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RESEARCH

Effects of SARS-CoV-2 vaccine (Vero cells) on disease activity in patients with inflammatory bowel disease in China: a multicenter study

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Abstract

Aims To evaluate the impact of SARS-CoV-2 vaccine on IBD activity.

Methods Adult IBD patients from five large IBD centers in China were enrolled and followed up for 6 months. Patients were divided into vaccinated and unvaccinated groups according to vaccination status. Demographic and clinical data were collected.

Results A total of 280 individuals (213 UC and 67 CD patients) were enrolled in the study. The unvaccinated and vaccinated groups of UC patients were comparable for basic characteristics, including age ($t=-0.8$, $p=0.425$), sex ($\chi^2=0.980$, $p=0.322$), course of disease ($z=-0.513$, $p=0.608$), surgical conditions ($\chi^2=1.042$, $p=0.838$), disease extent ($\chi^2=4.853$, $p=0.088$), or baseline drug therapy ($\chi^2=7.784$, $p=0.064$). In the subgroup of UC patients, there was no association between vaccination and disease activities, according to the medium disease activity scores for two groups: unvaccinated patients having scores (IQR) 1(2.75), 1(2), 1(2), and 1(2) at baseline, 1, 3, and 6 months, respectively, whereas vaccinated patients having scores (IQR) 1(2), 1(2), 1(2), and 1(2). Similar conclusions were also derived in the subgroup of CD patients. There were also no statistically significant differences in age ($t=-1.48$, $p=0.144$), sex ($\chi^2=0.003$, $p=0.957$), course of disease ($z=-0.074$, $p=0.941$), surgical conditions ($\chi^2=0.613$, $p=0.594$), localization ($\chi^2=6.261$, $p=0.199$), or baseline drug therapy ($\chi^2=5.881$, $p=0.114$) between 2 groups of CD patients. The medium disease activity scores (IQR) of the unvaccinated group at baseline, 1, 3, and 6 months were 1(4), 1(3), 1(3), and 1(3), respectively, whereas those of vaccinated group were 2.5(3.75), 2.5(3.75), 3(2), and 2(2), respectively. Overall, very few participants in this study described worsening IBD disease activity requiring a change or addition of medication.

Conclusions SARS-CoV-2 vaccine has no adverse effect on disease activity in IBD population. IBD patients should be recommended to receive SARS-CoV-2 vaccine in time.

Keywords SARS-CoV-2 vaccination · Inflammatory bowel diseases · Disease activity · Crohn's disease · Ulcerative colitis

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Introduction

The severe acute respiratory syndrome coronavirus (SARS-CoV-2) has caused a global health crisis. Vaccination is a key strategy to control transmission and protect populations. Inflammatory bowel diseases (IBD) mainly include ulcerative colitis (UC) and Crohn's disease (CD). Patients with IBD have been considered at high risk for infection and complications of SARS-CoV-2. Patients with IBD or other immune-mediated inflammatory diseases receiving immunosuppressive and biologic therapies were underrepresented in inactivated SARS-CoV-2 vaccine trials. There was a lack of evidence on the safety and efficacy of vaccination in patients with IBD. Although numerous groups and experts supported the importance of adequate vaccination of IBD patients [1–3], the percentage of physicians that routinely recommend vaccination to IBD patients was low. Research showed that IBD patients who received SARS-CoV-2 mRNA vaccination had similar adverse reactions to the general population [4, 5]. However, there has been some concern that vaccine-triggered immune activation could trigger immune dysregulation and exacerbate IBD. Patients and physicians were more concerned on the potential adverse effects, although there was no evidence to demonstrate that other vaccinations triggered flares of IBD. There have been few studies explicitly exploring the impact of SARS-CoV-2 vaccination on disease outcomes in IBD. This research is a prospective multicenter study consisting of five large general hospitals in China, to evaluate the effects of the SARS-CoV-2 vaccine (Vero cells) on IBD activity.

Objects and methods

Objects

This is a prospective, observational, multicenter cohort study. Adult patients (≥ 18 years old) with an established diagnosis of IBD receiving long-term treatment and follow-up in Beijing Tsinghua Changgung Hospital, Peking University People's Hospital, Aerospace Central Hospital, the First Affiliated Hospital of Xi'an Jiaotong University, and Shaanxi Provincial People's Hospital were enrolled. Exclusion criteria included malignancy, other systemic serious diseases, and uncontrolled infection. All patients were Chinese.

