ACPA and RF as Predictors of Sustained Clinical Remission in Rheumatoid Arthritis Patients: Data From a Rheumatoid Arthritis Cohort

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BACKGROUND

- Positive serology for anti-citrullinated protein antibody (ACPA) and rheumatoid factor (RF) are included in the 2010 ACR/EULAR classification criteria for rheumatoid arthritis (RA).

- Previous studies have shown that the presence of autoantibodies are positive predictors of response in RA patients treated with some biologics.

OBJECTIVES

- To evaluate the interaction of RF and ACPA in predicting sustained clinical response in a large observational registry of RA patients followed in routine clinical care.

METHODS

- The Ontario Best Practices Research Initiative (OBRI) includes a clinical registry of RA patients (OBRI-RA registry) followed in routine care in Ontario, Canada.

- RA patients enrolled in the OBRI, with active disease (≥1 swollen joint), available autoantibody information, and at least 1 follow-up assessment were included in the analysis.

- Sustained clinical remission was defined as CDAI ≤ 2.8 in at least 2 sequential visits separated by at least 3 and maximum 12 months.

- Time to sustained remission was assessed by plotting cumulative incidence curves and multivariate Cox regression analysis.
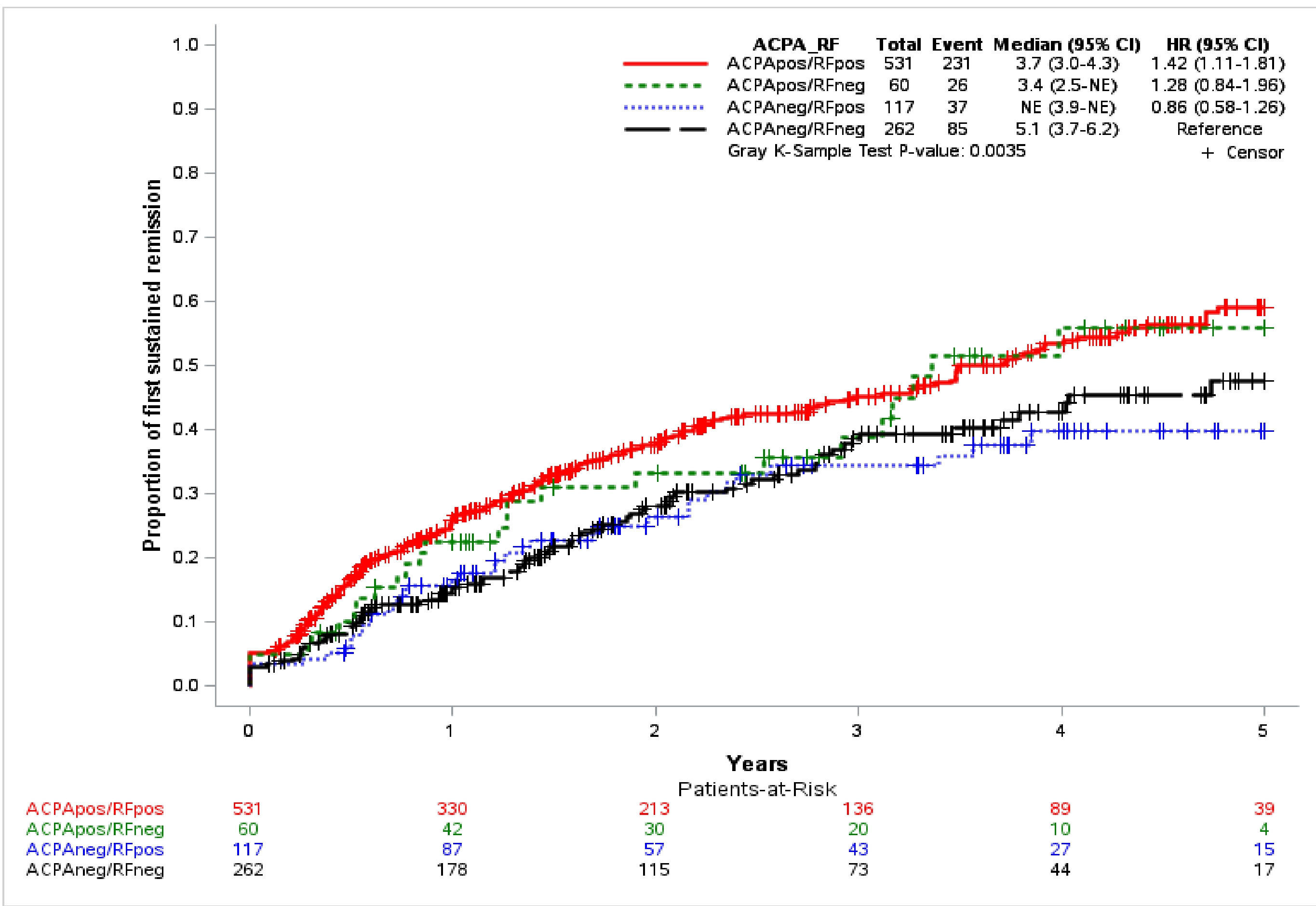
RESULTS

- A total of 970 out of 3251 patients in the registry were included in the analysis.

- At baseline, significant differences were observed between groups in age (p=0.02), Clinical Disease Activity Index (CDAI) (p=0.03), Health Assessment Questionnaire Disability Index (HAQ-DI) (p=0.002) and number of comorbidities (p=0.02)(Table 1).

