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Original Article

Profile of Patients with Rheumatoid Arthritis-Associated Interstitial Lung Disease: A Single-Center

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Abstract

Background: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is a well-described complication of rheumatoid arthritis (RA). The authors sought to describe the characteristics, treatment strategies, and outcomes of RA-ILD patients at 6 and 12 months.

Methods: Patients treated at the medical center between 2010 and 2019 with ICD9 and ICD10 codes for RA and interstitial lung disease (ILD) meeting American College of Rheumatology 1987 or 2010 ACR/European League Against Rheumatism classification criteria were considered for inclusion. The diagnosis of RA-ILD was based on clinical features, pulmonary function testing (PFT), and high-resolution computed tomography (HRCT) findings. Baseline demographics, body mass index , serologic status, tobacco use, PFT and HRCT findings, and RA-ILD treatments at 0, 6, and 12 months were extracted and analyzed.

Results: Forty-seven patients diagnosed with RA-ILD were included in this analysis. The median age at diagnosis was 64.7 years, and the median duration of follow-up was 30 months. Thirty-two patients (68.09%) had follow-up data available at 6 months and 27 (57.45%) had follow-up data at 12 months. Twenty-three (48.9%) patients received treatment for RA-ILD. Forty-three (90.6%) and 42 (88.9%) patients exhibited stability/improvement of RA-ILD at 6 and 12 months of follow-up, respectively. Progression of RA-ILD at 6 months was associated with tobacco use ($P = .025$); however, no specific variable was associated with RA-ILD progression at 12 months.

Conclusions: Patients with RA-ILD receiving treatment tend to show improvement or stability in lung disease at 6 and 12 months, although high attrition rate and short follow-up preclude finding of additional factors associated with ILD.

Trial registration: Not applicable.

Keywords: Rheumatoid arthritis, interstitial lung disease, disease progression

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Background

The age and sex-adjusted annual incidence of RA in the United States between 2005 and 2014 was 41/100 000 people, which is roughly in keeping with global trends during the same timeframe.[1,2] While inflammatory arthritis is by far the most common manifestation of RA, other extraarticular manifestations substantially impact the outcome of these patients. Interstitial lung disease (ILD) is one of the most serious extraarticular manifestations and carries a high degree of morbidity, mortality, and decreased quality of life among affected patients.[3]

The average prevalence of RA-ILD among RA patients in a systematic review from 2021 was found to range from 1.8% to 67%, with a median prevalence of 24.9%.[4] This variability is due in part to heterogeneous methods and definitions used to identify RA-ILD and limited sample sizes. Older age, male sex, duration of RA, and RF and ACPA positivity are well-established factors for the development and progression of RA-ILD.[5,6] Because of the relatively low prevalence of RA-ILD, most of the data regarding epidemiology, natural history, and treatment outcomes available are derived from small retrospective cohort studies and their meta-analyses.

RA-ILD is diagnosed based on clinical symptoms, radiographic findings, and pulmonary function testing. Radiographically, RA-ILD can exhibit a variety of patterns, however, usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP) are the most common.[7] Key imaging features include reticular patterns, peribronchovascular interstitial thickening, interlobular septal thickening, and traction bronchiectasis.[6,7] Pulmonary function tests (PFTs) typically demonstrate a restrictive pattern and decreased forced

vital capacity (FVC) and decreased diffusing capacity of the lungs for carbon monoxide (DLCO).[8,9]

