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Authors

Schmajuk, Gabriela
Montgomery, Anna D
Leonard, Samuel
et al.

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Factors Associated With Hospitalization and Death After COVID-19 Diagnosis Among Patients With Rheumatic Disease: An Analysis of Veterans Affairs Data

Gabriela Schmajuk,[1] [iD] Anna D. Montgomery,[1] [iD] Samuel Leonard,[1] Jing Li,[2] Milena Gianfrancesco,[2] [iD]
Andrea Seet,[2] Zara Izadi,[2] [iD] Jinoos Yazdany,[2] [iD] and Salomeh Keyhani[1]

Objective. Individuals with autoimmune rheumatic disease (RD) are considered to be at increased risk for infection. However, few US population-based studies have assessed whether these patients are at increased risk of hospitalization or death due to COVID-19 compared with those without RD.

Methods. We performed a retrospective cohort study using national Veterans Affairs Health Care System data for individuals who tested positive for SARS-CoV-2. Outcomes of interest were hospitalization or death due to any cause within 30 days of COVID-19 diagnosis. Outcomes were compared among veterans with RD and those without RD by using propensity score matching (PSM) and mixed-effects multivariate logistic regression.

Results. Of 26,116 veterans with COVID-19, 501 (1.9%) had an underlying RD. Prior to matching, patients with RD were more likely to have poor outcomes compared with controls (37.7% vs. 28.5% hospitalized; 6.4% vs. 4.5% died). In the PSM analysis, RD was not a significant predictor for poor outcomes; however, patients with prescriptions for glucocorticoids had increased odds of poor outcomes in a dose-dependent manner (odds ratio [95% confidence interval] for hospitalization or death: 1.33 [1.20-1.48] for doses >0 and ≤10 mg/day; 1.29 [1.09-1.52] for doses >10 mg/day).

Conclusion. Among US veterans with COVID-19, we did not find a significant association between RD and hospitalization or death. Poor outcomes appear to be mostly driven by age and other comorbidities, similar to the general veteran population. However, we observed an increased risk for poor outcomes among patients who received glucocorticoids, even at daily doses less than or equal to 10 mg.

INTRODUCTION

Individuals with autoimmune rheumatic diseases (RDs) are considered to be at increased risk for infection because of their underlying condition or exposure to immunosuppressive drugs. However, few population-based studies have assessed whether these individuals are at significantly increased risk of hospitalization or death due to infection with SARS-CoV-2 compared with individuals without RDs. Most of these studies come from Europe: for example, reports from a Swedish nationwide database showed that among patients with inflammatory joint disease, the risks of hospitalization, intensive care unit (ICU) admission, and death due to COVID-19 were slightly increased compared with

among population referents, and most antirheumatic drugs (with the exception of rituximab and Janus kinase [JAK] inhibitors) were not associated with increased risks for poor COVID-19 outcomes (1). Other population-based European studies have generally shown a slightly increased risk of poor outcomes for patients with RD (2–4).

Fewer studies have focused on US populations, in part because of limited availability of nationwide data. D'Silva et al (5) used a multi-institutional electronic health record data set to report on COVID-19 outcomes in patients with RD compared with the general population and found that patients with RD with COVID-19 were at higher risk of hospitalization, ICU admission, acute renal failure, and venous thromboembolism compared

with matched controls, although differences attenuated for all of these outcomes, except venous thromboembolism, when comorbidities and medications were accounted for. England et al (6) used US Veterans Affairs Healthcare System (VAHCS) data to examine COVID-19 outcomes but limited their comparison group to patients with rheumatoid arthritis (RA).

The VAHCS is unique in providing an integrated health care system for US veterans and provides information on diagnoses, medications, laboratory studies, and health care use for all participating patients. In this study, we aimed to assess the risk of hospitalization or death due to COVID-19 in a cohort of US veterans with any RD compared with the general veteran population.