Patients were divided into vaccinated and unvaccinated groups according to vaccination status. The vaccines injected were all inactivated SARS-CoV-2 vaccines (Vero cells), including the Sinovac COVID-19 vaccine (Vero cell) inactivated and Sinopharm [Vero cell] inactivated COVID-19 vaccine. We recorded baseline conditions before vaccination and postvaccination symptoms associated with the primary disease (e.g., abdominal pain, diarrhea, blood in the stool) after the first vaccine dose among those who received at least one dose.

Clinical data

Basic demographic data on age, gender, and disease-specific data such as disease course, type of IBD (CD vs. UC), range of lesion involved, operation, disease activity, and IBD treatment (sulfasalazine/mesalamine, biologic, immunosuppressor, steroid) were recorded. All patients were followed up for 6 months, and disease activity was recorded at 1, 3, and 6 months. Patients who were not vaccinated were also followed up for 6 months from the enrollment date, recording disease activity at baseline, 1 month, 3 months, and 6 months.

Type of IBD

The IBD types involved in this study were UC and CD.

The disease extent of UC patients was divided into E1 (proctitis), E2 (left-sided UC; proximal extent of inflammation is distal to the rectosigmoid), and E3 (extensive UC; involvement extends proximal to the splenic flexure) according to the Montreal classification.

The localization of CD patients was divided into L1 (terminal ileum), L2 (colon), L3 (ileocolon), and L4 (upper gastrointestinal) according to the Montreal classification.

Disease activity was scored according to the partial Mayo score (UC) and simplified Crohn's disease activity index (CD). See the supplemental tables for details.

The primary outcome of IBD exacerbation was either treatment escalation or undergoing surgery related to the disease.

Statistics

SPSS 26.0 statistical software was used for analysis. The measurement data were expressed by mean ± standard deviation or median (interquartile range, IQR), the comparison between normal measurement data groups was performed by two independent samples *t*-test or one-way variance test, while the comparison between non-normal measurement data and grade data groups was performed by rank sum test of two or more independent samples. The counting data were expressed as percentages, tested by χ^2 test or Fisher's exact probability method. $P < 0.05$ indicated a statistically significant difference.

Results

Baseline clinical characteristics

A total of 280 participants with IBD (42.9% female, mean age 47.6 ± 15.9 years, 76.1% UC) were included in the study. Full details regarding medication distribution, demographics, and IBD clinical characteristics are presented in Table 1.

UC patients consisted of 117 males (54.9%) and 96 females, with an average age of 49.9 ± 15.3 years old. The course of the disease ranged from 0 to 47 years, with a median of 5 years. Four patients (0.02%) had undergone surgical treatment, mainly partial colectomy. No participant reported a history of COVID-19 infection. A majority of participants were taking sulfasalazine/mesalamine therapies at baseline.

UC patients were divided into two groups: 145 in the vaccinated group and 68 in the unvaccinated group. Vaccinated patients consisted of 83 males (57.2%) and 62 females, with an average age of 50.5 ± 15.5 years old. The course of the disease ranged from 0 to 47 years, with a median of 5 years. According to the classification of Montreal, E1, E2, and E3 accounted for 26.9% (39 cases), 30.3% (44 cases), and 42.8% (62 cases), respectively. Unvaccinated patients consisted of 34 males (50%) and 34 females, with an average age of 48.7 ± 14.9 years old. The course of the disease ranged from 0 to 30 years, with a median of 4 years. E1, E2, and E3 accounted for 20.6% (14 cases), 20.6% (14 cases), and 58.8% (40 cases) respectively.

CD patients included 43 males (64.2%) and 24 females, with an average age of 40.1 ± 15.5 years old. The course of the disease ranged from 0 to 33 years, with a median of 5 years. Twenty-five patients (37.3%) had undergone surgical treatment, mainly partial bowel resection. No participant reported a history of COVID-19 infection. A majority of participants were taking biologic therapies at baseline.

