Burden of Disease in Refractory Rheumatoid Arthritis

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BACKGROUND

- Despite major advances in RA treatment, a substantial number of patients are refractory to multiple biologics
- Definitions for refractory RA (reRA) have been arbitrary and there is no universally accepted definition
- Depending on definition and cohort, prevalence of reRA is estimated at 6-21%
- To understand the mechanisms behind reRA and ultimately improve therapies, a better understanding of outcomes and associated factors is necessary; for this reason, there is a need for more thorough analyses of the burden of reRA in a real-world setting

METHODS

- Data were provided by adults with RA in FORWARD, The National Databank for Rheumatic Diseases (a US-wide longitudinal observational registry), with no history of biologic use at study entry and subsequent exposure to one or more biologics
- reRA: 3+ biologics during observation; non-refractory: use of a single biologic for 2+ years
- Descriptive statistics were calculated for reRA and non-refractory groups at initiation of first biologic and at the point of becoming refractory (for reRA) or two years after initiation of first biologic (for non-refractory)
- Characteristics at biologic initiation associated with becoming refractory and factors that varied significantly at the point of meeting reRA criteria were identified with logistic regression

RESULTS

- Of 2,769 participants who met inclusion criteria, 531 (19.2%) met criteria for reRA
- Numerous baseline characteristics varied significantly by comparison group (Table 1), but some were attenuated in models (Figure 1)
- Significant associations with future incidence of reRA included younger age, female sex, higher education, and glucocorticoid use (Figure 1A)
- After meeting reRA criteria, younger age, longer RA duration, higher education, history of smoking, higher BMI, GI disorder, heart disease, concomitant glucocorticoid use, lack of concomitant csDMARD use, patient global, and higher rate of rheumatology visits were associated with reRA (Figure 1B)

CONCLUSION

- Baseline factors associated with risk of reRA were consistent with existing literature
- Participants with reRA had more comorbidities, higher rates of smoking, more frequent use of glucocorticoids, and higher health care resource use
- Our findings characterize differences in disease burden and patient experience between non-refractory and reRA patients

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Individuals with refractory RA experience a higher comorbidity burden, greater healthcare resource use, are more likely to use glucocorticoids, and are less likely to use csDMARDs.

Table 1. Characteristics of FORWARD participants with RA by non-refractory and refractory subgroups at baseline and follow up. Baseline for both comparison groups was at initiation of first biologic. Follow up for reRA was the point of meeting the definition of refractory. Follow up for non-refractory was two years following the initiation of their only biologic.

