Changes in immunosuppressive medication because of COVID-19 by patients with chronic inflammatory rheumatic diseases: anxiety was not a major driver

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Abstract

Objective

To study treatment decisions of patients with chronic inflammatory rheumatic diseases (CIRD) at the beginning of the SARS-CoV-2 pandemic in relation to disease characteristics with focus on anxiety.

Methods

A total of 970 CIRD patients diagnosed with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriasis arthritis (PsA) and connective tissue diseases (CTD), selected from our records who had presented to our hospital at least twice during last year, were contacted by telephone to be asked about medication changes, health status and therapy satisfaction. Standardised tools were used to assess disease activity, anxiety and depression, the latter by Hospital Anxiety and Depression Score (HADS) with a score ≥8 denoting definite anxiety and/or depression. The cut-off for RADAI was set at ≥3.2 and for BASDAI ≥4. Compliance with prevention rules and vaccination status were assessed.

Results

Complete interviews of 557 patients (57.4%) made between April and July 2020 were available for analysis.

The median age was 55 (47–63), disease duration 9.0 (4.5–17.0) years, 61.9% females. A recent change in medication was reported by 197 patients (35.4%), 51.2% of which admitted that this decision was mainly made due to the pandemic with more changes occurring with bDMARDs (21.8%) than cDMARDs (6.6%) and corticosteroids (5.4%). There was no major difference between patients who changed because of the pandemic or self-reported inactive disease versus patients who did not change therapy regarding disease activity, depression and anxiety (41%, 17.2%, 31.3% vs. 47.5%, 22.5%, 35.0% vs. 48.9%, 27.7%, 34.1%). More than 90% of patients reported that they rigorously followed Corona prevention rules. The majority of patients were vaccinated against influenza (55.3%) and pneumococci (61.3%), respectively.

Conclusion

Anxiety, depression and disease activity did not play an important role in decisions favouring change of therapy, even though many patients changed medication due to the pandemic. Patients probably protected themselves by strictly adhering to hygiene recommendations. Vaccination rates against influenza and pneumococci were better than previously reported, but still too low.

Key words

rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, connective tissue diseases, SARS-CoV-2, pandemic, anxiety
Introduction

Whether patients with chronic inflammatory rheumatic diseases (CIRD) are more at risk for a severe course of COVID-19 infections than the general population is still unclear, but the known risk factors male gender, age, pulmonary and cardiovascular disease are also relevant for patients with common CIRD, such as rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), including ankylosing spondylitis (AS), psoriasis arthritis (PsA) and connective tissue diseases (CTD) (1). The benefits of treatment with conventional (c), biologic (b) or targeted synthetic (ts) disease-modifying anti-rheumatic drugs (DMARDs) to neutralise pro-inflammatory cytokines are well established in patients with CIRD (2). However, there are also risks such as a minor increase in infections, but no excess of mortality associated with corticosteroids, b- and tsDMARDs (3, 4). These aspects are potentially relevant for the current pandemic.

In the early days of the pandemic not much was known about the outcome of SARS-CoV-2 infections in patients with CIRD, especially under immunosuppressive therapy. This was the reason why this study had initially been started. An early report has already been published (5). In the meantime, several reports on the outcome of SARS-CoV-2 infections in patients with CIRD became available from other countries (6-9). The region our hospital is mainly serving is North Rhine-Westphalia (NRW) with 17.93 million inhabitants. By the end of February 2021 there were 544,937 subjects infected (3% of the population), 13,380 of which died (case fatality rate 2.5%) (10). These rates are not much different from national ones (10). The function and structure of our specialised tertiary care centre has recently been described in detail (15). Starting on April 15th 2020, 10 experienced rheumatologists interviewed patients with one of these four diagnoses as identified from the records: RA, axSpA, PsA, and CTD. All patients had been seen at least twice in our outpatient department during the last 2 years. No other selection process was in place. At least two telephone calls were made at different times of the day to reach a high number of patients. Patients with insufficient language skills and those who did not agree to participate were not included. The interviews were based on a pre-designed questionnaire and planned to last 10 to 15 minutes. Subsequently, questionnaires assessing disease activity, anxiety and depression were mailed to patients who had been interviewed. The data obtained until July 3rd 2020 are reported here.

