Prevalence of Depressive Symptoms in Patients With Psoriatic Arthritis: Have Numbers Changed During the COVID-19 Pandemic?

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This longitudinal analysis compares the prevalence of depressive symptoms in patients with psoriatic arthritis in the context of the COVID-19 pandemic. Data from a national patient register in Germany were analyzed regarding the Patient Health Questionnaire 2 (PHQ-2) to identify cases suspicious for depression at two time points, i.e., before and during the COVID-19 pandemic. Only patients with complete concurrent information on the Disease Activity in Psoriatic Arthritis Score (DAPSA) were included in the analysis. The frequency of depressive symptoms in psoriatic arthritis patients during the COVID-19 pandemic did not differ from the prevalence rates measured before. In addition, prevalence rates for depressive symptoms did not differ when stratifying the patient sample for DAPSA levels of disease activity measured before the pandemic. These results were confirmed further in a sensitivity analysis, limiting the second PHQ-2 assessment to lockdown periods only. However, longitudinal data on the prevalence of depressive symptoms in patients with rheumatic diseases, in general, and psoriatic arthritis, in particular, are scarce in the context of the COVID-19 pandemic. For a sensible comparison of prevalence rates for depressive symptoms in the future, underlying SARS-CoV-2 infection rates and resulting local healthcare disruptions need to be taken into account, besides the potential use of different depression screening tools to evaluate resulting numbers sensibly and draw corresponding conclusions for patient care.

Keywords: arthritis, psoriatic arthritis, depressive symptoms, COVID-19, SARS-CoV-2, depression
INTRODUCTION
Depression is acknowledged as frequent comorbidity in inflammatory arthritis (1–4). Psoriatic arthritis (PsA) is one of the diseases summarized under the “inflammatory arthritis” label, with reported prevalence rates for depression of about 13–20% (1, 2). PsA is found in 0.1–1% of the general population and is particularly frequent in patients with psoriasis (≈20%) involving the skin, nails, joints, and entheses (5). PsA patients typically face a combination of dermal and musculoskeletal symptoms impacting the health-related quality of life and social life, resulting in everyday minor and major challenges. Accordingly, recommendations for rheumatologists and dermatologists to screen and manage PsA patients regarding the underlying risk of depression were developed (6). However, regular depression screening has not been implemented into routine rheumatology care yet to help identify patients needing professional mental healthcare support. While depression screening still needed broader implementation into rheumatology care, another challenge occurred in December 2019 caused by a new coronavirus strain (SARS-CoV-2), later referred to as COVID-19. With its global spread and despite the successful initial containment of the first SARS-CoV-2 cases in late January 2020, the first wave eventually hit Germany in early March 2020, resulting in a first national shutdown by March 22nd. The temporal unavailability of face masks further stressed the situation for healthcare professionals and patients in Germany. Although resident rheumatologists and hospitals had taken quick action to refine sanitation and hygiene protocols to reduce SARS-CoV-2 infection risk for staff and patients as far as possible, many routine consultations had to be canceled and postponed. Similar and even more severe disruptive changes in rheumatology care were reported among patients with rheumatic and musculoskeletal diseases in the United States and other European countries (7, 8). In a corresponding qualitative analysis of reported perceptions given by patients referring to the pandemic, the following key themes were identified: emotions in response to the pandemic, perceptions of risks from immunosuppressive medications, protective measures to reduce risk of SARS-CoV-2 infection, and disruptions in accessing rheumatic disease medications (7). Given underlying health concerns, PsA patients perceived SARS-CoV-2 as a larger threat to their health than patients with psoriasis, whereas patients on biologics were more concerned about SARS-CoV-2 and potential outcomes of a SARS-CoV-2 infection (9). Importantly, if health concerns remain unaddressed over a longer time, disregarded feelings of helplessness may lead to depression. Systematic reviews and meta-analyses have consequently reported a high prevalence of depression in the general population, in (front-line) healthcare professionals, and patients diagnosed with SARS-CoV-2 during the pandemic (10–14). However, longitudinal data on this topic are scarce and, thus, little is known about whether the prevalence of depressive symptoms in PsA patients has increased during the COVID-19 pandemic. This retrospective analysis of PsA patient data aims to add some information to this gap and addresses whether depressive symptoms were more frequent during the COVID-19 pandemic than they were before.

