EULAR European E-Congress of Rheumatology 2020
From 3 June

Examination of interstitial lung disease in patients with rheumatoid arthritis – prevalence, time to onset and clinical characteristics

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Disclosures

- JZ and SL: employee and shareholder: Bristol-Myers Squibb Company
- QZ, YW, CG, DH, LX: employee: STATinMED Research, a paid consultant to Bristol-Myers Squibb Company
- KK: employee: Discus Analytics; consultant: Bristol-Myers Squibb Company
- GC: employee: Arthritis Northwest and VP of Discus Analytics; consultant and speakers bureau: Bristol-Myers Squibb Company

Background and objectives

- Interstitial lung disease (ILD) is a common extra-articular manifestation of RA and is associated with increased morbidity and mortality
- Studies have shown variability in the prevalence, clinical characteristics and risk factors of RA-associated ILD (RA-ILD)[1]

Objectives

- To evaluate the prevalence and time to onset of ILD in patients with RA
- To compare the clinical characteristics of patients with RA with and without ILD

1. Spagnolo P, et al. *Arthritis Rheumatol* 2018;70:1544-1554.

Methods: data source, endpoints and inclusion criteria

Data source

- Discus Analytics JointMan database: a large real-time rheumatology tracking platform

Endpoints

- Primary: prevalence and time to onset of ILD
- Secondary: demographics, co-morbidities, RA characteristics and disease activity in the baseline period[a] for patients with RA only (no diagnosis of ILD) versus RA-ILD (diagnosis of ILD after RA)

Inclusion criteria

- For the primary endpoint:
  - Diagnosis of RA at any time
- For the secondary endpoint:
  - RA diagnosis between 1 Jan 2009 and 20 Sept 2019
  - Age ≥18 years
  - ≥1 encounter after the initial encounter date
  - No diagnosis code for ILD prior to RA diagnosis
  - No diagnosis code for drug-induced ILD at any time during the study period

Diagnosis codes		
	RA	ILD
ICD-9-CM code	714.0	516.0, 516.2, 516.3, 516.4, 516.5, 516.8, 516.9
ICD-10-CM code	M05, M06	J84.0, J84.1, J84.2, J84.81, J84.82, J84.83, J84.89, J84.9

[a]6 months prior to or on date of initial RA diagnosis.

ICD-9-CM=International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease.

Methods: statistical analyses

Primary endpoint:

- Prevalence of first observed ILD diagnosis during follow-up was calculated
- Time to ILD diagnosis examined using unadjusted KM survival curves

Secondary endpoint:

- Numbers and percentages for dichotomous and polychotomous variables; Chi squared tests for significance
- Mean and SD for continuous variables; t tests for significance

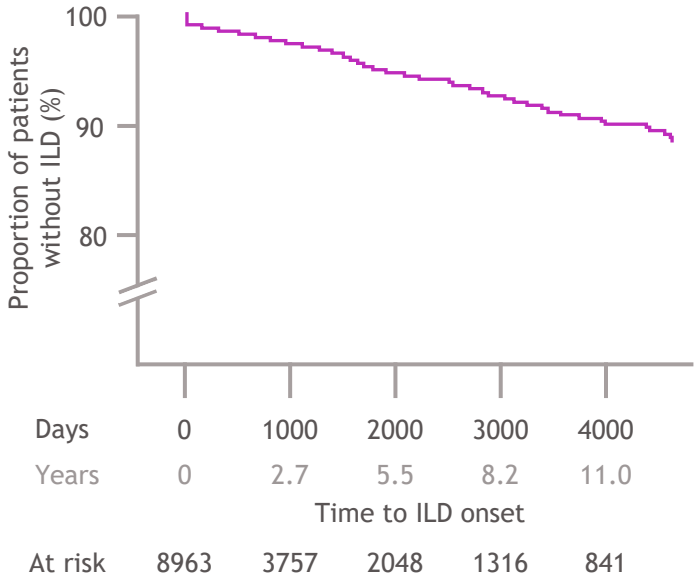
ILD=interstitial lung disease; KM=Kaplan-Meier.

Prevalence of ILD among patients with RA

- 8963 patients with RA identified
- 3.8% (337) had ILD after or at first RA diagnosis (overall follow-up period)

Time to ILD onset after RA diagnosis	Incidence (n=337)
Mean, years	3.3
Median, years	2.3
Years, n (%)	
0	70 (21)
>0 and <2	87 (26)
≥2 and <4	59 (18)
≥4 and <6	53 (16)
≥6	68 (20)

Survival estimate: time to ILD onset after RA diagnosis



ILD=interstitial lung disease.

