, azathioprine, tacrolimus, rituximab, and methotrexate) and antifibrotic therapy (pirfenidone). As ^{18}F-FDG PET/CT scans were performed between 2015 and 2024, a relatively long period, some variation in management protocols, particularly regarding the use of rituximab, may have occurred. Data are presented according to the STROBE checklist (See online Supplementary file).

Ethics

This study was approved by the Institutional Review Board (IRB) of the Severance Hospital, Seoul, Korea (IRB no. 4-2020-1071) and was conducted in accordance with the Declaration of Helsinki. Due to the retrospective design and the use of anonymised patient data, written informed consent was waived.

Diagnosis of ILD

The diagnosis of ILD was based on HRCT findings. ILD patterns were classified as either usual interstitial pneumonia (UIP) or non-UIP, according to the HRCT.

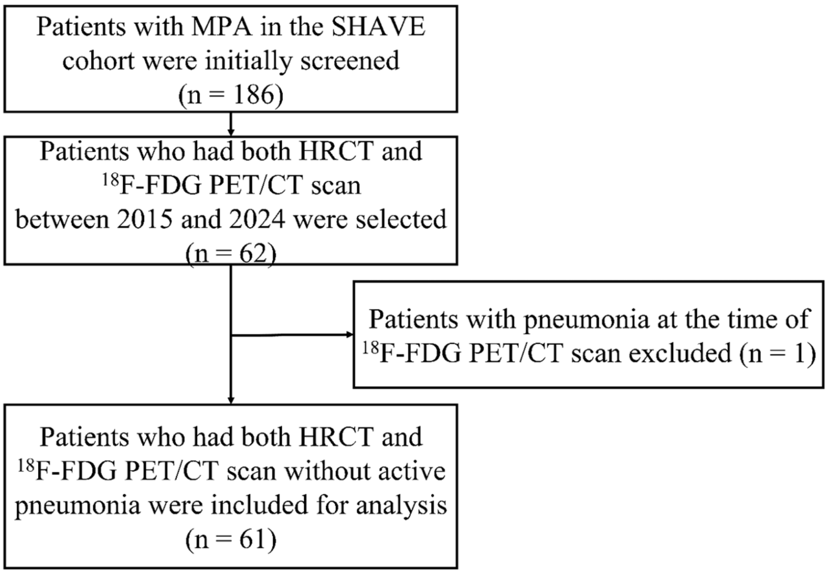

Fig. 1. Flowchart of study population selection.
FDG: fluorodeoxyglucose; HRCT: high-resolution computed tomography; MPA: microscopic polyangiitis; PET/CT: positron emission tomography/computed tomography; SHAVE: severance hospital ANCA-associated vasculitides.

^{18}F-FDG PET/CT

^{18}F-FDG PET/CT was performed to assess lung inflammation within 3 months of HRCT. Scans were obtained using dedicated scanners (Discovery STE [GE Healthcare] or Biograph 40 TruePoint [Siemens Medical Systems]), following previously established protocols (26). Patients fasted for six hours before imaging, and the blood glucose threshold was $<$140 mg/dL. The administered dose of ^{18}F-FDG was 5.5 MBq/kg, and the scan was performed 60 minutes after injection. To minimise motion and respiratory artifacts, patients were instructed to maintain shallow, steady breathing throughout the scan. All images were reconstructed using an ordered-subset expectation-maximisation algorithm incorporating attenuation correction.

The ^{18}F-FDG PET/CT results were analysed as a binary variable (^{18}F-FDG uptake in lung parenchyma: yes or no), which was based on the official reading by a single experienced nuclear medicine physician. The official reading was recorded as a binary variable (presence or absence of uptake), rather than semi-quantitatively. The evaluation included all parenchymal areas, irrespective of honeycombing or reticulation. The reader was not blinded to HRCT and clinical data.

Prognosis

The prognosis was assessed based on pulmonary function changes over the year following ILD diagnosis. Specifically, changes in FVC and DLCO from baseline to 1 year were evaluated. Δ was defined as (value at 1-year)–(value at baseline), with positive indicating improvement. The proportion of patients achieving minimal clinically important differences (MCID) for % predicted FVC and % predicted DLCO, defined as a change of $\geq$5%, was also assessed.