METHODS
Patient Sample and Setting
Routine clinical data from patients with an established diagnosis of PsA coming from eight centers in Germany participating in the RheumaDatenRhePort (RHADAR) register were included. RHADAR is a real-world longitudinal register for adult patients with rheumatic diseases in Germany. After informed consent, patients’ pseudonymized data are added to the database. For this report, patients having consented until March 31st, 2021, were part of the data analysis. Further details on the RHADAR register can be found elsewhere (15). Symptoms of depression were assessed using the Patient Health Questionnaire-2 (PHQ-2), a brief two-item depression screening tool, which had previously been validated in patients with rheumatoid arthritis, demonstrating good sensitivity and specificity (16, 17). The PHQ-2 sum score ranges from 0 (best) to 6 (worst), with scores ≥3 indicating depressive symptomatology. The RHADAR database was queried for patients who had had a first PHQ-2 assessment in the 12 months preceding the confirmation of the first SARS-CoV-2 cases in Germany (T1: January to December 2019, first SARS-CoV-2 cases in Germany: January 27th 2020) and had another assessment during the pandemic, i.e., after the first national lockdown taking effect on March 22nd 2020 (T2). If multiple PHQ-2 assessments for T1 were available, the first of them was chosen. The second assessment was supposed to be including PsA patients whose appointments had previously been postponed to cover changes in affective mood, resulting from potential healthcare disrupting effects. In addition, all patients included had to have an assessment of the Disease Activity in Psoriatic Arthritis Score (DAPSA) corresponding to each PHQ-2 assessment (18). Additional sample characteristics include information on sex, age, disease duration, the Hannover Functional Ability Questionnaire (HFAQ) as a measure of physical functioning, which is equivalent to the Health Assessment Questionnaire Disability Index (HAQ-DI), the Body Surface Area (BSA) for skin involvement, and anti-rheumatic treatment, aggregated by drug class (19). Besides the RHADAR inclusion criteria and the mandatory availability of data on PHQ-2 and DAPSA before and during the SARS-CoV-2 pandemic, no further inclusion or exclusion criteria were applied.

Statistical Data Analysis and Analysis Software
Descriptive characteristics of quantitative variables are presented as mean ± standard deviation and as absolute frequencies (per cent) for nominal data if not stated otherwise. Data on prescribed medication were aggregated into the following drug classes: conventional-, targeted synthetic-, and biological disease-modifying anti-rheumatic drugs (cDMARDs, tsDMARDs, bDMARDs), non-steroidal anti-inflammatory drugs (NSAIDs), and glucocorticoids (GCs). Due to combination therapies, the reported total number of prescriptions may exceed the sample size. Missing values were not imputed to preserve the original information of the available raw data. Differences in the prevalence of symptoms of depression and the prescription...
frequencies of aggregated standard anti-rheumatic therapies for PsA were investigated by McNemar's tests for paired nominal data, including Yate's correction for continuity. PHQ-2 sum scores were dichotomized using a sum score cutoff $\geq 3$, which is the standard threshold to identify cases suspicious for depression. For both time points, before and during the pandemic, the frequencies of the dichotomized PHQ-2 scores were compared. In a subsequent step, this analysis was repeated, stratified for DAPSA levels of disease activity, i.e., $\leq 4$ for remission, $>4$ and $\leq 14$ for low disease activity, $>14$ and $\leq 28$ for moderate disease activity and $>28$ for high disease activity (20). The stratified PHQ-2 analysis as well as the analysis of drug class-specific prescription frequencies were adjusted for multiple comparisons using Bonferroni-Holm correction to control type I error probability. Inferential test results include test coefficient, $p$-value and effect size, i.e., odds ratios with corresponding 95% confidence intervals. McNemar test-related odds ratios were calculated from the division of the off-diagonal cells in the respective contingency table (Supplementary File). An additional sensitivity analysis regarding PHQ-2-related outcomes was conducted to investigate whether the choice of the T2 assessment impacted the results. For this analysis, only patients with a second PHQ-2 assessment during lockdown periods were included. The data analysis was conducted using R (version 4.1.0.) and RStudio IDE (version 1.4.1103) (21, 22). $P \leq 0.05$ were considered statistically significant in cases with no multiple testing adjustment.