The goal of managing RA-ILD is to halt progression, improve/stabilize pulmonary function, and optimize quality of life while minimizing the undesirable side effects of medications. However, corticosteroids, conventional synthetic and biologic disease-modifying antirheumatic drugs (csDMARDs and bDMARDs), and antifibrotic agents are the mainstay of medical therapy.[10] The csDMARDs methotrexate (MTX) and leflunomide (LEF) are well-recognized to stabilize PFTs and protect against morbidity and mortality in patients with RA-ILD.[11,12] Other agents such as mycophenolate mofetil, azathioprine, and cyclophosphamide have also been found to be effective.[13] The B-cell targeting agents rituximab (RTX) and abatacept have also been shown to be effective, though further data on the long-term safety and efficacy of these agents is needed.[14,15] Tumor necrosis factor (TNF) inhibitors were associated with progression of RA-ILD in earlier studies; however, more recent evidence suggests this is not the case but rather that they are less efficacious than other DMARDs.[16] The antifibrotic agents pirfenidone and nintedanib have also been employed in select refractory patients with variable results.[13] In addition to immune suppression, smoking cessation, and vaccination against respiratory pathogens are recommended in the management of RA-ILD. A multidisciplinary team of rheumatologists, pulmonologists, and radiologists is required to effectively diagnose and treat RA-ILD.

This study highlights the baseline characteristics, treatment exposure, and outcomes of patients with RA-ILD managed at a large academic medical center in the Deep South with a diverse patient population and documents their response to RA-ILD treatment at 6 and 12 months.

Main Points

- In this retrospective cohort study of 47 patients with rheumatoid arthritis-associated interstitial lung disease (RA-ILD), 90.6% and 88.9% exhibited stability/improvement of RA-ILD at 6 and 12 months of follow-up, respectively.
- Tobacco use was associated with the progression of RA-ILD at 6 months but not at 12 months of follow-up.
- Limited sample size and study attrition may have precluded the finding of additional factors associated with ILD.

Material and Methods

Study design

The authors conducted a retrospective study to identify patients with RA-ILD between January 2010 and December 2019 treated at the institution. The authors utilized the University of Alabama at Birmingham (UAB) i2b2 electronic health record (EHR) database to identify candidate patients with both an ICD9 and/or ICD10 code for RA (714.0, M05, and M06) and an ICD9 and/or ICD10 code for ILD (515, J84, J84.1, J84.9, and J84.8). These patients' EHRs were then manually reviewed for potential inclusion in the final study population. The study was conducted in compliance with the Helsinki Declaration and was

Table 1. Characteristics of Patients with Rheumatoid Arthritis and Interstitial Lung Disease

		Baseline, n=47	At 6 months, n=32 (68.09%)	At 12 months, n=28 (59.57%)
Sex	Male, n (%)	23 (48.9)	16 (50)	13 (46.4)
	Female, n (%)	24 (51.1)	16 (50)	15 (53.6)
Race	African American, n (%)	14 (29.8)	9 (28.1)	9 (32.1)
	Caucasian, n (%)	31 (66.0)	22 (68.8)	17 (60.7)
	Asian, n (%)	2 (4.3)	1 (3.1)	2 (7.1)
History of smoking	Never, n (%)	22 (46.8)	19 (59.4)	15 (53.6)
	Past or present, n (%)	25 (53.2)	13 (40.6)	13 (46.4)
GERD or using PPI	Yes, n (%)	32 (68.1)	23 (71.9)	19 (67.9)
	No, n (%)	11 (23.4)	7 (21.9)	6 (21.4)
	Missing, n (%)	4 (8.5)	2 (6.2)	3 (10.7)
History of lung disease other than ILD	No, n (%)	25 (53.2)	17 (53.1)	15 (53.6)
	Yes, n (%)	18 (38.3)	12 (37.5)	9 (32.1)
	Missing, n (%)	4 (8.5)	3 (9.4)	4 (14.3
Current treatment for ILD	Yes, n (%)	23 (48.9)	17 (53.1)	16 (57.1)
	No, n (%)	24 (51.1)	15 (46.9)	12 (42.9)
RF	Positive, n (%)	41 (87.2)	27 (84.4)	24 (85.7)
	Negative, n (%)	6 (12.8)	5 (15.6)	4 (14.3)
ACPA	Present, n (%)	41 (87.2)	28 (87.5)	23 (82.1)
	Absent, n (%)	6(12.8)	4 (12.5)	5 (17.9)
ACPA and RF	Both present, n (%)	38 (80.9)	26 (84.2)	22 (78.6)
	One present, n (%)	6 (12.8)	3 (9.4)	3 (10.7)
	None, n (%)	3 (6.4)	3 (9.4)	3 (10.7)
Lung imaging pattern	UIP, n (%)	21 (44.7)	16 (50.0)	15 (53.6)
	NSIP, n (%)	1 3(27.7)	9 (28.1)	8 (26.6)
	OP, n (%)	2 (4.3)	0 (0)	1 (3.6)
	Other, n (%)	11 (23.4)	7 (21.9)	4 (14.3)
Transbronchial lung biopsy h/o	No, n (%)	39 (83.0)	26 (81.2)	22 (78.6)
	Yes, n (%)	8 (17.0)	6 (18.8)	6 (21.4)
BMI (kg/m^2)	Number, median (IQR)	45 31.4 (26-36.6)	30 30.7 (26.3-34.4)	28 29.9 (25.8-34.5)
Duration of follow-up (months)	Number, median (IQR)	40 30.1 (18.3-46.5)	30 28 (15.7-39.3)	25 31.1 (20.4-48.7)