PATIENTS AND METHODS

Study design and data source. We performed a retrospective cohort study of veterans with RD who were diagnosed with COVID-19 using data from the US Department of Veterans Affairs (VA) Corporate Data Warehouse (CDW) (7). Briefly, the CDW contains variables such as inpatient and outpatient diagnoses, medications, and laboratory codes. The CDW also contains information on dates of death, which are updated quarterly. This study included veterans who had their first test result of RNA positivity for SARS-CoV-2 between March 2 and September 30, 2020, documented in the CDW. March 2, 2020, was chosen as the study start date because that is the first date a positive polymerase chain reaction result for SARS-CoV-2 was reported in the CDW. All-cause mortality data were collected from both the CDW and the VA Vital Status File. Veterans were observed for 30 days after their first positive SARS-CoV-2 test result or COVID-19 diagnosis for the outcomes of hospitalization or death.
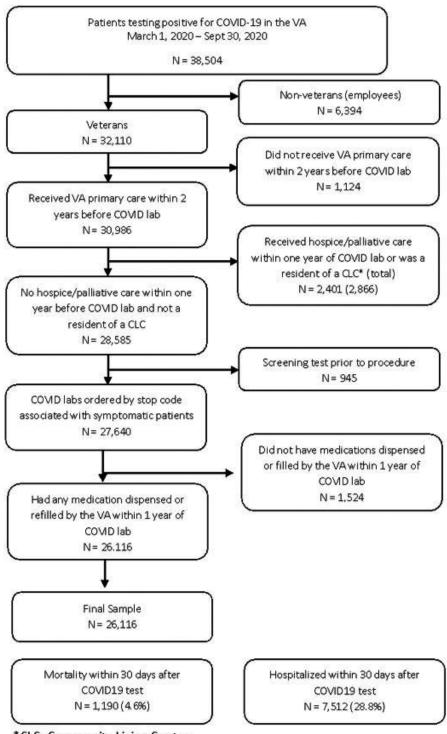
Exclusion criteria. We excluded nonveteran employees who received care through the VAHCS, veterans who did not receive VA primary care within 2 years before their SARS-CoV-2/COVID-19 test result (to ensure reliable capture of comorbid conditions), and veterans who did not have any medications dispensed by the VA within 1 year before their COVID-19 test (to ensure reliable capture of medications). We also excluded veterans who received hospice or palliative care within 1 year before their index test result, veterans who were residents of a community living center (nursing home setting within the VA), and veterans who had a positive SARS-CoV-2/COVID-19 test result as part of surveillance or screening prior to a procedure or infusion (Figure 1).

Predictors and covariates. Primary independent variables included RDs and antirheumatic medications. Autoimmune RDs were identified as veterans with two or more *International Classification of Diseases, 10th Revision* (ICD-10) codes within the same disease category, separated by 30 or more days, within 2 years prior to the patient's COVID-19 test date. Specific RDs included RA, sarcoidosis, polymyalgia rheumatica (PMR), systemic lupus

erythematosus (SLE), or other autoimmune rheumatic diseases that were less prevalent (those with less than 5% prevalence, including antiphospholipid syndrome, other inflammatory arthritis, inflammatory myopathies, antineutrophil cytoplasmic antibody–associated vasculitis, other vasculitis, giant cell arteritis, mixed connective tissue disease, psoriatic arthritis, systemic sclerosis, other spondyloarthritis, and undifferentiated connective tissue disease). Although it was possible for an individual to meet criteria for more than one RD diagnosis, for the purposes of this analysis, we categorized each patient as only having a single rheumatic condition based on a diagnostic hierarchy (from highest priority to lowest: systemic sclerosis, vasculitis, inflammatory myositis, SLE, RA). Therefore, patients with RA did not carry any of the other listed diagnoses.