RESULTS

Description of the Patient Sample

Eighty-nine PsA patients with 48 female patients (53.93%) and 41 male patients (46.07%) were included in the analysis. On average, patients were 54.16 $\pm$ 11.66 years of age and had a disease duration of 9.33 $\pm$ 9.02 years at T1. Mean T1 DAPSA was 10.38 $\pm$ 14.56, suggesting patients had low disease activity on average, whereas the subgroup analysis revealed the following distribution across DAPSA categories: 38 (42.70%) remission, 31 (34.83%) low disease activity, 12 (13.48%) moderate disease activity, and 8 (8.99%) high disease activity. Mean DAPSA at T2 was 7.91 $\pm$ 10.31, whereas DAPSA confidence intervals for both time points indicated comparable disease activity (Table 1). With potential scores ranging from 0 (worst) to 100 (best), average HFAQ-scores showed mild impairment of physical functioning at both time points (T1: 80.83 $\pm$ 21.77, T2: 82.51 $\pm$ 20.30). Further descriptive information is presented in Table 1.

At T1, cDMARDs were the most frequent drug ($n = 57$, 64.04%), followed by NSAIDs ($n = 45$, 50.56%), bDMARDs ($n = 35$, 39.33%), GCs ($n = 15$, 16.85%), and tsDMARDs ($n = 1$, 1.12%). Complete data on anti-rheumatic medication was available for 88 (98.88%) patients at T1 and 85 (95.51%) patients at T2. Except for GCs ($X^2(1) = 7.11$, $p = 0.008$), which were prescribed less frequent at T2 than at T1, prescription frequencies between the time points of interest did not differ (see section 1 of Supplementary File for further information). The corresponding odds ratio for GCs could not be calculated as division by 0, given by the contingency table, is undefined. However, the change in the prescription frequency of GCs remained significant after multiple testing adjustments (critical $p_{adj} = 0.01$). Importantly, our results did indicate that neither cDMARDs [$X^2(1) = 0.36$, $p = 0.55$, 95%CI$_{OR}$ = 0.17–1.95] nor bDMARDs [$X^2(1) = 0$, $p = 1.0$, 95%CI$_{OR}$ = 0.14–7.10] were prescribed more or less often during the pandemic than before.

Prevalence of Depressive Symptoms

PHQ-2 frequency analysis showed that the majority of the patients in our sample had a PHQ-2 sum score $\leq 2$, which is below the cutpoint for an indication of depressive symptoms at both time points (T1: $n = 74$, 83.15%; T2: $n = 76$, 85.39%). A total of 15 (T1) and 13 (T2) patients were found to show depressive symptomatology. Accordingly, the prevalence of symptoms of depression, identified by a PHQ-2 sum score $\geq 3$, was 16.85% at T1, and 14.61% at T2, respectively. The corresponding inferential McNemar analysis did not reveal any significant changes regarding depressive symptoms when comparing data from before SARS-CoV-2 to data during the pandemic [$X^2(1) = 0.06$, $p = 0.803$, 95%CI$_{OR}$ = 0.48–3.45]. Corresponding frequency data even suggested a slight (although non-significant) decrease in prevalence rates. When PHQ-2 data were stratified for DAPSA levels of disease activity, each of the resulting four categories did not indicate any significant changes in prevalence rates for depressive symptoms. With $p$-values ranging from 0.617 to 1.000 and 95% odds ratio confidence intervals encompassing 1, prevalence rates seemed equal over time irrespective of the DAPSA stratification for disease activity. Further details on PHQ-2 test results are shown in Tables 2, 3; contingency tables are shown in section 2 of the Supplementary File. The sensitivity analysis reduced longitudinal comparisons only to those patients that had their second assessment during one of the two national lockdowns. The corresponding results confirmed the previous findings, again, suggesting prevalence rates for depressive symptoms before and during the SARS-CoV-2 pandemic to be comparable in our sample [$X^2(1) = 0.25$, $p = 0.617$, 95%CI$_{OR}$ = 0.31–28.84; $X^2(1) = 1.50$, $p = 0.221$, 95%CI$_{OR}$ = 0.58–42.80; see section 3 of the Supplementary File for corresponding contingency tables].