ACPA, anti-citrullinated protein antibodies; BMI, body mass index; COPD, chronic obstructive pulmonary disease; GERD, gastroesophageal reflux disease; h/o, History; ILD, interstitial lung disease; IQR, interquartile ranges; NSIP, nonspecific interstitial pneumonia; OP, organizing pneumonia; PPI, protein pump inhibitor; RF, rheumatoid factor; UIP, usual interstitial pneumonia.

approved by the Institutional Review Board (IRB) at the UAB.

Ethics Approval and Informed Consent

This study was conducted in accordance with the principles of the Declaration of Helsinki and received approval from the IRB at the University of Alabama with the number IRB-300004585 . All procedures involving human participants adhered to the ethical standards of the institutional and national research committees. Given the retrospective nature of the study, no direct patient involvement occurred. The requirement for informed consent was waived by the University of Alabama at Birmingham in accordance with institutional policies (IRB-300004585).

Study Population

Patients were considered for inclusion if they were adults, had an age of RA onset > 18 years, had a confirmed diagnosis of RA-ILD by a board-certified pulmonologist, and had been seen at least once in the rheumatology clinic and twice in the pulmonology clinic. The diagnosis of RA was based on the American College of Rheumatology (ACR) 1987 or 2010 ACR/European League Against Rheumatism (EULAR) classification criteria.[17] The diagnosis of RA-ILD was based on the presence of clinical features (i.e., cough and dyspnea), PFTs, and HRCT findings.[18] Lung images were interpreted by 2 independent reviewers (1 pulmonologist and 1 radiologist). Disagreements were resolved by consensus or a third party if needed. Patients were excluded if they had a diagnosis of another systemic autoimmune disease, end-stage renal disease, liver disease, or active cancer.

Data Collection

The following data were extracted from the EHR: demographics (age, race, sex, and body mass index (BMI)); lifestyle habits (e.g., smoking); antibody status: rheumatoid factor (RF), and anti-cyclic citrullinated peptide antibody (ACPA); PFT measurements (e.g., diffusing capacity of the lungs for carbon monoxide (DLCO) and forced vital capacity (FVC)) and HRCT findings. Clinical data collected included age at the time of diagnosis of RA, age at the time of diagnosis of ILD, age at the time of diagnosis of RA-ILD, medications used for RA and RA-ILD. RA-ILD duration was defined as the time between the age at RA-ILD diagnosis and the current age at study enrollment. Progression of ILD was defined according to the Outcome Measures in Rheumatology (OMERACT) definition of decline in FVC of ≥10%, or a decline in FVC of 5% to 10% along with a decline in DLCO of ≥15% over 12 months. Patients with an FVC decline of less than 5% over 12 months were defined as stable. These definitions were selected as they are in line with internationally recognized outcome measures on the subject.[18,19]