Statistical analyses

Descriptive analysis was used to summarise patient characteristics. Continuous variables with normal and non-normal distributions were presented as mean±standard deviation and median (interquartile range), respectively. The normality of continuous variables was assessed using the Shapiro-Wilk test. Categorical variables were presented as frequencies (%). For comparisons between two groups, the independent t-test or Mann-Whitney U-test was used for continuous variables with normal or non-normal distributions, respectively. Categorical variables were compared using either the chi-square test or Fisher's exact test, as appropriate. The diagnostic performance of ^{18}F-FDG PET/

Table I. Characteristics of 61 patients with MPA.

Characteristics	n=61
Demographics	
Age, year, mean±SD	65.7 ± 11.0
Male sex, n (%)	29 (47.5)
Ever-smoker, n (%)	2[a] (3.3)
Vasculitis features	
ANCA profile, n (%)	
MPO-ANCA (or P-ANCA) positive	60 (98.4)
PR3-ANCA (or C-ANCA) positive	4 (6.6)
Both ANCA positive	4 (6.6)
Both ANCA negative	1 (1.6)
Organ involvement, n (%)	
General	31 (50.8)
Cutaneous	8 (13.1)
Mucous and ocular	3 (4.9)
Otorhinolaryngological	17 (27.9)
Pulmonological	54 (88.5)
Cardiovascular	7 (11.5)
Gastrointestinal	3 (4.9)
Renal	42 (68.9)
Nervous system	16 (26.2)
Lung physiology	
Presence of ILD, n (%)	54 (88.5)
Isolated ILD, n (%[b])	7 (13.0)
Other organs involved, n (%[b])	47 (87.0)
Pattern of ILD, n (%[b])	
UIP	38 (70.4)
Non-UIP	16 (29.6)
Pulmonary function tests, mean ± SD	
FVC, L	2.93 ± 0.88
FVC, % predicted	79.0 ± 14.2
DLCO, % predicted	68.4 ± 17.1
Antifibrotic ever-use, n (%)	7 (11.5)
^{18}F-FDG uptake, n (%)	34 (55.7)

ANCA: antineutrophil cytoplasmic antibody; C: cytoplasmic; DLCO: diffusing capacity of the lung for carbon monoxide; FDG: fluorodeoxyglucose; FVC: forced vital capacity; ILD: interstitial lung disease; MPA: microscopic polyangiitis; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; UIP: usual interstitial pneumonia.

[a] One patient was an ex-smoker with a 15.5 pack-year smoking history, and the other was an ex-smoker with a 12 pack-year smoking history.

[b] Calculated using 54 patients with ILD as the denominator.

CT for detecting ILD was evaluated using HRCT as the gold standard. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), and negative likelihood ratio (LR-) with their respective 95% confidence intervals (CIs) were estimated. Multivariable linear regression analyses adjusted for age, sex, smoking, baseline FVC/DLCO, HRCT pattern (UIP *vs.* non-UIP), myeloperoxidase (MPO)-ANCA positivity, extra-pulmonary involvement, antifibrotic use, cumulative GC dose, and immunosuppressive agent use were used to assess associations between ^{18}F-FDG uptake and Δ in FVC and DLCO. Sensitivity analyses in different subgroups of patients (patients with a UIP pattern, patients with a non-UIP pattern, and patients excluding those with isolated ILD) were performed. There were no missing data in the 1-year FVC and DLCO. $p<0.05$ was considered statistically significant. All analyses were conducted using SPSS software (v. 28.0; IBM Corporation, Armonk, NY, USA).

Results

Patients' characteristics

The characteristics of the study population are summarised in Table I. The mean age at diagnosis of MPA was 65.7±11.0 years, and 47.5% of the patients were men. MPO-ANCA (or perinuclear-ANCA) was positive in 98.4% of the patients. Among the 61 patients included in the study, ILD was diagnosed in 54 (88.5%). At the time of ILD diagnosis, 13.0% of patients had isolated ILD, while 87.0% had involvement of additional organs. A UIP pattern was observed on HRCT in 38 patients (70.4%), whereas 16 patients (29.6%) exhibited a non-UIP pattern. The mean FVC was 2.93±0.88 L, with a % predicted FVC of 79.0±14.2% and a % predicted DLCO of 68.4±17.1% at the time of ILD diagnosis. Increased ^{18}F-FDG uptake was observed in 34 patients (55.7%).

Diagnostic performance of ^{18}F-FDG uptake for detecting ILD

The diagnostic performance of ^{18}F-FDG uptake for detecting ILD in patients with MPA is presented in Table II. The sensitivity, specificity, PPV, and

Table II. Diagnostic accuracy of ^{18}F-FDG uptake.