Veterans were considered users of antirheumatic medications if they were given a greater than or equal to 28-day supply of any of the following within 1 year and up to 7 days prior to their positive SARS-CoV-2/COVID-19 test result: conventional disease-modifying antirheumatic drugs (DMARDs) (including azathioprine, cyclophosphamide, cyclosporine, hydroxychloroquine, leflunomide, methotrexate, mycophenolate mofetil, mycophenolic acid, sulfasalazine, and tacrolimus), biologic or targeted synthetic DMARDs (including abatacept, adalimumab, anakinra, apremilast, baricitinib, belimumab, certolizumab, denosumab, etanercept, golimumab, infliximab, natalizumab, rituximab, secukinumab, tofacitinib, tocilizumab, vedolizumab, and ustekinumab), and glucocorticoids (including oral dexamethasone, hydrocortisone, methylprednisolone, prednisone, prednisolone, and triamcinolone; topical creams, eye drops, and steroidal injections were excluded). For glucocorticoids, the medication dose in milligrams per day was calculated by using the dose amount in the prescription order multiplied by the number of doses per day. The average daily dose was calculated by taking the sum of daily doses for that medication over the duration of the supply divided by the number of days. When the number of doses per day were missing (58.8% of orders), we assumed once-daily dosing. Prior to limiting the days' supply to greater than or equal to 28 days, when the days' supply was not available (16.5% of orders), we assumed it to be a prescription for 30 days. Glucocorticoid use was categorized into two dose categories: more than 0 but less than 10 mg/day and greater than or equal to 10 mg/day.

Other covariates included age (<55, 55-59, 60-64, 65-69, 70-74, 75-79, ≥80), race/ethnicity (non-Hispanic White, Black, Hispanic, other/unknown), marital status (yes or no), body mass index (BMI) (<18.5, 18.5-24.9, 25-29.9, ≥30, unknown), month of positive SARS-CoV-2 test result (March to September), and geographic region (Northeast, Southeast, Continental, or Pacific). We also gathered information on behavioral risks, eg, current tobacco use (8) and/or alcohol abuse; number of inpatient admissions in the 12 months prior to the index date (9); and comorbid conditions (hypertension, ischemic heart disease, atrial fibrillation, stroke, diabetes mellitus, congestive heart failure, chronic kidney disease [CKD], dialysis, chronic obstructive pulmonary disease [COPD], asthma, pneumonia, sleep apnea, deep vein thrombosis [DVT] or pulmonary

Figure 1. Study population flowchart and hospitalizations and death following a COVID-19 diagnosis. CLC, community living center; lab, laboratory test; VA, Department of Veterans Affairs.

embolism [PE], home oxygen use, cancer, human immunodeficiency virus or acquired immunodeficiency syndrome, dementia, and cirrhosis or hepatitis. Comorbidities were defined as one or more inpatient ICD-10 code or two or more outpatient diagnosis codes within 2 years prior to the patient's positive SARS-CoV-2 test result date.

Outcomes. The combined primary outcome variable was hospitalization or death after a diagnosis of COVID-19. Hospitalization was identified by using codes for inpatient admission within 30 days of the first laboratory-confirmed SARS-CoV-2 infection. Death was defined as all-cause mortality measured in the 30-day

Table 1. Description of baseline characteristics for veterans with rheumatic disease versus controls in unmatched and PSM matched cohorts