Patient demographics and primary insurance category at baseline

Patients with ILD were significantly:

- more likely to be older, male, white and have Medicare as their primary insurance category
- less likely to have commercial as their primary insurance category

	RA only (n=5612)	RA-ILD (n=205)	p value
Age, years	59.1 (14.2)[a]	65.8 (11.8)[a]	<0.001
18-54	1938 (35)	29 (14)	<0.001
55-64	1550 (28)	60 (29)	0.604
65-74	1360 (24)	72 (35)	<0.001
75-79	412 (7)	20 (10)	0.195
≥80	352 (6)	24 (12)	0.002
Sex, male	1375 (25)	72 (35)	0.005
Race			
Black/African American	365 (7)	9 (4)	0.226
White	4014 (72)	165 (80)	0.005
Other/missing	1233 (22)	31 (15)	0.020
Primary insurance category			
Commercial	2407 (43)	51 (25)	<0.001
Medicare (alone or with other)	1596 (28)	97 (47)	<0.001
Medicaid (alone or with commercial)	132 (2)	4 (2)	0.709
No insurance	419 (7)	20 (10)	0.223
Missing	1058 (19)	33 (16)	0.321

Data are n (%) unless stated otherwise. Highlighted p values are significant ($p<0.05$).

[a]Mean (SD).

ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease.

Co-morbidities at baseline

Patients with ILD were significantly:

- more likely to have a history of COPD
- less likely to have a history of GERD or obesity

A similar proportion of patients with/without ILD had a history of smoking

	RA only (n=5612)	RA-ILD (n=205)	p value
CCI score	0.2 (0.6)[a]	0.2 (0.4)[a]	0.963
Co-morbidities			
History of COPD[b]	102 (3)	8 (7)	0.006
Diabetes[b]	341 (9)	9 (8)	0.699
Hyperlipidaemia[b]	481 (13)	14 (12)	0.915
Hypertension[b]	900 (23)	23 (20)	0.395
Serious infection[b]	38 (1)	3 (3)	0.091
Coronary artery disease	28 (<1)	1 (<1)	0.982
GERD	251 (4)	3 (1)	0.038
Obesity[c]	1686 (30)	50 (24)	0.002
Smoking status: current or former[b]	220 (6)	10 (9)	0.179

Data are n (%) unless stated otherwise. Highlighted p values are significant ($p<0.05$).

[a]Mean (SD); [b]Among patients with non-missing RA characteristics data; RA-only cohort, n=3846; RA-ILD cohort, n=115; [c]Diagnosis code or BMI ≥30 kg/m^2.

CCI=Charlson Comorbidity Index; COPD=chronic obstructive pulmonary disease; GERD=gastroesophageal reflux disease; ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease.

RA characteristics and medication use at baseline

For patients with RA-ILD versus RA only:

- Most RA characteristics or manifestations were significantly more prevalent
- Anti-CCP and ESR levels were significantly higher
- Medication use at the time of RA diagnosis was similar

	RA only (n=5612)	RA-ILD (n=205)	p value
RA characteristics	*n=3846*	*n=115*	
RF positive	1388 (36)	69 (60)	<0.001
Joint stiffness	1092 (28)	39 (34)	0.197
Rheumatoid nodules	153 (4)	17 (15)	<0.001
Erosions	459 (12)	23 (20)	0.009
Extra-articular disease[a]	487 (13)	29 (25)	<0.001
Anti-CCP antibodies[b]	1505 (27)	94 (46)	<0.001
Joint evaluation	*n=4929*	*n=181*	
Swelling	2861 (58)	123 (68)	0.008
Tenderness	3728 (76)	138 (76)	0.851
Laboratory tests[c]			
	n=2952	*n=128*	
ESR, mm/h	22.0 (22.6)	30.1 (25.5)	<0.001
	n=2997	*n=132*	
CRP, mg/L	22.5 (13.0)	60.6 (25.0)	0.086
Medication use at time of RA diagnosis			
Glucocorticoids	262 (5)	15 (7)	0.151
DMARDs[d]	4858 (87)	187 (91)	0.132
MTX	3700 (66)	129 (63)	0.373

Data are n (%) unless stated otherwise. Highlighted p values are significant (p<0.05).