Statistical Analysis

Data were collected and analyzed using Statistical Package for Social Studies, version 25 (IBM SPSS Corp.; Armonk, NY, USA). Qualitative variables were summarized as frequencies and percentage proportions, and quantitative variables were presented as median and interquartile ranges (IQR). Mann-Whitney *U* test was used in univariate non-parametric analysis to associate predictors with outcomes, with outcomes defined dichotomously as either progression or improvement/stability of RA-ILD over the observation period. For more than 2 subgroup comparisons, Friedman *P* values were calculated. Binary regression using the step-out method was used for the multivariate model to study the interaction of independent risk factors on the progression of ILD at 6 months and 12 months. A 2-sided *P* value of <.05 was considered statistically significant.

Results

Patient Characteristics

Forty-seven patients with RA-ILD receiving care at UAB between 2010 and 2019 met criteria for inclusion in this study. A total of 51.1% of the patients were female and 29.8% of the patients were African American, and 53.2% of the patients had a current or history of tobacco use. The median age at RA diagnosis was 57 years (IQR 48; 65), and the median age at RA-ILD diagnosis was 64.7 years (IQR 58.9; 72.8). The median interval between RA diagnosis and RA-ILD onset was 100.8 months (IQR 32.4; 190.8). The demographic and baseline RA and ILD characteristics are shown in Tables 1 and 2.

RA Treatments

DMARDs that patients were using during the enrollment period and previously

Table 2. Baseline Characteristics Comparison Between Patients Lost to Follow-Up and Those Retained at 6 and 12 Months

		Six Months Follow-Up			Twelve Months Follow-Up		
		Completed (n = 32)	Not completed (n = 15)	Validation	Completed (n = 27)	Not completed (n = 20)	Validation
Sex	Male	16	7	*P* = .84	13	10	*P* = .9
	Female	16	8		14	10	
Age	<50 years	10	5	*P* = .88	9	6	*P* = .82
	≥ 50 years	22	10		18	14	
Race	African American	9	5	*P* = .84	8	6	*P* = .83
	Caucasian	22	9		17	14	
	Asian	1	1		2	0	
History of smoking	Never	19	3	*P* = .01	14	8	*P* = .4
	Past or present	13	12		13	12	
History of lung disease other than ILD	No	17	8	*P* = .92	15	10	*P* = .78
	Yes	12	6		9	9	
	Missing	3	1		3	1	
Pre FVC/DLCO	Median	0.72	0.84	Z = - 0.04	0.72	0.86	Z = - 1.1
	IQR	(0.57-0.94)	(0.53-0.96)	*P* = 1.0	(0.56-0.90)	(0.55-1.0)	*P* = .29

DLCO, diffusion capacity of the lung for carbon monoxide; FVC, forced vital capacity; IQR, interquartile ranges; ILD, interstitial lung disease; TLC, total lung capacity.

treated with are documented in Table 3. Prednisolone, MTX, hydroxychloroquine, LEF, adalimumab, azathioprine, and etanercept were the medications used to treat RA or RA-ILD. PFT at the time of enrollment and 6, 12, and 24 months after RA-ILD treatment are reported in Tables 4 and 5. Out of the initial 47 patients who met inclusion criteria, 32 (68.09%) and 27 (57.45%) patients had follow-up data (including pulmonary function testing) available for analysis at 6 and 12 months, respectively.

RA-ILD Progression Status at 6 and 12 Months

At 6 months, 29 out of 32 (90.6%) of patients for whom follow-up PFT data were available showed stabilization or improvement in their ILD. Based on tipping point analysis, this could be as low as 61.7% if considering all 15 cases lost to follow-up as progressed and 93.6% if considering all 15 lost to follow-up as stable or improved. At 12 months, 24 out of 27 (88.9%) of patients for whom follow-up data were available showed stabilization or improvement in their ILD. Based on tipping point analysis, this could be as low as 51.1% if considering all 20 patients lost to follow-up as progressed and 93.6% if considering all 20 lost to follow-up as stable or improved.

