

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.

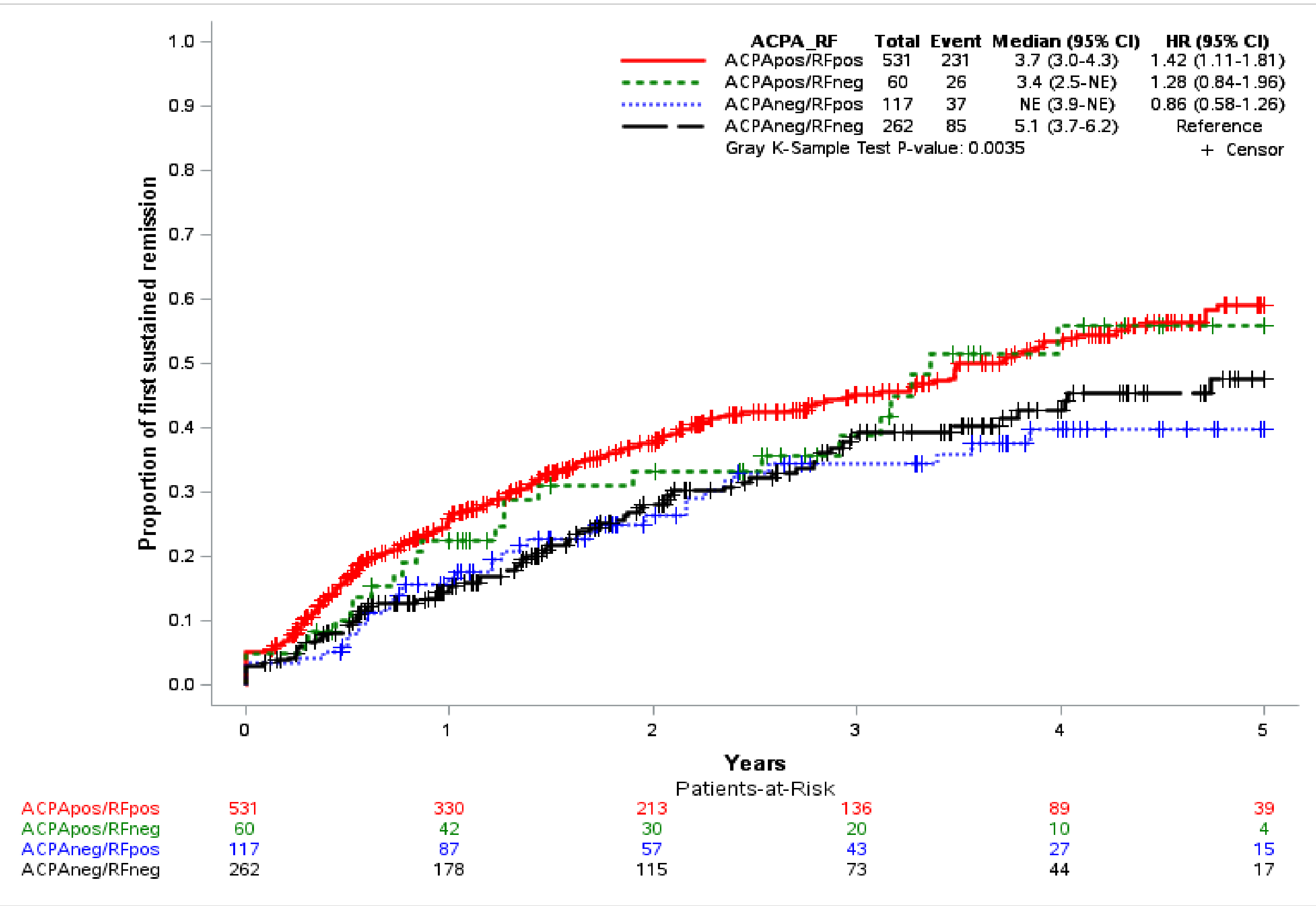
RESULTS

- 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				p-value
	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)	
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 (%)					0.27
- Never	125 (47.7)	26 (43.3)	46 (39.3)	236 (44.4)	
- Past	87 (33.2)	27 (45.0)	47 (40.2)	187 (35.2)	
- Current	34 (13.0)	5 (8.3)	19 (16.2)	90 (16.9)	
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



- Over three years mean follow-up, sustained remission was achieved in 43.5% of anti-CCP^{pos}/RF^{pos} patients, 43.3% of anti-CCP^{pos}/RF^{neg} patients, 31.6% of anti-CCP^{neg}/RF^{pos} patients and 32.4% of anti-CCP^{neg}/RF^{neg} 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-CCP^{pos}/RF^{pos} vs. anti-CCP^{neg}/RF^{neg} 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				p-value
	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)	
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}	Ref	Ref
- Anti-CCP ^{neg} /RF ^{pos}	0.86 (0.58-1.26), 0.26	0.82 (0.56-1.20), 0.31
- Anti-CCP ^{pos} /RF ^{neg}	1.28 (0.84-1.96), 0.44	1.16 (0.74-1.80), 0.52
- Anti-CCP ^{pos} /RF ^{pos}	1.42 (1.11-1.81), 0.01	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.

OBRI Investigators: Drs. Ahluwalia, V., Ahmad, Z., Akhavan, P., Albert, L., Alderdice, C., Aubrey, M., Aydin, S., Bajaj, S., Bensen, B., Bhavsar, S., Bobba, R., Bombardier, C., Bookman, A., Cabral, A., Carette, S., Carmona, R., Chow, A., Ciaschini, P., Cividino, A., Cohen, D., Dixit, S., Haaland, D., Hanna, B., Haroon, N., Hochman, J., Jaroszynska, A., Johnson, S., Joshi, R., Kagal, A., Karasik, A., Karsh, J., Keystone, E., Khalidi, N., Kuriya, B., Larche, M., Lau, A., LeRiche, N., Leung, Fe., Leung, Fr., Mahendira, D., Matsos, M., McDonald-Blumer, Midzic, I., Milman, N., H., Mittoo, S., Mody, A., Montgomery, A., Mulgund, M., Ng, E., Papneja, T., Pavlova, P., Perlin, L., Pope, J., Purvis, J., Rohekar, G., Rohekar, S., Ruban, T., Samadi, N., Shaikh, S., Shickh, A., Shupak, R., Smith, D., Soucy, E., Stein, J., Thompson, A., Thorne, C., Wilkinson, S.