SARS-CoV-2 Vaccination in Patients With Inflammatory Bowel Disease—Fear and Desire

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Introduction

The current SARS-CoV-2 pandemic has led to significant changes in societies and health care systems worldwide. In Europe, more than 30,000,000 people have tested positive for SARS-CoV-2 (as of February 3, 2021); the mortality of COVID-19 is 2.4%.1 In patients with inflammatory bowel disease (IBD), no increased susceptibility to SARS-CoV-2 infections or mortality is evident—however, 17% of patients with IBD infected with SARS-CoV-2 have had to be hospitalized worldwide.2

On December 21, 2020, the mRNA vaccine BNT162b2 (BioNTech/Pfizer) was the first vaccine against SARS-CoV-2 to be approved by the European Medicines Agency, and shortly thereafter the second mRNA vaccine (mRNA-1273, Moderna) was approved. The International Organization for the Study of Inflammatory Bowel Disease and very recently the COVID-19 European Crohn’s & Colitis Organisation task force recommended vaccinating all patients with IBD as soon as they are able to receive the vaccination, regardless of immune-modifying therapies.3,4 However, the vast amount of detailed scientific material and false and misleading information have sparked a controversial discussion about the benefits and risks of SARS-CoV-2 vaccines. This leaves patients with IBD skeptical about whether to get vaccinated. In this study, we aimed to explore the acceptance rates of patients with IBD regarding getting vaccinated with one of the mRNA vaccines available. For comparison, we asked for the participants’ attitudes toward and history of influenza vaccination and compared the results to a non-IBD control cohort.

METHODS

At 5 German specialized IBD centers, successive patients with IBD aged ≥18 years were invited to participate in our anonymous survey from January 8, 2021 until February 3, 2021. In addition, patients were recruited via the communication channels of the German organization for patients with IBD (Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung e.V., representing nearly 22,000 members with IBD). Health care–affiliated volunteers without IBD were recruited as a control group through the social media channels of 2 university hospitals (Facebook); these volunteers participated using the online survey tool LimeSurvey (version 2.05).
The questionnaire consisted of 20 questions on baseline characteristics (see Table 1), vaccination history regarding influenza, attitudes towards influenza and SARS-CoV-2 vaccinations, and history of SARS-CoV-2 infection. The questionnaire allowed for additional free-text comments.

Immunosuppressive medication was defined as the use of steroids, thiopurines, tumor necrosis factor-α antibodies, vedolizumab, ustekinumab, calcineurin inhibitors, or small molecules such as tofacitinib.

For statistical analysis, SPSS 26 (IBM Corp., Armonk, NY) and Prism 6 (GraphPad, La Jolla, CA) were used. Significance testing was performed using the Pearson χ² test for comparing frequencies and the Student t test for comparing the mean values of the 2 groups. The study was approved by the ethics committee of the medical faculty at the University Halle-Wittenberg, Halle, Germany (registration number 2020–227).

RESULTS

A total of 1442 questionnaires were answered by 1032 patients with IBD and 410 control patients. Of the patients with IBD, 373 (36.1%) were diagnosed with ulcerative colitis, 632 (61.4%) with Crohn disease, and 27 (2.6%) with microscopic or undetermined colitis. Details regarding sociodemographic and disease-related characteristics and comorbidities are presented in Table 1, and details regarding current IBD activity and medication are given in Supplementary Table 1.

Overall, 604 patients with IBD (58.5%) planned to get a SARS-CoV-2 vaccination as soon as possible or had already been vaccinated, results that were significantly lower than in the control patients (n = 267, 65.1%, P = 0.013); see Fig. 1A. Significantly more patients with IBD stated that they would prefer a vaccine type other than mRNA vaccines or reported that they would postpone their vaccination for 6 months to get more information on potential adverse effects (25.1% vs 18.5%, P = 0.007; Fig. 1B). We found that 11.1% of patients with IBD and 13.2% of the control patients generally opposed the SARS-CoV-2 vaccination. Self-reported activity of IBD or the type of IBD medical caregiver (university, non-university hospital, outpatient clinic) did not correlate to SARS-CoV-2 vaccination intent (data not shown).