Comparison of Participants Who Completed 12 Months of Follow-Up Versus Those Who Were Lost to Follow-Up

The authors compared baseline known risk factors in 27 RA-ILD patients who completed 12 months follow-up to 20 patients who were lost to follow-up. Age ($P = .89$), interval between diagnosis of RA and ILD ($P = .99$), BMI ($P = .46$), gender ($P = .57$), UIP pattern ($P = .2$), anti-CCP ($P = .27$), and current ILD treatment ($P = .22$) were not significantly different between the 2 groups. However, the history of smoking (present or past) was significantly higher in those lost to follow-up ($P = .036$).

Table 3. Medications Used to Treat RA and RA-ILD

Medication Class	At Baseline, n (%)	Prior Treatments, n (%)
CsDMARDs		
Hydroxychloroquine	10 (21.3)	18 (38.3)
Methotrexate	7 (14.9)	32 (68.1)
Leflunomide	9 (19.1)	15 (31.9)
Sulfasalazine	2 (4.3)	8 (17.0)
bDMARDs		
Anti-TNF		
Adalimumab	3 (6.4)	15 (31.9)
Etanercept	1 (2.1)	11 (23.4)
Infliximab	2 (4.3)	7 (14.9)
Certolizumab	0	2 (4.3)
Anti-IL6		
Tocilizumab	4 (8.5)	8 (17.0)
Other biologics		
Rituximab	6 (12.8)	9 (19.1)
Abatacept	2 (4.3)	5 (10.6)
TsDMARDs		
Tofacitinib	3 (6.4)	3 (6.4)
Antifibrotic		
Nintedanib	0	1 (2.1)
Pirfenidone	0	1 (2.1)
Other medications		
Glucocorticoids	14 (29.8)	41 (87.2)
Azathioprine	8 (17.0)	15 (31.9)
Mycophenolate mofetil	5 (10.6)	11 (23.4)
Mycophenolic acid	2 (4.3)	2 (4.3)
Immunoglobulins	0	1 (2.1)

bDMARDs: biological disease-modifying antirheumatic drugs; CsDMARDs, conventional synthetic DMARDs; TsDMARDs, targeted DMARDs.

RA-ILD and Smoking

Demographic and baseline characteristics were analyzed for correlation with progression or stability/improvement in ILD status at 6 and 12 months of treatment (Table 6). Never smokers were protected from

Table 4. Pulmonary Function Test Results at Presentation and Follow-Up Visits (6, 12, and 24 Months)

	Before	After Treatment			
	At Time of Enrollment (n = 47)	At 6 Months n = 32)	At 12 Months (n = 28)	At 24 Months (n = 31)	Validation (Friedman P)
FEV1% median (IQR)	72.5 (64-87)	74 (63.8-88.3)	70.1 (60.3-85.0)	74 (64.5-85)	.521
FVC % median (IQR)	68.0 (55-79)	65 (56.8-76.5)	67 (57-75)	70.5 (59.3-82.5)	.068
TLC% median (IQR)	58.0 (47.8-70.3)	58 (46-65)	55 (45-66)	55 (48-64)	.332
DLCO median (IQR)	49 (39.5-66.5)	44 (33-63)	54 (32.5-62.5)	56 (41-71.5)	.863
DLCO/FVC median (IQR)	0.73 (0.56-0.93)	0.64 (0.46-0.86)	0.77 (0.52-0.84)	0.84 (0.61-0.93)	.540

DLCO, cdiffusion capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; IQR, interquartile range; TLC, total lung apacity.