In addition, information about tests performed to search for a SARS-CoV-2 infection was collected. Anti-SARS-CoV-2 IgG antibodies were examined in 309 of 557 patients using the Euroimmun kit (16). Data obtained from May 6th to September 1st, 2020 are reported here.

Data management and statistics

Study data were collected and managed using REDCap (Research Electronic Data Capture) (17). Exported data were
processed in Microsoft Excel (Microsoft Inc., Redmond, WA) and prepared for statistical analyses using SigmaPlot 14 (Systat Software Inc., San Jose, CA). The data were described as numbers (percentage proportions), means ± standard deviations or medians (interquartile ranges). Groups were compared using appropriate statistical tests (Chi-square test with Yates correction for proportions, and Mann-Whitney U or ANOVA for ranks for continuous data that regularly failed the Shapiro-Wilk normality test). All p-values are two-tailed and a value <0.05 was considered statistically significant.

Patients
A large number of patients with RA, axSpA, PsA and CTD were contacted to obtain information about demographics, self-reported disease activity, current medication, satisfaction with the ongoing therapy and changes in treatment, as well as comorbidities, smoking, employment and self-reported health status. To assess risk factors for a COVID-19 infection we especially asked about cardiovascular events, arterial hypertension, malignancy in the last 5 years, osteoporosis, diabetes mellitus and chronic lung disease. The information obtained from the patients was confirmed by checking patients’ records. Additional information about social behaviour regarding the pandemic, as well as the vaccination status against pneumococci and influenza was collected. In addition, we compared CIRD patients who changed (group 1) versus those who did not change (group 2) during the pandemic. The patients in group 1 were further subdivided into those who reported to have changed therapy because of the pandemic (group 1a), because of high disease activity (group 1b) or because of inactive disease (group 1c).

Any changes in DMARD and CS therapy that had taken place in the last 6–8 weeks were explicitly asked about. The timepoint of any change including changes of dose, application interval, discontinuation, and whether the change of therapy was independently decided or after consultation with the rheumatologist, and the reason for change were recorded.

Self-reported health status was assessed using patient global assessment (PGA) (18) with a numerical rating scale (NRS) ranging from 0 to 10 (0 meaning very good health and 10 very bad health). A good health status was assumed if the scores were <4 and a bad or not so good one for scores ≥4. The subjective evaluation of the effectiveness of therapy (‘are you satisfied with your therapy?’) was determined by dichotomous answers (yes/no).

The Bath AS disease activity index (BASDAI) was used for axSpA (19) and the RA disease activity index (RA-DAI) for RA and PsA to assess disease activity (20). High disease activity was assumed if RADAI ≥3.2 and BASDAI ≥4. Due to the heterogeneity of patients with CTD a simple score to assess disease activity was developed, and currently active disease was assumed if 2 out of the following 4 items were positive: whole-body pain, not being satisfied with therapy, any increase in medication, or changed medication.

The Hospital Anxiety and Depression Score (HADS) (21) was collected to assess anxiety and depression levels of our patients. This self-assessment questionnaire depicting generalised anxiety and panic attacks consists of 14 questions with four-level response options (scores from 0–3), 7 relating to anxiety and 7 to depression, respectively. This allows for differentiation between anxiety and depression scales. A cut-off value of ≥8 points in the HADS-A (anxiety) and HADS-D (depression) subscales showed a good sensitivity and specificity (22).

Questions related to social distancing as recommended by the main German Institute in charge, the Robert-Koch Institute (RKI), wearing a face mask, avoiding of groups, frequent washing of hands and staying at home were asked to evaluate the compliance with COVID-19 containment measures. To approximately judge the number of contacts with other people during the pandemic, we asked about the average time spent outside of one’s own property during the last week. The assessment of difficulty in complying with these rules was tested on a Likert scale (5 possible answers): very easy, easy, neither easy nor hard, rather and very hard.

Results
Out of a total of 1,519 patients of our clinic, 315 were not reached by telephone despite several attempts (20.7%), and 190 patients refused to participate during the interview (12.5%). Language barriers led to exclusion of 32 patients, and 12 patients had died before the pandemic started. Finally, a total of 970 patients agreed to be interviewed (63.9%), 557 of which (57.4%) completed both, the telephone interview and the questionnaires. Thus, 549 patients did not participate at all (36.1%) for various reasons, and complete data were available of 36.7% of all patients originally identified from the records.