[a]Including nodules, sicca, uveitis, vasculitis and Felty's syndrome; [b]Binary (anti-CCP >20 U/mL considered positive) and continuous; RA-only cohort, n=5552; RA-ILD cohort, n=115; [c]Mean (SD); [d]Hydroxychloroquine, leflunomide, minocycline, MTX or sulfasalazine.

Anti-CCP=anti-cyclic citrullinated peptide; RA-ILD=RA-associated interstitial lung disease.

Disease activity at baseline (1/2)

Patients with RA-ILD versus RA only had significantly higher mean scores for:

- CDAI
- DAS28 (CRP)
- DAS28 (ESR)

	RA only (n=5612)	RA-ILD (n=205)	p value
CDAI	*n=4548*	*n=159*	
Mean (SD) score	16.4 (12.7)	18.9 (15.7)	0.049
Disease activity categories			
Remission	342 (8)	16 (10)	0.205
Low disease activity	1387 (30)	44 (28)	0.128
Moderate disease activity	1644 (36)	45 (28)	0.361
High disease activity	1175 (26)	54 (34)	0.073
DAS28 (CRP) score	*n=2476*	*n=97*	
Mean (SD) score	2.6 (1.2)	3.1 (1.4)	0.004
Disease activity categories			
Remission	1152 (47)	31 (32)	0.048
Low disease activity	291 (12)	11 (11)	0.447
Moderate disease activity	750 (30)	33 (34)	0.953
High disease activity	283 (11)	22 (23)	<0.001
DAS28 (ESR) score	*n=2484*	*n=95*	
Mean (SD) score	3.3 (1.4)	3.9 (1.5)	<0.001
Disease activity categories			
Remission	873 (35)	20 (21)	0.021
Low disease activity	394 (16)	11 (12)	0.800
Moderate disease activity	960 (39)	41 (43)	0.647
High disease activity	257 (10)	23 (24)	<0.001

Data are n (%) unless stated otherwise.
Highlighted p values are significant ($p<0.05$).
RA-ILD=RA-associated interstitial lung disease.

Disease activity at baseline (2/2)

- Mean RAPID3 scores were similar among patients with/without ILD
- Mean SDAI scores were significantly higher for patients with RA-ILD versus RA only

	RA only (n=5612)	RA-ILD (n=205)	p value
RAPID3	*n=4897*	*n=175*	
Mean (SD) score	12.2 (6.4)	12.3 (6.6)	0.482
Disease activity categories			
Remission	486 (10)	18 (10)	0.973
Low disease activity	531 (11)	12 (7)	0.071
Moderate disease activity	1331 (27)	56 (32)	0.206
High disease activity	2549 (52)	89 (51)	0.999
SDAI	*n=2452*	*n=95*	
Mean (SD) score	20.2 (23.9)	28.6 (47.3)	0.031
Disease activity categories			
Remission	152 (6)	7 (7)	0.995
Low disease activity	668 (27)	16 (17)	0.020
Moderate disease activity	1025 (42)	33 (35)	0.426
High disease activity	607 (25)	39 (41)	0.002

Data are n (%) unless stated otherwise. Highlighted p values are significant ($p<0.05$).

ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease; RAPID3=Routine Assessment of Patient Index Data 3.

Conclusions

- This large, real-world study provides insight into the increased burden of disease among patients with RA-ILD versus RA only
- Of the 8963 patients with RA identified, 3.8% had ILD after or at first RA diagnosis and a mean of 3.3 years (1220 days) for onset of ILD after RA diagnosis
- No correlation was found between cigarette smoking and ILD despite the higher prevalence of anti-CCP in the RA-ILD versus RA-only group
- Further analysis is warranted to assess risk factors for RA-ILD and its prognosis

Patients with RA-ILD versus RA only were significantly more likely to be older, male, white and RF positive; they were more likely to have Medicare as their primary insurance category, a history of COPD, rheumatoid nodules, erosions, extra-articular disease, anti-CCP antibodies, higher anti-CCP and ESR levels and higher DAS28 (CRP), DAS28 (ESR), CDAI and SDAI scores

Anti-CCP=anti-cyclic citrullinated peptide; COPD=chronic obstructive pulmonary disease; ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease.

Acknowledgements

- This study was sponsored by Bristol-Myers Squibb Company. Professional medical writing and editorial assistance was provided by Lola Parfitt, MRes, at Caudex and was funded by Bristol-Myers Squibb Company

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