Table 5. Pulmonary Function Test Results Among Those With Stable and Progressive Rheumatoid Arthritis-Related Interstitial Lung diseases

	At 6 Months			At 12 Months		
	Stable/ Improved, Median (IQR)	Progressed ILD, Median (IQR)	Validation Coefficient, Z (P)	Stable/ Improved, Median (IQR)	Progressed ILD, Median (IQR)	Validation Coefficient, Z (P)
FEV1%	77 (64-87)	69 (63-73)	- 0.9 (.39)	77 (64-101)	69.5 (60.3-80.5)	- 1.1 (.24)
FVC%	65 (57-87)	61 (55-70)	- 0.68 (.54)	69 (58-91)	63.5 (55.8-72.5)	- 0.97 (.36)
TLC%	54.5 (46-69)	60 (42- 65)	- 0.07 (.95)	69.5 (55-84)	49.5 (42-57)	- 1.3 (.27)
DLCO	45.5 (39-67.5)	22 (18-32)	- 2.4 (.01)	15 (12.6-58)	55 (37-65)	- 1.7 (.1)
DLCO/FVC	0.72 (0.5-0.87)	0.32 (0.31-0.52)	- 1.9 (.05)	0.3 (0.19-0.77)	0.81 (0.66-0.91)	- 2.0 (.05)

DLCO, diffusion capacity of the lung for carbon monoxide; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; IQR: interquartile ranges; TLC, total lung capacity.

deterioration of ILD status at 6 months compared to past and present smokers ($P = .025$), although the association became non-significant at 12 months of treatment ($P = .506$). The remaining demographic variables were nonsignificant.

Discussion

Most patients with RA-ILD at a large academic medical center in the South showed stable to improved lung function with treatment at 6 and 12 months. The cohort is notable in that a sizeable portion of patients were female and of African American race, which is unique and has been reported[17,20] when compared to most other RA-ILD cohorts, which have featured relatively fewer women and patients of color.[21,22] This observation is reinforced by McFarlane et al, which investigated RA-ILD in a predominantly Black population, revealing that 93.7% of the patients were female and 89% were Black.[17]

RA-ILD was stable or improved in 90.6% of this cohort at 6 months and 88.9% of this cohort at 12 months. In comparison, a prospective cohort of RA-ILD patients in China published by Chen et al found 33% improved, 35% remained unchanged/stable, and 32% progressed by 5 years of follow-up.[23] A retrospective study of RA-ILD patients in Tunisia found 18.2% had progression of ILD over a 7-year period.[24] In a prospective cohort study carried out in Spain by Mena-Vazquez et al, at 60

Table 6. Status of Rheumatoid Arthritis—Interstitial Lung Disease After 6 and 12 Months of Treatment and Determinants

		At 6 Months AfterTreatment				At 12 Months AfterTreatment			
Variable		Progressed	Stable	Improved	*P* value	Progressed	Stable	Improved	*P* value
Sex	Male	1	15	0	$X^2 = 6.8$,	3	9	1	$X^2 = 4.8$,
	Female	2	9	5	$P = .076$	0	10	4	$P = .184$
Smoking	Never	0	15	4	$X^2 = 5.4$,	1	9	4	$X^2 = 2.2$,
	Smokers	3	9	1	$P = .025$	2	10	1	$P = .506$
Lung disease	None	0	14	3	$X^2 = 3.1$,	2	11	1	$X^2 = 2.9$,
	Present	3	10	2	$P = .314$	1	8	4	$P = .075$
Current ILD treatment	Yes	1	14	2	$X^2 = 1.1$,	1	10	4	$X^2 = 1.74$,
	No	2	10	3	$P = .616$	2	9	1	$P = .376$
Race	African	0	7	2	$X^2 = 1.9$,	1	6	2	$X^2 = 2.2$,
	White	3	16	3	$P = .888$	2	12	2	$P = .534$
	Asian	0	1	0		0	1	1	
UIP	Present	1	13	2	$X^2 = 2.3$,	2	10	2	$X^2 = 0.7$,
	Absent	4	11	1	$P = .324$	1	9	3	$P = .599$
ACPA positivity	Present	4	21	3	$X^2 = 3.3$,	3	12	2	$X^2 = 22$,
	Absent	1	3	0	$P = .710$	1	3	0	$P = .362$
Methotrexate treatment	Yes	3	15	3	$X^2 = 3.3$,	1	10	5	$X^2 = 2.7$,
	No	2	9	0	$P = .213$	2	9	0	$P = .1$
Age(years)	≤ 50	1	7	1	$X^2 = 2.1$,	0	9	1	$X^2 = 0.294$,
	51 and more	4	17	4	$P = .554$	3	10	4	$P = .235$
BMI(kg/m^2)	<30	2	9	3	$X^2 = 3.2$,	2	8	3	$X^2 = 0.141$,
	30 and more	0	14	2	$P = .366$	1	11	2	$P = .793$
Age (year)			r = 0.139, $P = .411$				r = - 0.141, $P = .710$		
Duration of follow-up (months)			r = 0.116, $P = .154$				r = 0.09, $P = .368$		
Body Mass Index (kg/m^2)			r = 0.371, $P = .044$				r = 0.08, $P = 0.235$		