Among the 557 patients, 212 were male (38.1%) and 345 female (61.9%), with a median age of 55 (47–63) years. The median disease duration was 9 (4.5–17.0) years, and the median body mass index (BMI) 26.8 (23.4–30.6) kg/m²; 64.5% were ever smokers. There were no significant differences between groups with respect to age, disease duration and BMI. A detailed presentation of demographic and clinical data is shown in Table I.

Overall, 229 patients had RA (41.1%), 72.4% of which were anti-CCP positive, and 286 had SpA, 31.2% with axSpA (64.3% HLA B27+) and 20.1% with PsA, while 42 patients had CTD (7.5%). No significant differences between groups with regard to comorbidities were found (Table II).

A change in medication due to the pandemic (group 1a) was reported by 46 of all RA patients (20.1%) 37 axSpA (21.3%) and 17 PsA patients (15.2%), respectively (Table I). For comparison, in group 2, no change in therapy was reported by 131 RA (57.2%), 120 axSpA (69.0%) and 73 PsA patients (65.2%), respectively. Only 1 patient with CTD changed therapy because of the pandemic (2.3%).

There were no significant differences between CIRD patients including PsA, RA, axSpA and CTD in terms of disease activity, as assessed by BASDAI, RADAI and CTD (group 1b excluded). Subgroup analyses showed that patients in group 1a with RA and PsA had lower RADAI scores than in group 2 but there was no significant difference to group
Table I. Patient demographics

<table>
<thead>
<tr>
<th>Item</th>
<th>All</th>
<th>No recent change in medication (group 2)</th>
<th>Reason for change**</th>
<th>Active disease (group 1b)</th>
<th>Inactive Disease (group 1c)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N*** (%)</td>
<td>557</td>
<td>360 (64.6)</td>
<td>101 (53.4)</td>
<td>40 (21.2)</td>
<td>40 (21.2)</td>
<td>0.581</td>
</tr>
<tr>
<td>Age, y</td>
<td>55 (47–63)</td>
<td>55 (46.25–63)</td>
<td>55 (46–63)</td>
<td>51.5 (43.5–62.75)</td>
<td>55 (51–64)</td>
<td>0.048b</td>
</tr>
<tr>
<td>Male patients</td>
<td>212 (38.1)</td>
<td>135 (63.7)</td>
<td>48 (47.5)</td>
<td>10 (25.0)</td>
<td>12 (30.0)</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>26.8 (23.4–30.6) [2]</td>
<td>26.9 (23.2–30.6) [1]</td>
<td>26.8 (24.0–31.2)</td>
<td>25.7 (23.0–29.2)</td>
<td>25.9 (23.5–28.9)</td>
<td>0.641</td>
</tr>
<tr>
<td>Currently smoking</td>
<td>153 (27.6)</td>
<td>99 (27.6)</td>
<td>24 (23.8)</td>
<td>15 (37.5)</td>
<td>13 (32.5)</td>
<td>0.373</td>
</tr>
<tr>
<td>Never smoked</td>
<td>198 (35.5)</td>
<td>129 (35.8)</td>
<td>41 (40.6)</td>
<td>11 (27.5)</td>
<td>14 (35.0)</td>
<td></td>
</tr>
</tbody>
</table>

Main diagnosis

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>All</th>
<th>No recent change</th>
<th>Reason for change**</th>
<th>Active disease (group 1b)</th>
<th>Inactive Disease (group 1c)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active</strong></td>
<td>279</td>
<td>176 (48.9)</td>
<td>42 (41.6)</td>
<td>32 (80.0)</td>
<td>19 (47.5)</td>
<td></td>
</tr>
</tbody>
</table>

**Percentage across row, for reasons relative to patients who did recently change medication.

Numbers are N (%) or median (interquartile range). Numbers in square brackets indicate the number of missing values. *p (change vs. no change) and p (different reasons vs. no change), respectively (p-values: Chi-square test, ANOVA, or Kruskal-Wallis ANOVA on ranks).