Characteristics	Unmatched cohorts		PSM model 1 matched cohorts[a]	
	Veterans with rheumatic disease (n = 501)	Controls (n = 25,615)	Veterans with rheumatic disease (n = 501)	Controls (n = 501)
Age (y), n (%)				
<55	160 (31.9)	10,249 (40.0)	160 (31.9)	160 (32.0)
55-59	60 (12.0)	2,661 (10.4)	60 (12.0)	60 (13.9)
60-64	64 (12.8)	3,037 (11.9)	64 (12.8)	64 (12.9)
65-69	47 (9.4)	2,686 (10.5)	47 (9.4)	47 (9.5)
70-74	94 (18.8)	3,693 (14.4)	94 (18.8)	95 (18.9)
75-79	45 (9.0)	1,566 (6.1)	45 (9.0)	45 (9.0)
≥80	31 (6.2)	1,723 (6.7)	31 (6.2)	30 (6.0)
Male sex, n (%)	391 (78.0)	22,742 (88.8)	391 (78.0)	391 (78.0)
Race, n (%)				
White	207 (41.3)	11,721 (44.4)	207 (41.3)	207 (41.3)
Black	223 (44.5)	8,991 (35.1)	223 (44.5)	223 (44.5)
Hispanic	40 (8.0)	3,572 (13.9)	40 (8.0)	40 (8.0)
Other	31 (6.2)	1,690 (6.6)	31 (6.2)	31 (6.2)
Married, n (%)	255 (50.9)	11,721 (45.8)	255 (50.9)	201 (40.1)
Number of inpatient hospital visits in the past year, mean (SD)	0.45 (0.99)	0.22 (0.74)	0.43 (0.99)	0.21 (0.90)
Behavioral risk, n (%)				
Current tobacco use	97 (19.4)	4,749 (18.2)	97 (19.4)	76 (15.2)
Alcohol abuse	80 (16.0)	5,015 (19.6)	80 (16.0)	92 (18.4)
Comorbid conditions, n (%)				
Hypertension	341 (68.1)	14,185 (55.4)	341 (68.1)	280 (55.9)
Ischemic heart disease	117 (23.4)	3,832 (15.0)	117 (23.4)	84 (16.8)
Atrial fibrillation	54 (10.8)	1,973 (7.7)	54 (10.8)	50 (10.0)
Stroke	24 (4.8)	720 (2.8)	24 (4.8)	13 (2.6)
Diabetes mellitus	185 (36.9)	8,298 (32.4)	185 (36.9)	153 (30.5)
CHF	70 (14.0)	2,103 (8.2)	70 (14.0)	39 (7.8)
CKD	145 (28.9)	6,891 (26.9)	145 (28.9)	147 (29.3)
Dialysis	13 (2.6)	412 (1.6)	13 (2.6)	11 (2.2)
COPD	130 (25.9)	2,892 (11.3)	130 (25.9)	57 (11.4)
Asthma	51 (10.2)	1,418 (5.5)	51 (10.2)	37 (7.4)
Pneumonia	42 (8.4)	845 (3.3)	42 (8.4)	6 (1.2)
Home oxygen in past year	34 (6.8)	782 (3.1)	34 (6.8)	37 (7.4)
Sleep apnea	143 (28.5)	4,660 (18.2)	143 (28.5)	72 (14.4)
DVT or PE	35 (7.0)	631 (2.5)	35 (7.0)	13 (2.4)
Cancer	55 (11.0)	2,004 (7.8)	55 (11.0)	51 (10.2)
HIV and AIDS	4 (0.8)	327 (1.3)	4 (0.8)	6 (1.2)
Dementia	26 (5.2)	967 (3.8)	26 (5.2)	19 (3.8)
Cirrhosis or hepatitis	64 (12.8)	1,930 (7.5)	64 (12.8)	36 (7.2)
BMI, n (%)				
≥30	260 (51.9)	13,018 (50.8)	260 (51.9)	254 (50.7)
25.0-29.9	160 (31.9)	7,533 (29.4)	160 (31.9)	148 (29.5)
18.5-24.9	59 (11.8)	3,094 (12.1)	59 (11.8)	63 (12.6)
<18.5	5 (1.0)	110 (0.4)	5 (1.0)	5 (1.0)
Unknown BMI	17 (3.4)	1,860 (7.3)	17 (3.4)	31 (6.2)
Rheumatic diseases, n (%)[b]				
Rheumatoid arthritis	222 (44.3)	-	222 (44.3)	-
Sarcoidosis	113 (22.6)	-	113 (22.6)	-
Polymyalgia rheumatica	32 (6.4)	-	32 (6.4)	-
SLE	30 (6.0)	-	30 (6.0)	-
Psoriatic arthritis	28 (5.6)	-	28 (5.6)	-
Other rheumatic diseases[c]	76 (15.2)	-	76 (15.2)	-
Rheumatic medications, n (%)				
csDMARDs	211 (42.1)	460 (1.8)	211 (42.1)	9 (1.8)
bDMARDs/tsDMARDs	98 (19.6)	185 (0.7)	98 (19.6)	4 (0.8)

