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Association Between Anti-Citrullinated Protein Antibody Status, Erosive Disease and Healthcare Resource Utilization in Patients With RA

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Introduction

- RA is a destructive autoimmune disease driven by pathogenic autoantibodies and proinflammatory cytokines.[1,2]
- The persistently elevated levels of autoantibodies and cytokines in patients with RA result in increased clinical and disease activity, structural damage, functional impairment and socioeconomic costs.[1–4]
- Anti-citrullinated protein antibodies (ACPAs) are highly specific serological biomarkers,[5] which can be predictive of the development of more aggressive disease, extra-articular manifestations, premature mortality and therapeutic response in RA.[6–8]
- Little is known regarding the impact of poor prognostic factors, such as ACPAs and erosive disease, on healthcare resource utilization (HCRU).[9]

Objective

- To characterize the rate of HCRU between anti-cyclic citrullinated peptide positive (anti-CCP+; a surrogate for ACPA) patients with RA, with or without erosions who initiated biologic (b)DMARD treatment.

Methods

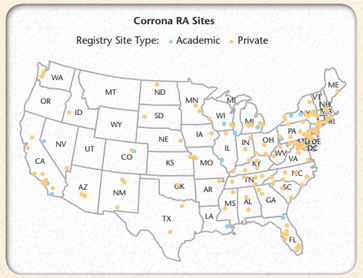
Data source

- The Corrona RA registry is an independent, prospective, national, observational cohort in which treatment and outcomes data for patients with RA are collected and analyzed.
  - Patients are recruited from 177 private practices and academic sites with 736 participating rheumatologists across 42 US states (Figure 1).
  - As of June 2018, the Corrona RA registry included information on approximately 49,162 patients.
  - Data on 373,064 patient visits and approximately 173,389 patient-years of follow-up observation time have been collected.
  - The mean time of patient follow-up is 4.4 years (median, 3.3 years).

Study population

- This analysis included adult patients with RA enrolled between October 2001 and August 2017.
- Patients with RA initiating a bDMARD who were aged ⩾18 years at enrollment and had known erosions, as measured by radiography, and anti-CCP+ status at or prior to bDMARD initiation visit, and a 12-month (±3 months) follow-up visit were included in this analysis.

Figure 1. Corrona Sites From Inception of Registry



- bDMARDs included TNF inhibitors (TNFis; adalimumab, certolizumab pegol, etanercept, golimumab or infliximab) and non-TNFis (abatacept, rituximab, tocilizumab).
- Anti-CCP+ status was defined as an anti-CCP level ⩾20 units/mL.
- Data for follow-up visits were included regardless of switching status.

Study assessments

- HCRU was determined over 12 months from initiation visit using the following measures:
  - all-cause hospitalizations
  - all-site joint surgery visits
  - reported radiographic procedures
    - joint MRI and ultrasounds
  - use of assistive devices
    - devices used for dressing, special or built-up utensils, crutches, cane, special or built-up chair, wheelchair, walker, raised toilet seat, bathtub bar, long-handled appliances for reach, bathtub seat, long-handled appliances in the bathroom and jar opener.
- Outcomes were captured using physician/laboratory follow-up forms.

Statistical analysis

- A descriptive analysis of HCRU was carried out.
- Rates of HCRU per 100 patient-years and risk ratios were estimated with 95% CI using a Poisson regression model and adjusted for age.

Results

Patient disposition and baseline characteristics

- Of 13,914 biologic initiators included in the Corrona RA registry, 3333 had known CCP and erosion status and 12-month follow-up information.
  - Of these patients, 2047 were anti-CCP+ and therefore included in this analysis; 868 with and 1179 without erosions (Figure 2).
- At bDMARD initiation visit, anti-CCP+ patients with and without erosions had a mean (SD) age of 58.9 (12.5) and 55.9 (12.5) years and a mean (SD) disease duration of 11.7 (10.1) and 6.4 (7.5) years, respectively (Table 1).
- Baseline characteristics were generally well balanced between anti-CCP+ patients with or without erosions, except that compared with patients without erosions, those with erosions had a longer RA duration and had higher prior conventional synthetic DMARD, targeted synthetic DMARD and bDMARD use.

Healthcare resource utilization

- Over 12 months of follow-up, among anti-CCP+ patients, the rates of HCRU were higher for patients with versus without erosions at baseline bDMARD initiation visit (Figure 3).

Figure 2. Selection of Eligible Patients for Analysis

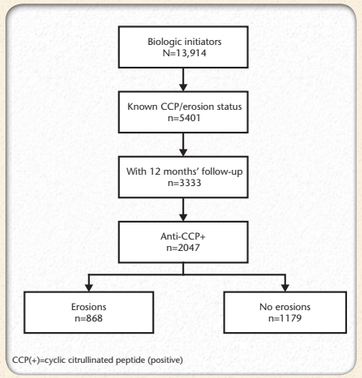


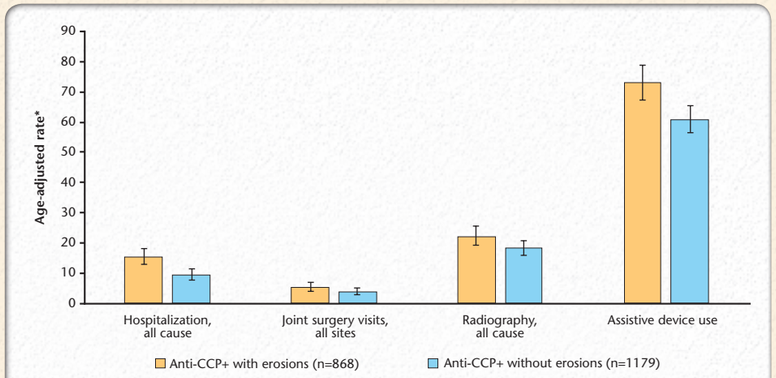
Table 1. Patient Demographics and Disease Characteristics at First bDMARD Initiation Visit