ACPA, anti-citrullinated protein antibodies; BMI, body mass index; ILD, interstitial lung disease; UIP, usual interstitial pneumonia. .

months of follow-up, 56.9% of patients had stable, 7.8% had improved, and 19.8% had worsening RA-ILD.[25] Although this analysis was limited by shorter duration of follow-up compared to other studies, it is possible that longer follow-up may have yielded results comparable to the existing literature.

A history of smoking was a significant risk factor for the progression of ILD at 6 months in this study, which is in line with other studies.[25-28] One prospective cohort study of RA-ILD found that current or past smoking history was associated with a hazard ratio of 2.5 for ILD progression in a Cox multivariate analysis.[25] This speaks to the importance of tobacco cessation in RA-ILD. Interestingly, the well-documented risk factors for RA-ILD progression of male sex, advanced age, duration of RA, as well as UIP pattern were not associated with progression of ILD in this study at 6 and 12 months of treatment.[5,6,8,29] This may have been related to sample size.

Patients in this cohort received a wide range of DMARDs, with HCQ, MTX, LEF, and RTX being the most common at the time of enrollment, along with a multitude of other agents. Due to the small size of the cohort, this study was not powered to assess whether a specific DMARD was superior in improving or stabilizing ILD. Future prospective studies are needed to explore this further. Additionally, future and ongoing studies subtyping patients with genomics and proteomics may elucidate whether an individual patient is more likely to benefit from a specific DMARD over another.[30,31]

Limitations

Our study has several limitations. As a single-center retrospective analysis, it was constrained by a smaller sample size and a short follow-up duration, both of which contribute to the potential for immortal time bias. Furthermore, a substantial proportion of patients were lost to follow-up, introducing an additional element of survivorship bias that may have impacted the findings. Due to the combination of loss to follow-up and the limited follow-up period, accurate assessment of mortality outcomes was not feasible.

Another notable limitation is the heterogeneity of treatment strategies within this cohort. This variability made it challenging to identify any RA-ILD-directed treatment as definitively superior to others. Additionally, this study did not address drug adherence, which could further influence the observed outcomes and introduce unmeasured confounding.

To mitigate these limitations and build on the findings, future studies should adopt a multicenter prospective design with larger cohorts, standardized treatment protocols, and extended follow-up periods to capture long-term outcomes more comprehensively. Addressing drug adherence and minimizing bias through robust study designs will be essential for deriving stronger, generalizable conclusions.

The management of RA-ILD is complex and requires periodic evaluation by an interdisciplinary team of rheumatologists, pulmonologists, and radiologists to manage both the pulmonary and articular manifestations of the disease. In general, RA-ILD stabilizes/improves in most patients at 6 and 12 months with immunosuppressive treatment.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This study was approved by the Ethics Committee of University of Alabama (Approval No: IRB-300004585).

Informed Consent: N/A.

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