	Baseline			Follow Up		
	Non-refractory	Refractory		Non-refractory	Refractory	
	n=2238	n=531	p-value	n=1868	n=531	p-value
Demographics						
Age, years, mean (SD)	61.4 (12.5)	56.8 (10.5)	<0.001	63.3 (12.4)	63.4 (11.1)	0.91
RA duration, years, mean (SD)	15.0 (11.0)	15.0 (10.5)	0.94	16.8 (11.0)	21.5 (11.5)	<0.001
Observation time, years, mean (SD)	3.4 (3.0)	3.1 (2.4)	0.04	5.0 (3.1)	9.7 (4.6)	<0.001
Female, %	79.3	86.8	<0.001	79.9	86.8	<0.001
White, %	92.7	90.1	0.05	93.5	90.1	0.01
Education, years, mean (SD)	13.6 (2.3)	14.0 (2.2)	<0.001	13.5 (2.4)	14.0 (2.2)	<0.001
Rural residence, %	26.5	29.0	0.24	27.6	29.0	<0.01
Hx smoking, %	40.5	36.2	0.07	33.7	45.6	<0.001
BMI, kg/m^2, mean (SD)	27.5 (6.3)	28.0 (6.3)	0.08	27.4 (6.4)	28.3 (6.8)	0.01
Comorbidities						
RDCI, 0-9, mean (SD)	1.6 (1.5)	1.6 (1.4)	0.57	1.7 (1.5)	2.1 (1.6)	<0.001
Hx cancer, %	11.7	11.1	0.69	16.3	25.6	<0.001
Hx pulmonary disorder, %	18.9	18.2	0.69	27.7	42.8	<0.001
Hx GI disorder, %	36.4	43.2	<0.01	51.7	71.9	<0.001
Hx heart disease, %	14.1	13.4	0.66	22.7	32.6	<0.001
Hx renal disorder, %	6.1	5.9	0.86	11.5	20.0	<0.001
Concomitant Medications						
Glucocorticoid use, %	42.6	49.2	<0.01	35.0	48.8	<0.001
csDMARD use, %	85.0	87.8	0.10	78.7	72.5	<0.01
PROs						
Pain VAS, 0-10, mean (SD)	3.5 (2.7)	4.1 (2.7)	<0.001	3.7 (2.7)	4.4 (2.6)	<0.001
Fatigue VAS, 0-10, mean (SD)	4.2 (2.9)	4.7 (3.0)	<0.01	4.3 (2.9)	5.0 (2.9)	<0.001
Patient global, 0-10, mean (SD)	3.4 (2.4)	3.8 (2.4)	<0.01	3.5 (2.4)	4.3 (2.3)	<0.001
HAQ-II, mean (SD)	0.98 (0.67)	1.01 (0.63)	0.50	1.05 (0.69)	1.25 (0.67)	<0.001
PAS-II, mean (SD)	3.4 (2.1)	3.7 (2.0)	0.04	3.5 (2.2)	4.3 (2.0)	<0.001
Healthcare Interactions						
Rheumatology visits, last 6 months, %						
0-2 visits	36.3	31.4		54.0	36.5	
3-4 visits	39.9	43.2	0.12	34.7	39.9	<0.001
>4 visits	23.8	25.5		11.3	23.6	
Health satisfaction, 0-4, mean (SD)	2.4 (1.2)	2.1 (1.2)	<0.001	2.3 (1.2)	1.9 (1.2)	<0.001

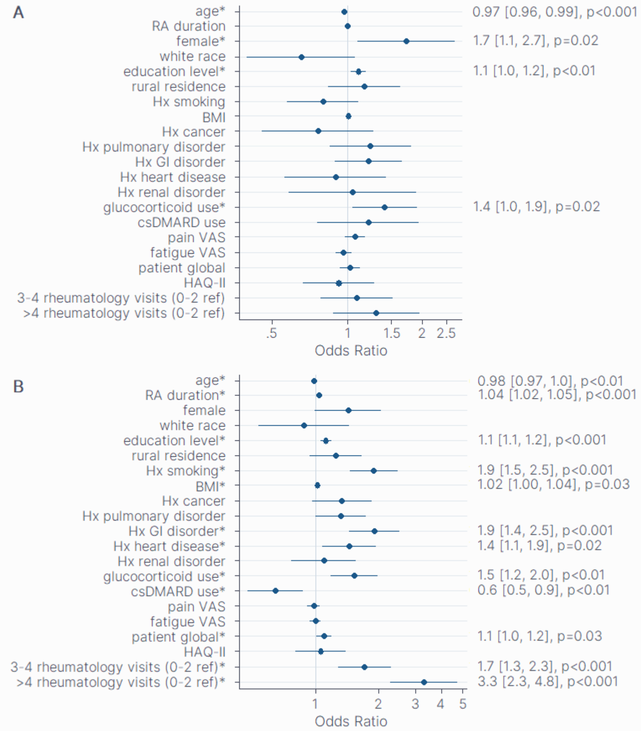

Figure 1. Odds ratios and 95% CI for factors associated with reRA. Covariates marked with an asterisk (*) are statistically significant (p<0.05) and have their associated odds ratios and p-values listed. (A) Baseline (initiation of first biologic) factors associated with reRA. (B) Follow up (meeting the definition of refractory vs 2-year mark on initial biologic) factors associated with reRA.

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The National Databank for Rheumatic Diseases

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