**Corona vs. Disease activity, p=0.024; **Corona vs. No change, p=0.015 and Corona vs. Disease activity, p=0.001; **Corona vs. Disease activity, p<0.001.

***Excluding 16 cases with other or unknown reasons (other reasons include undesired side effects [4], viral infection [3], accident [1]).

Table II. Patient demographics - comorbidities

<table>
<thead>
<tr>
<th>Item</th>
<th>All</th>
<th>No recent change in medication (group 2)</th>
<th>Reason for change**</th>
<th>Disease activity (group 1b)</th>
<th>Disease inactivity (group 1c)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N***</td>
<td>557</td>
<td>360 (64.6)</td>
<td>101 (53.4)</td>
<td>40 (21.2)</td>
<td>40 (21.2)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>57 (10.4) [10]</td>
<td>36 (10.1) [5]</td>
<td>10 (10.0) [1]</td>
<td>5 (12.8) [1]</td>
<td>3 (7.7) [1]</td>
<td>0.904</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>254 (45.8) [2]</td>
<td>157 (43.6)</td>
<td>48 (48.0) [1]</td>
<td>20 (51.3) [1]</td>
<td>18 (45.0)</td>
<td>0.738</td>
</tr>
<tr>
<td>Use of ACE inhibitors</td>
<td>180 (73.5) [9]</td>
<td>115 (75.2) [4]</td>
<td>33 (73.3) [3]</td>
<td>14 (70.0)</td>
<td>11 (64.7) [1]</td>
<td>0.796</td>
</tr>
<tr>
<td>Cancer</td>
<td>47 (8.9) [29]</td>
<td>29 (8.5) [19]</td>
<td>11 (11.5) [5]</td>
<td>2 (5.3) [2]</td>
<td>3 (7.5)</td>
<td>0.667</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>99 (18.2) [14]</td>
<td>65 (18.4) [7]</td>
<td>14 (14.3) [3]</td>
<td>9 (24.3) [3]</td>
<td>6 (15.4)</td>
<td>0.543</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>107 (20.4) [32]</td>
<td>65 (19.2) [21]</td>
<td>18 (18.9) [6]</td>
<td>10 (25.6) [1]</td>
<td>7 (17.9)</td>
<td>0.792</td>
</tr>
<tr>
<td>Number of comorbidities</td>
<td>2 (1–3); Range 0–13</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>2 (0–4)</td>
<td>2 (0.25–2.75)</td>
<td>0.785</td>
</tr>
</tbody>
</table>

Numbers are N (%) or median (interquartile range). Numbers in square brackets indicate the number of missing values. *p (change vs. no change) and p (different reasons vs. no change), respectively (p-values: Chi-square test, ANOVA, or Kruskal-Wallis ANOVA on ranks).

**Excluding 16 cases with other or unknown reasons (other reasons include undesired side effects [4], viral infection [3], accident [1]).

***Percentage across row, for reasons relative to patients who did recently change medication.

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4.9% of patients in gr.1a discontinued or reduced CS, compared to 37.5% of patients in group 1c ($p < 0.004$). The decision to change therapy in all groups was based on a shared decision between physicians and patients in >80% of cases (Table IV) – as reported by the patients. Compliance with the required corona prevention rules was reported by >90% of patients, with only 14.2% admitting that compliance was rather/very hard. As many as 61.7% of patients said that they regularly spent <2 hours per day away from home.

A history of vaccination against pneumococci was reported by 276 (61.3%) and against influenza by 267 patients (55.3%), respectively. Only 1 out of 37 patients under suspicion tested by PCR was positive for SARS-CoV-2 (0.2%). Patients tested had cough, sniffles and/or headache (39.1% each), sore throat (34.8%), shortness of breath (30.4%) and fever (21.7%). The only PCR-positive patient (female, age 37) suffering from cough and fever hospitalised for 7 days survived.