	No ILD, n	ILD, n	Diagnostic accuracy of ^{18}F-FDG uptake					
No ^{18}F-FDG uptake, n	7	20	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	LR+ (95% CI)	LR– (95% CI)
^{18}F-FDG uptake, n	0	34	0.630	1.000	1.000	0.259	N/A	0.370
Prevalence of ILD, (%)	88.5		(0.487–0.757)	(0.590–1.000)	(0.897–1.000)	(0.198–0.331)		(0.260–0.520)

CI: confidence interval; FDG: fluorodeoxyglucose; ILD: interstitial lung disease; LR: likelihood ratio; NPV: negative predictive value; PPV: positive predictive value.

Table III. Comparison of patients with MPA-associated ILD without and with ^{18}F-FDG uptake.

	No ^{18}F-FDG uptake (n=20)	^{18}F-FDG uptake (n=34)	*p*-value
Demographics			
Age, year, mean±SD	64.4 ± 14.4	66.9 ± 9.2	0.431
Male sex, n (%)	8 (40.0)	19 (55.9)	0.260
Ever-smoker, n (%)	1 (5.0)	1 (2.9)	>0.999
ANCA profile, n (%)			
MPO-ANCA (or P-ANCA) positive	20 (100.0)	33 (97.1)	>0.999
PR3-ANCA (or C-ANCA) positive	1 (5.0)	3 (8.8)	>0.999
Both ANCA positive	1 (5.0)	3 (8.8)	>0.999
Both ANCA negative	0 (0.0)	1 (2.9)	>0.999
Involvement of organs, n (%)			
Isolated ILD	1 (5.0)	6 (17.6)	0.239
Other organs involved	19 (95.0)	28 (82.4)	0.239
Pattern of ILD, n (%)			
UIP	16 (80.0)	22 (64.7)	0.235
Non-UIP	4 (20.0)	12 (35.3)	0.235
Pulmonary function tests			
FVC, L, mean±SD	2.69 ± 0.65	2.83 ± 0.95	0.631
FVC, % predicted, mean±SD	79.6 ± 14.1	76.1 ± 14.8	0.468
DLCO, % predicted, mean±SD	68.4 ± 16.6	65.2 ± 19.0	0.597
Δ[a] FVC, L, mean±SD (95% CI)	-0.09 ± 0.16 (-0.19–0.01)	0.12 ± 0.23 (0.02–0.22)	0.012
Δ[a] FVC, % predicted, mean±SD (95% CI)	-4.6 ± 7.0 (-8.7–-0.5)	4.2 ± 6.5 (1.3–7.1)	0.002
Δ[a] DLCO, % predicted, mean±SD (95% CI)	-6.7 ± 9.8 (-12.5–0.9)	1.6 ± 9.4 (-2.9–6.1)	0.033
MCID for FVC, % predicted, n (%)	0 (0.0)	16 (47.1)	<0.001
MCID for DLCO, % predicted, n (%)	2 (10.0)	12 (35.3)	0.041
Medications used			
Glucocorticoids, mg[b], median (IQR)	4923.8 (2588.8–7349.1)	3980.1 (2067.5–6595.0)	0.410
Cyclophosphamide, n (%)	8 (40.0)	9 (26.5)	0.301
Mycophenolate mofetil, n (%)	11 (55.0)	16 (47.1)	0.573
Azathioprine, n (%)	5 (25.0)	11 (32.4)	0.568
Tacrolimus, n (%)	1 (5.0)	1 (2.9)	>0.999
Rituximab, n (%)	4 (20.0)	9 (26.5)	0.746
Methotrexate, n (%)	1 (5.0)	2 (5.9)	>0.999
Pirfenidone, n (%)	3 (15.0)	4 (11.8)	>0.999

ANCA: antineutrophil cytoplasmic antibody; C: cytoplasmic; DLCO: diffusing capacity of the lung for carbon monoxide; FDG: fluorodeoxyglucose; FVC: forced vital capacity; ILD: interstitial lung disease; MCID: minimal clinically important differences; MPA: microscopic polyangiitis; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; UIP:, usual interstitial pneumonia.

[a] Δ=(1-year–baseline; positive=improvement).

[b] Cumulative dose of prednisolone or its equivalent.