Table 1: Baseline Characteristics of Included Sample

	Anti-CCP /RF status				
	Anti-CCP neg/RF neg (N=262)	Anti-CCP pos /RF neg (N=60)	Anti-CCP neg/RF pos (N=117)	Anti-CCP pos/ RF pos (n=531)	p-value
Female, n (%)	205 (78.2)	46 (76.7)	88 (75.2)	413 (77.8)	0.92
Age, mean (SD)	57.3 (13.7)	55.9 (12.1)	57.6 (11.9)	54.6 (13.7)	**0.02**
RA duration , mean (SD)	4.8 (7.6)	6.6 (8.9)	3.8 (6.6)	5.4 (8.4)	0.11
Early RA (duration <=1 yr.), n (%)	134 (51.2)	25 (41.7)	61 (52.1)	261 (49.2)	0.55
Post-secondary education, n (%)	165 (63.0)	38 (63.3)	64 (54.7)	309 (58.2)	0.18
Smoking status, n (%) - Never - Past - Current	 125 (47.7) 87 (33.2) 34 (13.0)	 26 (43.3) 27 (45.0) 5 (8.3)	 46 (39.3) 47 (40.2) 19 (16.2)	 236 (44.4) 187 (35.2) 90 (16.9)	0.27
DAS28-ESR, mean (SD)	4.3 (1.6)	3.8 (1.5)	4.1 (1.5)	4.3 (1.6)	0.10
Physician Global Assessment, mean (SD)	4.4 (2.5)	3.8 (2.0)	3.9 (2.4)	4.4 (2.6)	0.18
CDAI, mean (SD)	22.3 (14.0)	17.2 (11.6)	19.5 (13.0)	20.2 (13.7)	**0.03**
Patients with CDAI remission (CDAI≤ 2.8), n (%)	10 (3.8%)	3 (5.0%)	5 (4.3%)	34 (6.4%)	0.45
HAQ Disability Index, mean (SD)	1.1 (0.8)	0.9 (0.7)	1.2 (0.7)	1.0 (0.7)	**0.002**
Number of comorbidities, mean (SD)	3.7 (2.4)	3.7 (2.5)	3.8 (2.4)	3.2 (2.5)	**0.02**
Prior use of bDMARDs, n (%)	57 (21.8%)	20 (33.3%)	31 (26.5%)	130 (24.5%)	0.33
Prior use of csDMARDs, n (%)	205 (78.2%)	48 (80.0%)	95 (81.2%)	400 (75.3%)	0.47

Figure 1: Cumulative Incidence of Sustained Remission by ACPA/RF Status

ACPA_RF	Total	Event	Median (95% CI)	HR (95% CI)
ACPApos/RFpos	531	231	3.7 (3.0-4.3)	1.42 (1.11-1.81)
ACPApos/RFneg	60	26	3.4 (2.5-NE)	1.28 (0.84-1.96)
ACPAneg/RFpos	117	37	NE (3.9-NE)	0.86 (0.58-1.26)
ACPAneg/RFneg	262	85	5.1 (3.7-6.2)	Reference

Gray K-Sample Test P-value: 0.0035   + Censor

Patients-at-Risk

	0	1	2	3	4	5
ACPApos/RFpos	531	330	213	136	89	39
ACPApos/RFneg	60	42	30	20	10	4
ACPAneg/RFpos	117	87	57	43	27	15
ACPAneg/RFneg	262	178	115	73	44	17

- Over three years mean follow-up, sustained remission was achieved in 43.5% of anti-CCPpos /RFpos patients, 43.3% of anti-CCPpos /RFneg patients, 31.6% of anti-CCPneg /RFpos patients and 32.4% of anti-CCPneg/RFneg patients (p=0.01)(Table 2) .

- Significant differences were observed in the time to achieve sustained clinical remission based on anti-CCP status/RF status (p=0.004)(Figure 1).

- Multivariate Cox regression adjusting for baseline CDAI score, age and sex showed differences between groups which reached statistical significance in anti-CCPpos /RFpos vs. anti-CCPneg/RFneg patients (HR [95%CI]: 1.30 [1.01-1.67]; p=0.04)(Table 3).

Table 2: Frequency of Sustained Remission According to Anti-CCP and RF Status

Outcome	Anti-CCP /RF status				
	Anti-CCP neg/RF neg (N=262)	Anti-CCP pos /RF neg (N=60)	Anti-CCP neg/RF pos (N=117)	Anti-CCP pos/ RF pos (n=531)	p-value
First sustained CDAI remission during follow-up, n (%)	85 (32.4)	26 (43.3)	37 (31.6)	231 (43.5)	0.01

Table 3: Association Between Anti-CCP/RF Status and Sustained Remission

	Hazard Ratio (95% Confidence Interval), p-value	
	Unadjusted model	Adjusted model
Anti-CCP status - Anti-CCP neg/RF neg - Anti-CCP neg /RF pos - Anti-CCP pos /RF neg - Anti-CCP pos /RF pos	 Ref 0.86 (0.58-1.26), 0.26 1.28 (0.84-1.96), 0.44 **1.42 (1.11-1.81), 0.01**	 Ref 0.82 (0.56-1.20), 0.31 1.16 (0.74-1.80), 0.52 **1.30 (1.01-1.67), 0.04**
Female (Ref=male)	0.96 (0.74-1.23), 0.73	0.85 (0.67-1.08), 0.19
Age at baseline	**0.99 (0.98-1.00), 0.02**	**0.99 (0.98-1.00), 0.01**
CDAI at baseline	**0.97 (0.96-0.98), <0.0001**	**0.97 (0.96-0.98), <0.0001**

CONCLUSIONS

- These results suggest that anti-CCP but not RF positivity may be associated with a greater chance of sustained remission, possibly due to an improved treatment response.