Characteristic	Anti-CCP+ with erosions (n=868)	Anti-CCP+ without erosions (n=1179)
Female sex, n (%)	664 (76.5)	920 (78.2)
White race, n (%)	679 (78.6)	961 (81.7)
Age, years	58.9 (12.5)	55.9 (12.5)
Duration of RA, years	11.7 (10.1)	6.4 (7.5)
Co-morbidities, n (%)		
Diabetes	73 (8.4)	126 (10.7)
Malignancies*	233 (26.8)	264 (22.4)
CVD†	116 (13.4)	109 (9.3)
Hypertension	285 (32.8)	336 (28.5)
Serious infections‡	78 (9.0)	71 (6.0)
BMI	28.6 (6.4)	29.7 (6.9)
Current medication use, n (%)		
TNFi	588 (68.5)	888 (77.1)
Abatacept	130 (15.2)	158 (13.7)
Rituximab/tocilizumab	140 (16.3)	106 (9.2)
No. of prior csDMARDs, n (%)		
0	42 (4.8)	89 (7.6)
1	364 (41.9)	580 (49.2)
2+	462 (53.2)	510 (43.3)
No. of prior biologics/tsDMARDs, n (%)		
0	29 (3.3)	61 (5.2)
1	227 (26.2)	415 (35.2)
2+	612 (70.5)	703 (59.6)
CDAI	21.9 (14.0)	22.1 (14.4)
DAS28 (ESR)§	4.5 (1.5)	4.4 (1.6)
SJC (28)	6.5 (5.5)	6.8 (6.4)
TJC (28)	7.3 (7.0)	7.3 (7.3)
Physician Global Assessment‖	38.7 (22.9)	36.1 (22.4)
Patient Global Assessment‖	43.1 (27.7)	44.3 (26.9)
mHAQ (range: 0 to 3)	0.5 (0.5)	0.5 (0.5)
Patient pain‖	44.9 (28.6)	46.7 (28.2)
Fatigue‖	44.8 (30.1)	46.9 (29.7)

Data are presented as mean (SD) unless otherwise stated
*Malignancies include breast, lung, skin melanoma, lymphoma, other (excludes non-melanoma skin cancer)
†CVD includes MI, stroke, acute coronary syndrome, coronary artery disease, congestive heart failure, revascularization procedure including percutaneous coronary intervention, coronary artery bypass grafting or coronary artery stents, ventricular arrhythmia, cardiac arrest, unstable angina, peripheral ischemia, peripheral artery disease, other cardiovascular, deep vein thrombosis and transient ischemic attack
‡Infections were not included in the Corrona RA questionnaire until version 7 (late 2008)
§DAS28 (ESR) sample counts were lower due to visits without the lab results required for reporting the ESR component of the DAS28 algorithm
‖Data collection instrument: horizontal 100 mm visual analog scale
CCP+=cyclic citrullinated peptide positive; csDMARD=conventional synthetic DMARD; CVD=cardiovascular disease; mHAQ=modified Health Assessment Questionnaire; MI=myocardial infarction; TNFi=TNF inhibitor; tsDMARD=targeted synthetic DMARD

- Rates of all-cause hospitalization, all-cause radiography and assistive device use were significantly higher in those with versus without erosions.
- There was a non-significant trend toward increased rates of joint surgery visits in patients with versus without erosions.

Figure 3. Rates of HCRU in Anti-CCP+ Patients With RA, With and Without Erosions



	Age-adjusted risk ratio*† (95% CI)
Hospitalization, all cause	1.47 (1.14, 1.90)
Joint surgery visits, all sites	1.31 (0.86, 1.98)
Radiography, all cause	1.25 (1.03, 1.53)
Assistive devices	1.12 (1.00, 1.25)

*Rates per 100 patient-years with 95% CI based on Poisson distributed counts
†Reference group: anti-CCP+ and erosions
CCP+=cyclic citrullinated peptide positive; HCRU=healthcare resource utilization

Conclusions

- In patients with RA, ACPA seropositivity with erosive disease predicts high HCRU, suggesting that early therapeutic intervention may be warranted in anti-CCP+ patients with erosions to achieve better disease control and reduce complications from RA.

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Disclosures

LRH: employee: Corrona, LLC and the University of Massachusetts Medical School; shareholder: Corrona, LLC; grant/research support: Pfizer; consultancy fees: Bristol-Myers Squibb and Roche. LG, SR and YS: employees: Corrona, LLC. SEC and EA: employees and shareholders: Bristol-Myers Squibb. JMK: employee and shareholder: Corrona, LLC; consultant: AbbVie, Amgen, Bristol-Myers Squibb, Genentech, Lilly, Regeneron, Sanofi, Pfizer; grant/research support: AbbVie, Bristol-Myers Squibb, Genentech, Lilly, Novartis and Pfizer.