NPV were 0.630 (0.487–0.757), 1.000 (0.590–1.000), 1.000 (0.897–1.000), and 0.259 (0.198–0.331), respectively. The LR+ was not calculable because the specificity was 1.000, and the LR- was 0.370 (0.260–0.520). These findings indicate high specificity and PPV but limited sensitivity and NPV.

Comparison of patients without and with ^{18}F-FDG uptake

To assess the prognostic value of ^{18}F-FDG uptake for Δ in pulmonary function, we categorised patients with ILD into two groups based on the absence or presence of uptake. Their clinical outcomes are shown in Table III. The distribution of UIP and non-UIP patterns did not differ significantly between the groups (*p*=0.235). Similarly, baseline pulmonary function, including absolute FVC (*p*=0.631), % predicted FVC (*p*=0.468), and % predicted DLCO (*p*=0.597), was comparable between groups. However, compared with those without ^{18}F-FDG uptake, patients with ^{18}F-FDG uptake showed significantly more favourable Δ in pulmonary function. This included improvements in absolute FVC (-0.09±0.16 L *vs.* 0.12±0.23 L, p=0.012), % predicted FVC (-4.6±7.0% *vs.* 4.2±6.5%, *p*=0.002), and % predicted DLCO (-6.7±9.8% *vs.* 1.6± 9.4%, *p*=0.033). In addition, compared with patients without ^{18}F-FDG uptake, those with uptake showed a significantly higher proportion of patients achieving MCID for % predicted FVC (absolute difference: 0.0% *vs.* 47.1%, relative difference: 19.800 [95% CI 1.252–313.162], *p*<0.001) and % predicted DLCO (10.0% *vs.* 35.3%, relative difference: 3.529 [95% CI 0.878–14.189], *p*=0.041). The medications administered during the first year after ILD diagnosis did not differ between the two groups.

Comparison of patients with non-UIP pattern and UIP pattern

We next investigated whether ILD patterns on HRCT also have prognostic significance. Patients with ILD were divided into two groups based on HRCT findings: those with a non-UIP pattern and those with a UIP pattern. Clinical outcomes were compared between the groups, and the results are presented in Table IV. The proportion of patients with ^{18}F-FDG uptake did not differ significantly between the groups (75.0% *vs.* 57.9%, *p*=0.235). Baseline pulmonary function, including absolute FVC (*p*=0.499), % predicted FVC (*p*=0.365), and % predicted DLCO (*p*=0.863), was comparable between the groups. However, the Δ in absolute FVC (0.23±0.27 L *vs.* 0.00±0.20 L, *p*=0.030) and % predicted FVC (6.8±8.6% *vs.* -0.5±7.1%, *p*=0.037) were significantly more favourable in patients with a non-UIP pattern than in those with a UIP pattern. However, no significant differences were observed in the Δ in % predicted DLCO between the two groups (-5.8±10.1% *vs.* -0.6±10.2%, *p*=0.135). Likewise, the proportion of patients achieving MCID for % predicted FVC (absolute difference: 50.0% *vs.* 21.1%, relative difference: 2.375 [95% CI 1.081–5.217], *p*=0.033) was significantly higher in patients with a non-UIP pattern than in those with a UIP pattern, whereas the proportion of patients achieving MCID for % predicted DLCO did not differ between the two groups (absolute difference: 18.8% *vs.* 28.9%, relative difference: 0.648 [95% CI 0.208–2.016] *p*=0.515). The medications used during the first year following ILD diagnosis did not differ between the two groups.

Table IV. Comparison of patients with MPA-associated ILD according to the ILD pattern.