DISCUSSION

Regarding the prevalence of depressive symptoms identified by the PHQ-2, our results align with the numbers given by recent systematic reviews in PsA (1, 2). Surprisingly, the results of our data analysis suggest depressive symptoms not to occur more often during the SARS-CoV-2 pandemic compared to the 2019 data for patients having completed a depression screening at both time points. Except for GCs, that were prescribed less frequent at T2, our findings showed that anti-rheumatic medication remained unchanged in the vast majority of our sample. Thus, switches of anti-rheumatic medication do not seem to be a reason for the stable prevalence rates. With the help of a sensitivity analysis regarding the choice of the T2 time point, we were also able to show that results remained unchanged when limiting the second assessment to lockdown periods only. However, given the challenges the healthcare system and rheumatologists
were facing, particularly during the first national lockdown, the corresponding sample sizes were smaller (T2: first lockdown: \( n = 18 \), T2: second lockdown: \( n = 50 \)). A post-lockdown study confirmed a similar prevalence in patients with inflammatory arthritis and gave a plausible explanation of why depressive symptoms might not occur more frequently during the SARS-CoV-2 pandemic (23). According to Ciaffi et al., patients with inflammatory arthritis showed higher resilience scores than study participants from the general population—-independent of the patients’ age or disease duration (23). Resilience is a psychological construct implying resistance to environmental risk experiences or overcoming stress or adversity (24). The authors of the study above hypothesize whether higher resilience might result from the necessity for patients to adapt to everyday hassle resulting from inflammatory arthritis, in turn, training their abilities to cope more effectively in challenging situations.
Given comparable results regarding 95% confidence intervals of mean PHQ-2 scores of database patients with a single PHQ-2 assessment at T1 (i.e., patients who were not included into the analysis) and the patient sample presented, we assume that patients with a single PHQ-2 assessment at T1 did not show higher depressiveness on average than the patients included into the analysis of this manuscript (95%CI only T1: 1.44–1.68, 95%CI patient sample: 1.04–1.72). Hence, a potential selection bias resulting from a mandatory T1 and T2 documentation as inclusion criterion is unlikely. Unfortunately, longitudinal data for comparing the prevalence of depressive symptoms before and during SARS-CoV-2 are scarce in rheumatology, yet and, thus, would merit further, preferably large-scale data input leading to improved insights of what kind of circumstances still
can be handled by improved resilience capabilities of patients with rheumatic disorders and at which point even these might not suffice to bolster challenges such as those resulting from the pandemic.

In conclusion, our analysis showed similar prevalence rates of depressive symptoms before and during SARS-CoV-2 in PsA patients in Germany, irrespective of the patients’ DAPSA category or the timing of the during COVID-19 assessment. To the best of our knowledge, this is the first longitudinal investigation of depressive symptoms in patients with PsA during the COVID-19 pandemic.

**DATA AVAILABILITY STATEMENT**

The data analyzed in this study is subject to the following licenses/restricions: The raw data for this analysis are not openly available given the patients’ consent, allowing for the publication of aggregated data only. However, information on aggregated raw data is given in the contingency tables of the Supplementary Material. Requests to access these datasets should be directed to pmanagement@statscoach.de.

**ETHICS STATEMENT**

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

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**AUTHOR CONTRIBUTIONS**

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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**SUPPLEMENTARY MATERIAL**

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2021.748262/full#supplementary-material
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Conflict of Interest: WV, CD, SK, PB-B, CK, KK, SS-M, PA, and MW are members of RheumaDatenRhePort GbR. RHADAR GbR received honoraria from UCB Pharma GmbH, Sandoz Deutschland/Hexal AG, Lilly GmbH, and Galapagos Biopharma Germany GmbH, and research support from Novartis Pharma GmbH. ME received remunerations from RheumaDatenRhePort GbR for statistical data analyses and consultation for previous projects.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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