(Continued)

Table 1. (*Cont'd*)

	Unmatched cohorts		PSM model 1 matched cohorts[a]	
Characteristics	Veterans with rheumatic disease (n = 501)	Controls (n = 25,615)	Veterans with rheumatic disease (n = 501)	Controls (n = 501)
Glucocorticoids				
>0 and ≤10 mg daily	112 (22.4)	1284 (5.0)	112 (22.4)	0 (0.0)
> 10 mg daily	33 (6.6)	589 (2.3)	33 (6.6)	1 (0.2)

Abbreviations: AIDS, acquired immunodeficiency syndrome; ANCA, antineutrophil cytoplasmic antibody; bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DVT, deep vein thrombosis; HIV, human immunodeficiency virus; PE, pulmonary embolism; PSM, propensity score matching; SLE, systemic lupus erythematosus; tsDMARD, targeted synthetic disease-modifying antirheumatic drug.
[a] PSM model 1 was performed by using the nearest neighbor method. The exposure score included age, sex, marital status, BMI, and race/ethnicity.
[b] Rheumatic condition diagnosis data were derived from the number of veterans with two or more diagnoses within the same disease category separated by 30 d or more.
[c] Other rheumatic diseases included ANCA-associated vasculitis, other vasculitis, giant cell arteritis, other inflammatory arthritis, inflammatory myopathies, antiphospholipid syndrome, other spondyloarthritis, systemic sclerosis, mixed connective tissue disease, and undifferentiated connective tissue disease.

period after the first test date of the laboratory-confirmed SARS-CoV-2 infection/COVID-19 diagnosis.

Statistical analysis. Data were analyzed on the VA Informatics and Computing Infrastructure by using RStudio (version R-3.3. 1). Descriptive statistics were used to estimate the frequency of covariates across groups.

We performed propensity score matching (PSM) using the nearest neighbor matching approach between veterans with RD and a control group of veterans without RD. We used a caliper width equal to 0.2 of the pooled standard deviation of the logit of the propensity score. PSM model 1 included age, sex, race/ethnicity, BMI, and month of positive SARS-CoV-2 test result to generate a propensity score. PSM model 2 included all variables from PSM model 1 with the addition of individual comorbidities to generate a propensity score. We did not require the same controls to be matched to each RD case in the two PSM models. Covariate balance between the PSM cohorts was assessed by using Love plots, which showed that all covariates were matched with an absolute standardized mean difference below 0.1, denoting optimal matching performance (Supplementary Figures 1 and 2). We examined the association of RD and rheumatic medications in the matched cohorts and the outcome using multivariate logistic regression models, which included RD, antirheumatic medications, and individual comorbidities as independent variables for the PSM model 1 cohorts; and RD and antirheumatic medications as independent variables in the PSM model 2 cohorts.

Ethical statement. The Institutional Review Board of the University of California, San Francisco, approved this study and waived the need for patient consent because the research involved no more than minimal risk to participants.