	Non-UIP (n=16)	UIP (n=38)	*p*-value
Demographics			
Age, year, mean±SD	66.3 ± 14.2	65.9 ± 10.1	0.917
Male sex, n (%)	9 (56.3)	18 (47.4)	0.551
Ever-smoker, n (%)	1 (6.3)	1 (2.6)	0.509
ANCA profile, n (%)			
MPO-ANCA (or P-ANCA) positive	16 (100.0)	37 (97.4)	>0.999
PR3-ANCA (or C-ANCA) positive	3 (18.8)	1 (2.6)	0.073
Both ANCA positive	3 (18.8)	1 (2.6)	0.073
Both ANCA negative	0 (0.0)	1 (2.6)	>0.999
Involvement of organs, n (%)			
Isolated ILD	0 (0.0)	7 (18.4)	0.090
Other organs involved	16 (100.0)	31 (81.6)	0.090
^{18}F-FDG uptake, n (%)	12 (75.0)	22 (57.9)	0.235
Pulmonary function tests			
FVC, L, mean±SD	2.6 ± 0.54	2.83 ± 0.91	0.499
FVC, % predicted, mean±SD	75.1 ± 4.3	78.1 ± 16.3	0.365
DLCO, % predicted, mean±SD	65.4 ± 15.4	66.6 ± 18.9	0.863
Δ[a] FVC, L, mean±SD (95% CI)	0.23 ± 0.27 (0.02–0.44)	0.00 ± 0.20 (-0.08–0.08)	0.030
Δ[a] FVC, % predicted, mean±SD (95% CI)	6.8 ± 8.6 (0.0–13.7)	-0.5 ± 7.1 (-3.4–2.3)	0.037
Δ[a] DLCO, % predicted, mean±SD (95% CI)	-5.8 ± 10.1 (-13.9–2.3)	-0.6 ± 10.2 (-4.8–3.7)	0.135
MCID for FVC, % predicted, n (%)	8 (50.0)	8 (21.1)	0.033
MCID for DLCO, % predicted, n (%)	3 (18.8)	11 (28.9)	0.515
Medications used			
Glucocorticoids, mg[b], median (IQR)	5451.3 (3363.0–8533.6)	3808.8 (1562.5–6595.0)	0.058
Cyclophosphamide, n (%)	7 (43.8)	10 (26.3)	0.208
Mycophenolate mofetil, n (%)	10 (62.5)	17 (44.7)	0.233
Azathioprine, n (%)	6 (37.5)	10 (26.3)	0.517
Tacrolimus, n (%)	1 (6.3)	1 (2.6)	0.509
Rituximab, n (%)	3 (18.8)	10 (26.3)	0.732
Methotrexate, n (%)	0 (0.0)	3 (7.9)	0.547
Pirfenidone, n (%)	0 (0.0)	7 (18.4)	0.090

ANCA: antineutrophil cytoplasmic antibody; C: cytoplasmic; DLCO: diffusing capacity of the lung for carbon monoxide; FDG: fluorodeoxyglucose; FVC: forced vital capacity; ILD: interstitial lung disease; MCID: minimal clinically important differences; MPA: microscopic polyangiitis; MPO: myeloperoxidase; P: perinuclear; PR3: proteinase 3; UIP: usual interstitial pneumonia.

[a] Δ=(1-year–baseline; positive=improvement).

[b] Cumulative dose of prednisolone or its equivalent.

Table V. Multivariable linear regression models for the 1-year changes in PFT according to ^{18}F-FDG uptake or ILD pattern.

	β (95% CI)	R^2	*p*-value
Δ FVC, L			
^{18}F-FDG uptake	0.197 (0.016–0.378)	0.468	0.034
Non-UIP pattern	0.240 (0.012–0.467)		0.040
Δ FVC, % predicted			
^{18}F-FDG uptake	8.256 (2.873–13.638)	0.597	0.004
Non-UIP pattern	8.020 (0.661–15.378)		0.034
Δ DLCO, % predicted			
^{18}F-FDG uptake	7.375 (0.064–14.686)	0.632	0.048
Non-UIP pattern	0.664 (-8.829–10.156)		0.885

Multivariable model adjusted for age, sex, smoking, baseline FVC/DLCO, HRCT pattern (UIP *vs.* non-UIP), MPO-ANCA, extra-pulmonary involvement, antifibrotic use, cumulative GC dose, and immunosuppressive agent use.

DLCO: diffusing capacity of the lung for carbon monoxide; FDG: fluorodeoxyglucose; FVC: forced vital capacity; GC: glucocorticoid; HRCT: high-resolution computed tomography; ILD: interstitial lung disease; MPO-ANCA: myeloperoxidase-antineutrophil cytoplasmic antibody; PFT: pulmonary function test; UIP: usual interstitial pneumonia.

^{18}F-FDG uptake, HRCT patterns and outcomes

The results of the multivariable linear regression analyses are presented in Table V. The presence of ^{18}F-FDG uptake was significantly associated with favourable Δ in absolute FVC (β=0.197 [95% CI 0.016–0.378], *p*=0.034) and % predicted FVC (β=8.256 [95% CI 2.873–13.638], *p*=0.004). Similarly, a non-UIP pattern was significantly associated with favourable Δ in absolute FVC (β=0.240 [95% CI 0.012–0.467], *p*=0.040) and % predicted FVC (β=8.020 [95% CI 0.661–15.378], *p*=0.034). Moreover, ^{18}F-FDG uptake was also significantly associated with favourable Δ in % predicted DLCO (β=7.375 [95% CI 0.064–14.686], *p*=0.048), whereas the non-UIP pattern was not (β=0.664 [95% CI -8.829–10.156], *p*=0.885).

