Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Tumor necrosis factor inhibitors and methotrexate are associated with decreased COVID-19-related hospitalization: Follow up of "Clinical outcomes of COVID-19 in patients taking tumor necrosis factor inhibitors and methotrexate"

To the Editor: Earlier in the COVID-19 pandemic, we studied the effects of tumor necrosis factor inhibitors (TNFis) and methotrexate (MTX) on disease severity following COVID-19. There were fewer patients on these therapies who required hospitalization or died compared to controls; however, this association was insignificant.[1] A study conducted during this period by Veenstra and coworkers also examined the relationship between TNFi and COVID-19, and found these medications to be associated with less severe disease.[2] Another study found MTX was associated with reduced mortality.[3] Since a much greater number of COVID-19 cases are now available for analysis, we re-examined the TriNetX database to clarify the relationship between COVID-19 severity and MTX or TNFi exposure.

TriNetX is a global federated research network that provides access to statistics on electronic medical records across 66 health care organizations, as described previously.[1] Since our prior study, the TriNetX COVID-19 research network has almost doubled in size from over 53 million to over 95 million patients. Those with a COVID-19-related diagnosis since January 20, 2020 also increased from 32,076 to over 1.7 million. Among adults with documented COVID-19, 24,068 were exposed to a TNFi or MTX within 1 year before diagnosis compared with our previous cohort of 214 patients.

We queried the TriNetX COVID-19 research network on June 14, 2022 for adult patients with documented exposure to a TNFi (adalimumab, infliximab, etanercept, certolizumab, or golimumab) or MTX within 1 year of COVID-19 diagnosis. Outcomes examined were hospitalization or death within 45 days of COVID-19 diagnosis. Cohorts included TNFi and MTX as well as patients on both medications. 1:1 propensity score matching was performed for comorbidities associated with poor COVID-19-related outcomes (Supplementary Tables I and II, available via Mendeley at https://doi.org/10.17632/tvvwmbry4h.2).[4] Analyses were assembled using the *International Classification of Diseases, 10th Revision, Clinical Modification* diagnoses and terminology recommended by the World Health Organization and Centers for Disease Control and Prevention (Supplementary Appendix, available via Mendeley at https://doi.org/10.17632/tvvwmbry4h.2).

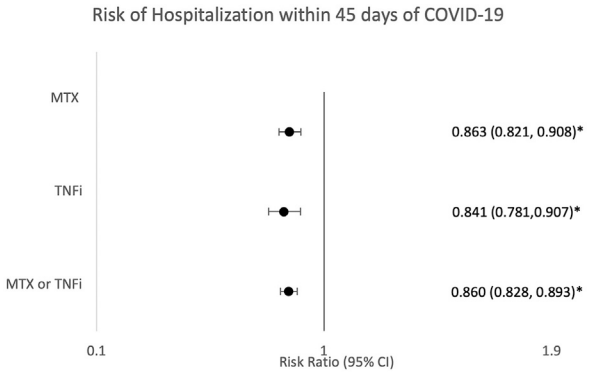

Fig 1. Risk of hospitalization within 45 days of COVID-19. Risk ratios and 95% CIs were calculated to assess the likelihood of hospitalization within 45 days of receiving a diagnosis associated with COVID-19 in patients on methotrexate or tumor necrosis factor inhibitor after 1:1 propensity matching. *MTX*, Methotrexate; *TNFi*, tumor necrosis factor inhibitor. *$P < .05$ was considered significant.

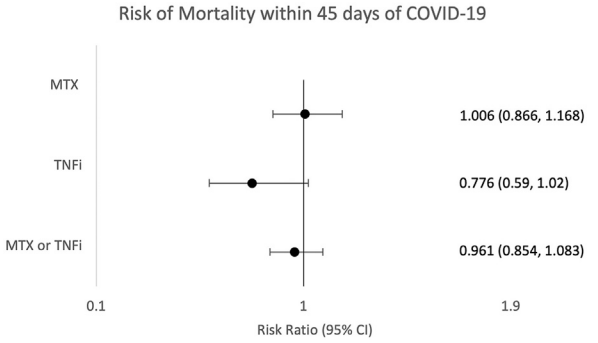

Fig 2. Risk of mortality within 45 days of COVID-19. Risk ratios and 95% CIs were calculated to assess the likelihood of mortality within 45 days of receiving a diagnosis associated with COVID-19 in patients on methotrexate or tumor necrosis factor inhibitor after 1:1 propensity matching. *MTX*, Methotrexate; *TNFi*, tumor necrosis factor inhibitor. *$P < .05$ was considered significant.

For each matched group, the likelihood of hospitalization was significantly decreased. Risk differences were 2.786% in the combined TNFi/MTX group (risk ratio [RR] = 0.860 [95% CI 0.828, 0.893]), 2.933% in the TNFi group (RR = 0.841 [95% CI 0.781, 0.907]), and 2.952% in the MTX group (RR = 0.863 [95% CI 0.821, 0.908]) for hospitalization (Fig 1). Mortality for matched groups did not reach significance with risk differences of 0.087% for TNFi/MTX, 0.385% for TNFi, and 0.016% for MTX (RR = 0.961 [95% CI 0.854, 1.083], RR = 0.776 [95% CI 0.59, 1.02], RR = 1.006 [95% CI 0.866, 1.168], respectively) (Fig 2).