RESULTS

We assessed 38,504 US veterans for eligibility in this study. After applying exclusion criteria, our final sample included 26,116 veterans (Figure 1). Of these, 501 (1.9%) were diagnosed with RD and 25,615 were included as controls. The most common RDs were RA (44.3%), followed by sarcoidosis (22.6%), PMR (6.4%), and SLE (6.0%). Less than half (42.1%) were prescribed conventional synthetic DMARDs (csDMARDs), and approximately one third (29.0%) were prescribed oral glucocorticoids at any dose (Table 1). The RD group was slightly older (mean [SD] 61.2 [13.6] years vs. 57.7 [16.1] for controls). Patients with RD were more likely to be female (22.0% vs. 11.2%), more likely to have had prior inpatient admissions (mean [SD] 0.45 [0.99] vs. 0.22 [0.74] for controls), and more likely to have nearly every comorbid condition listed (Table 1). Other patient characteristics, such as race/ethnicity, marital status, BMI, and behavioral risks, were similar in both groups.

Unmatched analysis. Overall, in the unmatched analysis, patients with RD were more likely to be hospitalized compared with controls (37.7% vs. 28.6%, respectively; *P* = 0.002). There were 1,190 deaths reported: 6.4% among patients with RD and 4.5% among controls (Table 2). The unadjusted odds ratio (OR) (95% confidence interval [CI]) for hospitalization or death for patients with any RD versus all others was 1.60 (1.34-1.92). When we stratified by specific RD, veterans with RA appeared more likely to be hospitalized and/or die compared with veterans without any RD (OR [95% CI] 1.98 [1.52-2.58]); however, patients with non-RA RDs did not appear to be at increased risk (Table 3, column 2). Veterans receiving csDMARDs or glucocorticoids had higher odds of hospitalization and/or death (OR [95% CI]: csDMARDs 2.12 [1.73-2.59]; glucocorticoids at doses >0 and <10 mg/day 2.17 [1.79-2.63]; glucocorticoids at doses ≥10 mg/day 3.62

Table 2. Proportion of patients with hospitalization or death within 30 d of COVID-19 diagnosis for veterans with rheumatic disease versus controls in unmatched and PSM matched cohorts

	Unmatched cohorts		PSM model 1 matched cohorts[a]		PSM model 2 matched cohorts[b]	
	Veterans with rheumatic disease (n = 501)	Controls (n = 27,136)	Veterans with rheumatic disease (n = 501)	Controls (n = 501)	Veterans with rheumatic disease (n = 497)	Controls (n = 497)
Hospitalized within 30 d of COVID-19 diagnosis, n (%)	189 (37.7)	7,323 (28.6)	189 (37.7)	149 (29.7)	185 (37.2)	179 (36.0)
Death within 30 d of COVID-19 diagnosis, n (%)	32 (6.4)	1,158 (4.5)	32 (6.4)	28 (5.6)	30 (6.0)	26 (5.2)

Abbreviations: BMI, body mass index; PSM, propensity score matching.
[a] PSM was performed by using the nearest neighbor method. The exposure score for PSM model 1 included age, sex, BMI, race/ethnicity, and month of positive SARS-CoV-2 test result.
[b] The exposure score for PSM model 2 included age, sex, BMI, race/ethnicity, month of positive SARS-CoV-2 test result, and individual comorbidities.

[3.18-4.12]). As expected, veterans who were older, male, Black or Hispanic, or current tobacco users or those who had various comorbid conditions (ischemic heart disease, diabetes mellitus, CKD, pneumonia, COPD, DVT or PE, dementia, and cirrhosis or hepatitis) were also more likely to be hospitalized or die (Supplementary Table 1).

PSM analyses. The PSM analyses included 501 veterans with RD and 501 controls in PSM model 1 and 497 veterans with RD and 497 controls in PSM model 2 (4 veterans with RD were unable to be matched within the confines of the propensity score).