The sensitivity analyses (Table VI) yielded favourable outcomes in patients with ^{18}F-FDG uptake among those with a UIP pattern and among those excluding isolated ILD, consistent with the main analysis. In patients with a non-UIP pattern, a similar trend toward favourable outcomes was observed, although statistical significance was lost, likely owing to the small number of patients (n=16), as reflected by the wide 95% CIs.

Discussion

In this study, we evaluated the diagnostic performance and prognostic value of ^{18}F-FDG PET/CT in detecting and monitoring the progression of ILD in patients with MPA. We found that ^{18}F-FDG uptake demonstrated high specificity and PPV for detecting ILD, although its sensitivity and NPV were limited. Notably, the presence of ^{18}F-FDG uptake was associated with favourable changes in pulmonary function over 1 year, suggesting a potential role as a prognostic marker. While the ILD pattern on HRCT, particularly the non-UIP pattern, was also associated

Table VI. Sensitivity analyses: association between ^{18}F-FDG uptake and 1-year changes in PFT in different subgroups.

	β (95% CI)	R^2	*p*-value
Δ FVC, L			
^{18}F-FDG uptake (patients with a UIP pattern)	0.155 (-0.007–0.318)	0.151	0.060
^{18}F-FDG uptake (patients with a non-UIP pattern)	0.366 (-0.387–1.119)	0.313	0.249
^{18}F-FDG uptake (excluding patients with isolated ILD)	0.239 (0.038–0.440)	0.225	0.022
Δ FVC, % predicted			
^{18}F-FDG uptake (patients with a UIP pattern)	7.471 (2.196–12.747)	0.282	0.008
^{18}F-FDG uptake (patients with a non-UIP pattern)	10.600 (-14.627–35.827)	0.254	0.308
^{18}F-FDG uptake (excluding patients with isolated ILD)	9.592 (3.098–16.087)	0.310	0.006
Δ DLCO, % predicted			
^{18}F-FDG uptake (patients with a UIP pattern)	8.533 (0.083–16.984)	0.182	0.048
^{18}F-FDG uptake (patients with a non-UIP pattern)	19.400 (-2.063–40.863)	0.612	0.066
^{18}F-FDG uptake (excluding patients with isolated ILD)	8.800 (1.618–15.982)	0.246	0.019

DLCO: diffusing capacity of the lung for carbon monoxide; FDG: fluorodeoxyglucose; FVC: forced vital capacity; PFT: pulmonary function test; UIP: usual interstitial pneumonia.

with better outcomes, the prognostic value of ^{18}F-FDG PET/CT appeared to be more consistent. These findings support the potential clinical utility of ^{18}F-FDG PET/CT as a complementary imaging tool alongside HRCT in the management of MPA-associated ILD. To the best of our knowledge, this is the first study to evaluate the role of ^{18}F-FDG PET/CT in the diagnosis and prognosis of ILD in patients with MPA. Although the specificity (1.000 [95% CI 0.590–1.000]) and PPV (1.000 [95% CI 0.897–1.000]) of ^{18}F-FDG PET/CT for detecting ILD were excellent, the sensitivity (0.630 [95% CI 0.487–0.757]) and NPV (0.259 [95% CI 0.198–0.331]) were relatively low. These results indicate that while a positive ^{18}F-FDG uptake strongly supports the presence of ILD, a negative result does not reliably exclude the diagnosis. Therefore, ^{18}F-FDG PET/CT should not be used as a primary screening tool for ILD in patients with MPA. Instead, its utility may lie in serving as a complementary modality, particularly in cases where HRCT findings are inconclusive or when assessing systemic disease activity.