SARS-CoV-2 antibody tests performed in 309 patients (55.5%), only 1.0% had detectable IgG Ab against SARS-CoV-2.
**Table III. Medication.**

<table>
<thead>
<tr>
<th>Item</th>
<th>All</th>
<th>No recent change in medication (group 2)</th>
<th>Reason for change** (group 1a)</th>
<th>Disease activity (group 1b)</th>
<th>Disease inactivity (group 1c)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N***</td>
<td>557</td>
<td>360 (64.6)</td>
<td>101 (53.4)</td>
<td>40 (21.2)</td>
<td>40 (21.2)</td>
<td></td>
</tr>
<tr>
<td>GC</td>
<td>166 (30.3) [9]</td>
<td>93 (26.3) [7]</td>
<td>26 (26.0) [0]</td>
<td>27 (67.5)</td>
<td>12 (30.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MTX</td>
<td>177 (32.4) [11]</td>
<td>114 (32.6) [10]</td>
<td>28 (27.7)</td>
<td>13 (32.5)</td>
<td>15 (38.5) [1]</td>
<td>0.648</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>11 (2.0) [17]</td>
<td>10 (2.9) [15]</td>
<td>0 [1]</td>
<td>1 (2.5)</td>
<td>0 [1]</td>
<td>0.253</td>
</tr>
<tr>
<td>HCQ</td>
<td>36 (6.7) [16]</td>
<td>29 (8.3) [12]</td>
<td>3 (3.1) [3]</td>
<td>4 (10.0)</td>
<td>0 [1]</td>
<td>0.076</td>
</tr>
<tr>
<td>SSZ</td>
<td>14 (2.6) [18]</td>
<td>10 (2.9) [16]</td>
<td>2 (2.0) [1]</td>
<td>1 (2.5)</td>
<td>1 (2.6) [1]</td>
<td>0.969</td>
</tr>
<tr>
<td>AZA</td>
<td>18 (3.5) [41]</td>
<td>17 (5.2) [32]</td>
<td>1 (1.0) [5]</td>
<td>0</td>
<td>0 [1]</td>
<td>0.067</td>
</tr>
</tbody>
</table>

**Table IV. Change of medication.**

<table>
<thead>
<tr>
<th>Item</th>
<th>Recent change in medication (group 1)</th>
<th>Reason for change* (Pandemic (group 1a))</th>
<th>Disease activity (group 1b)</th>
<th>Disease inactivity (group 1c)</th>
<th>p**</th>
</tr>
</thead>
<tbody>
<tr>
<td>N***</td>
<td>197 (35.4)</td>
<td>101 (53.4)</td>
<td>40 (21.2)</td>
<td>40 (21.2)</td>
<td></td>
</tr>
<tr>
<td>Base therapy</td>
<td>165 (83.8)</td>
<td>99 (98.0)</td>
<td>29 (72.5)</td>
<td>25 (62.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cDMARDs</td>
<td>41 (25.8)</td>
<td>17 (17.9)</td>
<td>13 (44.8)</td>
<td>8 (33.3)</td>
<td>0.009</td>
</tr>
<tr>
<td>bDMARDs</td>
<td>110 (69.2)</td>
<td>73 (76.8)</td>
<td>15 (51.7)</td>
<td>14 (58.3)</td>
<td>0.018</td>
</tr>
<tr>
<td>tsDMARDs</td>
<td>13 (8.2)</td>
<td>8 (8.4)</td>
<td>2 (6.9)</td>
<td>3 (12.5)</td>
<td>0.756</td>
</tr>
<tr>
<td>Stopped or Net dose reduction</td>
<td>124 (75.1)</td>
<td>91 (90.0)</td>
<td>5 (12.5)</td>
<td>17 (42.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GC therapy</td>
<td>51 (25.9)</td>
<td>9 (8.9)</td>
<td>22 (55.0)</td>
<td>16 (40.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stopped or Dose reduction</td>
<td>31 (60.8)</td>
<td>5 (4.9)</td>
<td>8 (20.0)</td>
<td>15 (37.5)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

**Discussion**

This study was successful in reaching a large number of patients on immunosuppressive therapy during the ongoing SARS-CoV-2 pandemic. The rate of active participants (n=557) was also relatively high for such a survey. Indeed, valid information on disease activity, actual medication, anxiety and depression was obtained in a large number of patients. In addition, the population of this cohort is very much what tertiary centres as ours are usually taking care of, and this includes comorbidity and medication.

Almost 20% of patients interviewed in our survey reported to have changed therapy because of COVID-19 in the beginning of the pandemic (18.1%). This is different from other reports in which much smaller (7) but also higher percentages have been reported (23). Such differences can be possibly explained by the level of information patients had on the pandemic at a certain point in time.