In PSM model 1, we found no significant effect for any specific RD on the odds of hospitalization or death (Table 3, column 3). Veterans receiving glucocorticoids at doses greater than 0 to less than 10 mg/day or greater than or equal to 10 mg/day had higher odds of hospitalization or death compared with those receiving none (OR [95% CI] 1.33 (1.20-1.48) and 1.29 [1.09-1.52], respectively). Similar to the unmatched models, the covariates of hypertension, heart disease, CKD, COPD, and pneumonia were also significant predictors of poor outcomes (Supplementary Table 1). PSM model 2, which matched on all the same variables as PSM model 1 with the addition of individual comorbid conditions, showed similar results (Table 3, column 4).

Table 3. Associations of rheumatic disease and rheumatic medications with combined outcome of hospitalization or death

	Unmatched unadjusted odds ratio (95% CI), total N = 26,116	PSM model 1 matched[a] odds ratio (95% CI), total n = 1,002	PSM model 2 matched[b] odds ratio (95% CI), total n = 994
n cases	501	501	497
Rheumatic disease (reference: none)			
Rheumatoid arthritis	**1.98 (1.52-2.58)**	1.06 (0.96-1.17)	1.02 (0.93-1.13)
Sarcoidosis	1.16 (0.77-1.70)	0.95 (0.86,1.05)	0.93 (0.85-1.03)
Polymyalgia rheumatica	1.85 (0.90-3.70)	0.99 (0.83-1.18)	0.98 (0.81-1.17)
SLE	1.81 (0.86-3.73)	1.04 (0.86-1.25)	0.99 (0.82-1.45)
Psoriatic arthritis	0.95 (0.39-2.08)	0.91 (0.75-1.11)	0.89 (0.74-1.09)
Other autoimmune rheumatic diseases[c]	1.46 (0.91-2.31)	1.00 (0.88-1.12)	0.99 (0.86-1.09)
Rheumatic medications (reference: none)			
csDMARDs	**3.60 (3.08-4.22)**	0.97 (0.89-1.07)	1.01 (0.92-1.10)
bDMARDs/tsDMARDs	1.21 (0.94-1.55)	1.08 (0.97-1.21)	1.08 (0.96-1.21)
Glucocorticoids			
>0 and ≤10 mg daily	**4.53 (4.05-5.07)**	**1.33 (1.20-1.48)**	**1.35 (1.23-1.48)**
>10 mg daily	**3.41 (2.91-4.01)**	**1.29 (1.09-1.52)**	**1.25 (1.10-1.43)**

Note: The bold values denote statistically significant ($p < 0.01$) Odds Ratios and their confidence intervals.
Abbreviations: ANCA, antineutrophil cytoplasmic antibody; bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; PSM, propensity score matching; SLE, systemic lupus erythematosus; tsDMARD, targeted synthetic disease-modifying antirheumatic drug; VA, Department of Veterans Affairs.
[a] PSM was performed by using the nearest neighbor method. In PSM model 1, the exposure score included age, sex, race/ethnicity, BMI, and month of positive SARS-CoV-2 test result. PSM model 1 included 501 veterans with RD and 501 controls.
[b] In PSM model 2, the exposure score included age, sex, race/ethnicity, BMI, month of positive SARS-CoV-2 test result, and individual comorbidities. PSM model 2 included 497 veterans with RD and 497 controls (4 veterans with RD were unable to be matched within the confines of the propensity score). Multivariate models in the PSM analysis included RD and rheumatic medications and geographic VA facility location as the clustering variable.
[c] Other autoimmune rheumatic diseases included antiphospholipid syndrome, other inflammatory arthritis, inflammatory myopathies, ANCA-associated vasculitis, other vasculitis, giant cell arteritis, mixed connective tissue disease, psoriatic arthritis, systemic sclerosis, other spondyloarthritis, and undifferentiated connective tissue disease.

DISCUSSION

In this study of US veterans with COVID-19, we did not find a significant association between RD and odds of hospitalization or death within 30 days of a COVID-19 diagnosis. Poor outcomes for veterans with RD appear to be driven by age and other comorbidities, similar to the control population. However, we did consistently observe a slightly increased risk for poor outcomes among veterans who received glucocorticoids, even at doses less than 10 mg.