Factors associated with the willingness to receive a SARS-CoV-2 vaccination were male sex (92.1% vs 85.8%, P = 0.004) and the presence of at least 1 severe SARS-CoV-2 infection (as defined by the need for hospital admission) among close friends or family members (SARS-CoV-2 vaccination in general: 93.9% vs 86.1%, P = 0.009; vaccination as soon as possible: 70.0% vs 59.4%, P = 0.044). Furthermore, patients with arterial hypertension were more willing to get a SARS-CoV-2 vaccination (94.0% vs 85.2%, P = 0.009), whereas other comorbidities were not associated with SARS-CoV-2 vaccination intent.

Patients without IBD medication were less willing to get vaccinated (no IBD medication: 82.9% vs any IBD medication: 88.9%, P = 0.011). This association still held true when we compared immunosuppressed and nonimmunosuppressed patients with IBD. Vedolizumab treatment was associated with a lower SARS-CoV-2 vaccine hesitancy (5.7% vs 12.7%, P = 0.024). No differences were found for tumor necrosis factor-α antibodies, other biologics, or small molecules.

In the 2020-2021 influenza season, patients with IBD received an influenza vaccination more frequently than the control patients (overall: 52.7%; IBD: 55.6%; control patients: 45.3%; P = 0.001). Three hundred thirteen patients with IBD (30.2%) and 166 control patients (40.4%) reported that they had never been vaccinated against influenza (P = 0.04), whereas 533 participants reported that they received the influenza vaccination during every influenza season (416 patients with IBD (40.3%), 117 control patients (28.5%), P < 0.001; Supplementary Fig. 1). Among the reasons for patients not receiving vaccination against influenza, the fear of adverse effects was significantly more frequent in patients

**Table 1. Baseline Characteristics of Patients and Control Patients**

|                                    | Patients With IBD (n = 1032) | Control Patients (n = 410) | P     |
|------------------------------------|------------------------------|---------------------------|-------|
| Sex, female                        | 690 (66.9%)                  | 328 (80%)                 | <0.001|
| Age, y                             | 43 (33/54)                   | 35 (26/42)                | <0.001|
| Body weight, kg                    | 72 (62/86)                   | 72.7 (63/87)              | 0.845 |
| Smoker                             | 177 (17.1%)                  | 89 (21.7%)                | 0.001 |
| Former smoker                      | 300 (29.1%)                  | 74 (18.4%)                | <0.001|
| No comorbidity                     | 597 (57.8%)                  | 141 (34.4%)               | <0.001|
| Stroke                             | 19 (1.8%)                    | 0                         | 0.073 |
| Pulmonary disease                  | 126 (12.2%)                  | 39 (9.5%)                 | 0.008 |
| Diabetes mellitus                  | 52 (5.0%)                    | 13 (3.2%)                 | 0.618 |
| Arterial hypertension              | 202 (19.6%)                  | 52 (12.7%)                | 0.092 |
| Coronary heart disease             | 19 (1.8%)                    | 4 (1.0%)                  | 1.000 |
| Peripheral arterial disease        | 12 (1.2%)                    | 1 (0.2%)                  | 0.522 |
| Chronic kidney disease             | 43 (4.2%)                    | 6 (1.5%)                  | 0.451 |
| Chronic liver disease              | 48 (4.7%)                    | 0                         | 0.003 |
| Rheumatic disease                  | 111 (17.8%)                  | 7 (1.7%)                  | 0.001 |
| Psoriasis                          | 86 (8.3%)                    | 14 (3.4%)                 | 0.486 |
| Cancer                             | 71 (6.9%)                    | 14 (3.4%)                 | 1.000 |
| Solid organ transplant             | 2 (0.2%)                     | 4 (1.0%)                  | 0.007 |

All data are presented as mean and first/third quartile or as number and percentage.
with IBD than in control patients (9.8% vs 5.6%, \( P = 0.001 \); Supplementary Fig. 2).