Of interest, there were no major differences in disease activity between patients who changed and those who did not. However, there was one sta-
tistically significant difference for RA-DAI scores suggesting that RA and PsA patients were more likely to be in remission when they decided to change therapy because of the pandemic. This makes sense from a patients’ perspective not knowing how the pandemic will affect them. On the other hand, about half of the patients who reported to have changed therapy actually had an active disease as assessed by BASDAI and RADAIs suggesting that patients had more respect for increased disease activity than fear of the virus. There was a high proportion of patients reporting active disease but most of them were satisfied with their current treatment, and this is consistent with other studies (24).

This study disproves the assumption that the pandemic may have induced more anxiety and depression in our patients thereby making it improbable that these factors played an important role in therapeutic decisions. In fact, there were no significant differences among the groups in this regard. However, a meta-analysis of pandemic survivors in the general population revealed a pooled prevalence of anxiety symptoms of 46% (25). Furthermore, the anxiety level of Japanese RA patients was higher than pre-pandemic levels which includes that patients using bDMARDs or those with more physical disability in the previous year had higher HADS anxiety scores during the pandemic, while – similar to our study – depression levels did not change (26).

Among patients who stated to have changed therapy because of the pandemic there were more patients on bDMARDs, especially TNFi, compared to those who did not change. Indeed, we found that significantly more changes of therapy occurring due to fear of COVID-19 were related to bDMARDs and only rarely to CS, with the former having been either discontinued or reduced. This suggests that many patients and doctors still think that bDMARDs are associated with a higher risk of infections than CS, which is reportedly not the case (27). However, at this point in time, there was limited evidence on potential risk factors, even though an early report from Italy had shown that CS were potentially harmful (28). In contrast, dexamethasone, similar to tocilizumab (29), is now approved and used for severe COVID-19 infections to reduce the cytokine storm in some countries (30).

Nevertheless, the majority of our patients were not very active and for these a cautious tapering of therapy may have been considered. Only a few patients who made changes due to inactive disease discontinued or reduced bDMARDs whereas more patients reduced CS. The percentage of changes was similar in PsA, axSpA and RA patients suggesting that age and the type of disease was not of importance for therapeutic decisions. In any case, patients who changed therapy because of pandemic were more often in remission than patients who did not change therapy at all. Almost no therapy changes were made by CTD patients – probably because they were afraid of having to experience higher disease activity.

Finally, what do we know now after living for more than a year with the pandemic in a situation where almost 5 million people worldwide have died? Similar factors as in the general population such as age and male gender, in CIRD patients moderate/high disease activity, not receiving DMARDs and a prednisolone dosage >10 mg/day were associated with death (31). Indeed, several large cohort studies showed a higher risk for a severe course of COVID-19 in patients with higher disease activity or high dose CS (28, 32) but no risk was demonstrated for biologics, especially not for TNFi (1, 28). For JAKi the situation is now clearer (33) – even though baricitinib seems to work against COVID-19 (34) – while therapy with RTX represents a problem in this regard (1).

A bit more than half of the patients in our study were vaccinated against influenza and pneumococci. This is fortunately better than in our previous study (35). In other studies lower/similar (36) rates were found in CIRD patients. Since there is some evidence that vaccination against influenza may protect against severe outcomes of COVID-19 (37) this is especially unfortunate. Expectedly, the prevalence of a SARS Cov-2 infection in our cohort was low (0.2%) and not much different from the general population (0.24%) (10). One possible explanation could be that patients with CIRD protect themselves more carefully by more strictly adhering to hygiene recommendations, which was actually the case.

One weakness of our study is the use of a disease activity tool in CTD that has not been evaluated. Since there was no tool such as RADAIs or BASDAI available for CTD, we just used a simple general score. In addition, we did not use clinical or laboratory parameters but only patient reported outcome (PRO) data. Finally, due to the nature of the data collection by telephone, we were unable to personally verify much of the information.

Taken together, our study shows that 18.1% of CIRD patients changed therapy because of the pandemic, mostly biologics, and anxiety does not appear to play a major role in this context. We are currently evaluating the outcome of those patients, both in terms of disease activity and safety related to the risk of acquiring COVID-19.

References
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