Consistent with the study by Veenstra and coworkers, our results suggest that patients on MTX

and TNFi are not at increased risk of more severe COVID-19-related sequelae and that TNFi may be associated with less severe disease.[2] Ours are among the first to suggest MTX may also be associated with milder COVID-19. These findings continue to support ongoing use of TNFi and MTX without interruption due to fear of worse COVID-19 outcomes and also support the rationale for ongoing randomized trials testing TNFi and MTX as therapy for COVID-19.[5]

Rachel Tallman Cahn, MD, Zachary Zinn, MD, and Michael S. Kolodney, MD, PhD

From the Department of Dermatology, West Virginia University, Morgantown, West Virginia.

Funding sources: None.

IRB approval status: Not applicable.

Key words: coronavirus; COVID-19; methotrexate; SARS-CoV-2; TNF-alpha; tumor necrosis factor-alpha inhibitor.

Correspondence to: Rachel Tallman Cahn, MD, Department of Dermatology, West Virginia University, 1 Medical Center Dr, HSC PO Box 9158, Morgantown, WV 26506-9158

E-mail: rmtallman@hsc.wvu.edu

Reprint requests: Michael S. Kolodney, MD, PhD, Department of Dermatology, West Virginia University, 1 Medical Center Dr, HSC PO Box 9158, Morgantown, WV 26506-9158

E-mail: michael.kolodney@hsc.wvu.edu

Conflicts of interest

None disclosed.

REFERENCES

1. Yousaf A, Gayam S, Feldman S, Zinn Z, Kolodney M. Clinical outcomes of COVID-19 in patients taking tumor necrosis factor inhibitors or methotrexate: a multicenter research network study. *J Am Acad Dermatol*. 2021;84(1):70-75. https://doi.org/10.1016/j.jaad.2020.09.009
2. Veenstra J, Buechler CR, Robinson G, et al. Antecedent immunosuppressive therapy for immune-mediated inflammatory diseases in the setting of a COVID-19 outbreak. *J Am Acad Dermatol*. 2020;83(6):1696-1703. https://doi.org/10.1016/j.jaad.2020.07.089
3. FAI2R /SFR/SNFMI/SOFREMIP/CRI/IMIDIATE consortium and contributors. Severity of COVID-19 and survival in patients with rheumatic and inflammatory diseases: data from the French RMD COVID-19 cohort of 694 patients. *Ann Rheum Dis*. 2021;80(4):527-538. https://doi.org/10.1136/annrheumdis-2020-218310
4. Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ*. 2020;368:m1198.
5. Hachem H, Godara A, Schroeder C, et al. Rapid and sustained decline in CXCL-10 (IP-10) annotates clinical outcomes following TNFα-antagonist therapy in hospitalized patients with severe and critical COVID-19 respiratory failure. *J Clin Transl Sci*. 2021;5(1):e146. https://doi.org/10.1017/cts.2021.805

https://doi.org/10.1016/j.jaad.2023.02.002

Association between psoriasis and celiac disease: A cross-sectional study in the All of Us Research Program

To the Editor: Psoriasis is an inflammatory skin and systemic disease associated with multiple comorbidities, including gastrointestinal disorders such as inflammatory bowel disease and non-alcoholic fatty liver disease.[1] Multiple studies have investigated the association between psoriasis and celiac disease (CD) with conflicting results.[2] We examined the association between psoriasis and CD using the All of Us Research Program, a National Institutes of Health database that contains clinical data on a socioeconomically diverse cohort of over 300,000 Americans.[3]

We performed a cross-sectional analysis of *All of Us*, which includes adults age 18 and older from 2018 to present. We used electronic health record data to identify psoriasis and CD based on Systemized Nomenclature of Medicine diagnostic codes. We identified psoriasis and CD cases using the Systemized Nomenclature of Medicine codes 9,014,002 and 396,331,005, respectively. We used $\chi 2$ test for categorical variables and unpaired *t* tests for continuous variables to compare patients with psoriasis against patients without psoriasis. We used logistic regression to calculate odds ratios and determine whether psoriasis was associated with CD. Our multivariable model was adjusted for age, sex, race/ethnicity, smoking status, autoimmune diseases independently associated with psoriasis and CD (systemic lupus erythematosus, rheumatoid arthritis, inflammatory bowel disease, type 1 diabetes mellitus, autoimmune thyroiditis, vitiligo, alopecia areata), and body mass index.[4,5]

We identified 316,166 patients (mean [SD] age, 54.1 [16.8] years; 58.6% female patients). Of the 6476 patients with psoriasis, 107 (1.65%) had CD, whereas out of 309,690 patients without psoriasis, 1520 (0.49%) had CD ($P < .001$). Patients with psoriasis significantly differed in age (mean, 61.4 vs 54.0; $P < .001$), race (69.1% vs 47.8% White; $P < .001$), body mass index (mean, 31.0 vs 29.8; $P < .001$), smoking (46.0% vs 39.4%; $P < .001$), and autoimmune disease (22.6% vs 6.4%; $P < .001$) compared to patients without psoriasis (Table I). In multivariable analysis, psoriasis remained significantly associated with CD (odds ratio, 2.05; 95% CI, 1.67-2.51; $P < .001$) (Table II).