Patients who received an influenza vaccine during the 2020-2021 or 2019-2020 influenza season were more frequently willing to receive the SARS-CoV-2 vaccine (97.1% vs 75.2% in 2020-2021 and 96.3% vs 84.4% in 2019-2020; both \( P < 0.001 \)). We found that 54 patients with IBD (5.2%) reported SARS-CoV-2 infection (compared to 19 control patients [4.6%]); 499 patients with IBD (48.3%) reported ≥1 SARS-CoV-2 infections among close friends or family as compared to 231 control patients (36.3%).

**Discussion**

The novel mRNA SARS-CoV-2 vaccines have proven to be efficacious in large phase III trials against COVID-19. Health care experts’ SARS-CoV-2 vaccination recommendations for patients with IBD are unequivocal: They should get vaccinated as soon as possible.\(^3\) However, despite the high fear of contracting a SARS-CoV-2 infection in patients with IBD,\(^5,6\) in this multicenter study of >1400 participants, patients with IBD were significantly more hesitant to get vaccinated than were control patients without IBD. In addition, the COVID-19 vaccination intent of patients with IBD was reduced in comparison to that of the corresponding general population: According to a survey of the German government’s central scientific institution in the field of biomedicine, the Robert Koch Institute, during 4 weeks in January and February 2021, 70.2% of the 1006 participants reported a high SARS-CoV2 vaccination intent or were already vaccinated.\(^7\)

In contrast, Dalal et al.\(^8\) recently reported from the United States that patients with IBD had a higher SARS-CoV-2 vaccination intent than expected from surveys among the general U.S. population. This discrepancy with our findings may be related to different cultural backgrounds and different vaccination priorities; the influenza vaccination rate among patients with IBD in the U.S. cohort was as high as 80.3%. In addition, the significantly higher cumulative incidence of COVID-19 in the United States (8.1% as of February 3, 2021)\(^9\) compared to Germany (2.7%) may have an impact on SARS-CoV-2 vaccination hesitancy. This concept is supported by our observation that patients with severe COVID-19 cases of infection among close friends or family were more ready for SARS-CoV-2 vaccination.

However, the patients in the Dalal et al.\(^8\) cohort reported similar reasons for vaccination hesitancy: Patients with IBD frequently reported concerns about the efficacy and safety of the novel mRNA vaccines and indicated that they preferred to wait for other types of vaccines (eg, conjugate vaccines) or that they would postpone SARS-CoV-2 vaccination for 6 months.

Our findings describe a paradoxical situation: patients with IBD were more afraid of COVID-19 than were control patients and were more frequently vaccinated against influenza. Meanwhile, they were more hesitant than control patients to get vaccinated against SARS-CoV-2 as soon as possible.

The self-reported influenza vaccination rate underlines that participants in our survey were not generally opposed to vaccinations. Still, a high compliance rate for influenza vaccination correlated to a higher readiness for SARS-CoV-2 vaccination.

The online self-recruiting of the control group for our study resulted in a selection bias, and for our study we considered it to be more appropriate to address a health care–affiliated control group (including health care workers and patients with other diseases than IBD) rather than a control group representative of the general population, because chronically ill patients and health care–affiliated workers have been assigned a higher SARS-CoV-2 vaccination priority by local authorities. A further potential limitation is the self-reporting of influenza vaccination history. However, the self-reported influenza vaccination status has been reported to be highly sensitive and specific in patients with IBD.\(^8\) Finally, considering the contrasting findings of Dalal et al.,\(^8\) our results may be more representative for regions with a low incidence of SARS-CoV-2.

**Conclusions**

The acceptance of SARS-CoV-2 vaccination in patients with IBD is hampered by concerns and anxieties especially regarding long-term safety, even in patients with a high influenza vaccination compliance (as a positive marker for the acceptance of vaccinations in general). It is therefore very important to actively address these concerns and to discuss potential concerns with our patients. Clear recommendations should be given regarding the SARS-CoV-2 vaccination; the most im-
portant of these recommendations should be: Get vaccinated as soon as possible.

**Supplementary Data**
Supplementary data are available at *Inflammatory Bowel Diseases* online.

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**Data Availability Statement**
The data underlying this article will be shared on reasonable request to philipp.reuken@med.uni-jena.de.

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