It is interesting to put our results in the context of other population-based studies. Our findings are distinct from the US-based population-based study of COVID-19 outcomes among patients with RD using TriNetX data, which described an increased risk for hospitalization, ICU admission, acute renal failure, and venous thromboembolism among patients with RD (5). These differences may stem from the veteran population being predominantly male, secular trends related to date of COVID-19 diagnosis, or other regional differences or may represent residual confounding because we were able to control for many more comorbid conditions, including individual comorbidities, as well as social factors such as, marital status and tobacco or alcohol use.

Our results were also different compared with the study of COVID-19 outcomes using VAHCS data among patients with RA (6). There are several key methodologic differences that could explain why we found a smaller effect size for patients with RD and, specifically, for patients with RA: First, we excluded patients who did not receive VAHCS primary care or who did not have at least one medication filled through the VAHCS pharmacy. This step was taken to minimize missing outcomes because patients not receiving VAHCS primary care are more likely to be hospitalized outside the VAHCS, which makes their outcomes more difficult to ascertain. Second, we excluded patients who were tested for SARS-CoV-2 as part of asymptomatic preprocedure screening protocols, including elective surgeries or infusions, which eliminated many asymptomatic patients who may have been included in the other study. Third, our definitions for rheumatic conditions were based on the presence of ICD-10 codes but did not require DMARD use, visits to a rheumatologist, or serologic tests. Our definition is therefore more sensitive but less specific than those used by England et al. (6,10).

Finally, a large study from Sweden found modest (20%-30%) increases in the hazard of hospitalization or death related to COVID-19 among patients with RA or other inflammatory joint diseases as well as increased risks among patients receiving rituximab and JAK inhibitors (1). We did not observe such risks, although we may have been limited by sample size in patients receiving these classes of medications. Importantly, the Swedish study did not account for glucocorticoid use or dose, which could explain some of the differences compared with this study. The risks we observed among veterans prescribed glucocorticoids were similar across glucocorticoid doses, whereas other studies have described a more dramatic dose-dependent risk (11).

Our study has several limitations. The veteran population is predominantly male and older, so findings may not be generalizable to non-VAHCS settings. Although our PSM model included a wide range of covariates across many domains and demonstrated balance across covariates, we cannot exclude residual confounding. We did not have data on disease activity, which has recently been shown to be an important factor in predicting COVID-19 outcomes (12). We defined medication exposure on the basis of prescription at any time during the 12 months preceding the index date, so the exposure to DMARDs or glucocorticoids in the weeks to months leading up to the COVID-19 diagnosis may have been misclassified. Glucocorticoid prescriptions in which daily dose could not be determined were assumed to be dosed just once per day, which may have resulted in an underestimation of daily dose for some patients. It is possible that some patients died of COVID-19 after a prolonged (>30 days) hospitalization, in which case we could not have captured some deaths related to COVID-19; however, it is unlikely that prolonged hospitalization and death would vary by exposure status. It is also possible for veterans to be admitted to non-VA hospitals, which would result in under-ascertainment of the hospitalization outcome. However, we included a population of veterans who were users of VA primary care, laboratory, and pharmacy services, which increases the likelihood that they would be hospitalized at the VA. Finally, although we excluded patients who were tested as part of preprocedure screening protocols, patients with RD may still have been screened and diagnosed with COVID-19 differentially compared with controls.

Strengths of the study include that this is a large population-based sample of veterans from across the United States coming from an integrated health care system in which diagnoses, medication use, and laboratory studies are all observable. We were able to control for a large number of comorbid conditions and social determinants of health, as mentioned above.

In conclusion, our study suggests that veterans with RD do not appear to be at higher risk for poor COVID-19 outcomes above the risk conferred by age and other comorbidities; however, glucocorticoid use did appear to increase risk of poor outcomes, even at lower doses.

AUTHOR CONTRIBUTIONS

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