The prognostic significance of ^{18}F-FDG PET/CT was especially compelling. Patients with ^{18}F-FDG uptake demonstrated significantly greater improvements in both FVC and DLCO over a 1-year period. One possible interpretation is that physicians may have administered more intensive immunosuppressive treatment in response to observed ^{18}F-FDG uptake, potentially influencing outcomes. However, our data show no significant differences in cumulative glucocorticoid dose or use of immunosuppressive agents between patients with and without ^{18}F-FDG uptake, suggesting that the prognostic association is independent of treatment intensity. Notably, although not statistically significant, patients without ^{18}F-FDG uptake received higher cumulative doses of glucocorticoids and were more frequently treated with immunosuppressive agents such as cyclophosphamide and mycophenolate mofetil. This may be due to the numerically higher proportion of patients with extra-pulmonary involvement in this group. These findings suggest that the improved pulmonary outcomes observed in patients with ^{18}F-FDG uptake are unlikely to be attributed to treatment intensity. The ^{18}F-FDG uptake in fibrotic areas (such as reticulation and honeycombing) of ILD could be attributable to increased expression of glucose transporter-1 in inflammatory cells within these fibrotic areas, where ongoing inflammation and neovascularisation occur (16, 27). In other words, the presence of ^{18}F-FDG uptake in these fibrotic areas may reflect ongoing, potentially reversible inflammatory activity rather than irreversible fibrosis alone. This could explain the better response to immunosuppressive therapy in patients with ^{18}F-FDG uptake and support its role as a prognostic indicator in MPA-associated ILD. However, this mechanistic interpretation remains speculative, as alternative sources of ^{18}F-FDG uptake (fibroblast activity, infection, atelectatsis, etc.) and technical factors (partial volume, motion, etc.) may also contribute.

HRCT patterns are widely recognised as prognostic indicators in ILD (28-30). Consistent with previous literature (28-30), our findings show that a non-UIP pattern is associated with better 1-year FVC outcomes compared with a UIP pattern. However, this prognostic advantage did not extend to changes in DLCO. This discrepancy may be due to the fact that DLCO is influenced by a broader range of factors beyond structural changes alone, including parenchymal and vascular inflammation that affect alveolar-capillary membrane function, factors not fully captured by HRCT-based structural patterns (31, 32). In this context, ^{18}F-FDG uptake, which reflects underlying inflammatory activity in both the interstitial and vascular compartments (33, 34), may serve as a more comprehensive and reliable prognostic indicator for DLCO changes. Indeed, when comparing the prognostic performance of ^{18}F-FDG uptake and HRCT patterns, ^{18}F-FDG uptake demonstrated stronger associations not only with FVC but also with DLCO changes, as supported in the linear regression analyses. Specifically, a significant association with DLCO changes was found only for ^{18}F-FDG uptake and not for HRCT patterns. Collectively, these results suggest that ^{18}F-FDG PET/CT may provide more accurate prognostic information than HRCT alone in patients with MPA-associated ILD.

This study has some limitations. First, we used ^{18}F-FDG uptake as a binary variable rather than quantifying its intensity (*e.g.* SUV_{mean}/SUV_{max} or lung-to-blood pool TBR). Consequently, we could not assess whether higher uptake levels offer greater prognostic value. However, from a clinical perspective, binary classification may be more practical than quantitative assessment in real-world clinical settings. Second, due to the small number of non-ILD cases (n=7), specificity and PPV may be imprecise or inflated; that is, this study is underpowered for a precise specificity estimation. Third, although we adjusted for medications in the multivariable linear regression analyses, residual confounding by treatment selection cannot be fully excluded due to the retrospective design. Nevertheless, a comparison of medication use between the no-uptake and uptake groups revealed no significant differences. Additionally, although not statistically significant, certain immunosuppressive agents were more frequently used in the no-uptake group, suggesting that the prognostic value of ^{18}F-FDG uptake is likely independent of treatment intensity. Fourth, our study was conducted in a single-centre cohort of Korean patients. External validation in diverse populations is needed to generalise our findings.

In summary, ^{18}F-FDG PET/CT demonstrated high specificity and PPV for detecting ILD in patients with MPA, though its limited sensitivity and NPV reduce its utility as a screening tool. However, its prognostic value appears substantial, as ^{18}F-FDG uptake was associated with significant improvements in pulmonary function over 1 year, independent of treatment intensity. Compared with HRCT-based ILD patterns, ^{18}F-FDG uptake showed stronger prognostic performance, particularly in predicting changes in DLCO. These findings suggest that ^{18}F-FDG uptake may reflect ongoing, reversible inflammation and could help identify patients more likely to benefit from immunosuppressive therapy. Therefore, ^{18}F-FDG PET/CT may serve as a complementary imaging modality may aid prognostic stratification in MPA-associated ILD.

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