CD patients were divided into vaccinated and unvaccinated groups, including 36 and 31, respectively. Vaccinated patients included 23 males (63.9%) and 13 females, with an average age of 42.7 ± 14.7 years old. The course of the disease ranged from 0.5 to 22 years, with a median of 5 years. According to the classification of Montreal, L1, L2, L3, and L4 accounted for 33.3% (12 cases), 33.3% (12 cases), 30.6% (11 cases), and 2.8% (1 case) respectively. Unvaccinated patients consisted of 20 males (64.5%) and 11 females, with an average age of 37.2 ± 16.2 years old. The course of the disease ranged from 0 to 33 years, with a median of 5 years. L1, L2, and L3 accounted for 19.4% (6 cases), 29.0% (8 cases), and 51.7% (16 cases) respectively.

Disease activity during follow-up

UC

There were no statistically significant differences in age ($t = -0.8$, $p = 0.425$), sex ($\chi^2 = 0.980$, $p = 0.322$), course of disease ($z = -0.513$, $p = 0.608$), surgical conditions ($\chi^2 = 1.042$, $p = 0.838$), disease extent ($\chi^2 = 4.853$, $p = 0.088$), or baseline drug therapy ($\chi^2 = 7.784$, $p = 0.064$) between non-vaccinated and vaccinated patients.

The disease activity scores of patients in the two groups during follow-up are shown in Table 2. The medium disease activity scores of the unvaccinated group at baseline,1, 3, and 6 months were 1(2.75), 1(2), 1(2), and 1(2), respectively, and the medium disease activity scores of the vaccinated group at baseline, 1, 3, and 6 months were 1(2), 1(2), 1(2), and 1(2), respectively. The differences were not statistically significant between the 2 groups ($p > 0.05$). During the 6-month follow-up period in UC patients, 4 unvaccinated patients (5.9%) and 5 vaccinated patients (3.4%) experienced treatment escalation, and the difference was not statistically significant ($\chi^2 = 0.678$, $p = 0.471$).

CD

There were no statistically significant differences in age ($t = -1.48$, $p = 0.144$), sex ($\chi^2 = 0.003$, $p = 0.957$), course of disease ($z = -0.074$, $p = 0.941$), surgical conditions ($\chi^2 = 0.613$, $p = 0.594$), disease extent ($\chi^2 = 6.261$, $p = 0.199$), or baseline drug therapy ($\chi^2 = 5.881$, $p = 0.114$) between non-vaccinated and vaccinated patients.

The disease activity scores of patients in the two groups during follow-up are shown in Table 3. The medium disease activity scores of the unvaccinated group at baseline, 1, 3, and 6 months were 1(4), 1(3), 1(3), and 1(3), respectively, and the medium disease activity scores of the vaccinated group at baseline, 1, 3, and 6 months were 2.5(3.75), 2.5(3.75), 3(2), and 2(2), respectively. The differences were not statistically significant between the 2 groups ($p > 0.05$). During the 6-month follow-up period in CD patients, 4 unvaccinated patients (12.9%) and 5 vaccinated patients (13.9%) experienced treatment escalation, and the difference was not statistically significant ($\chi^2 = 0.014$, $p = 1.000$).

Discussion

Vaccination against SARS-CoV-2 is the most effective strategy for managing the pandemic. Fear of precipitating an IBD flare is an important contributor to persistent vaccine hesitancy among patients with IBD. In general, vaccines are underutilized in patients treated with immunosuppressive regimens.

Table 1 Participant characteristics

	UC ($n=213$)		CD ($n=67$)	
	Vaccinated group	Unvaccinated group	Vaccinated group	Unvaccinated group
Age at enrollment				
Mean (SD)	50.5 ± 15.5	48.7 ± 14.9	42.7 ± 14.7	37.2 ± 16.2
[Min, max]	18–82	18–80	18–75	19–83
Sex				
Male	83 (57.2%)	34 (50%)	23 (63.9%)	20 (64.5%)
Female	62 (42.8%)	34 (50%)	13 (36.1%)	11 (35.5%)
Prior COVID infection				
No	145 (100%)	68 (100%)	36 (100%)	31 (100%)
Yes	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Duration (years) of IBD				
***M*(IQR)**	5(6)	4(8)	5(4.8)	5(4)
[Min, max]	0–47	0–30	0.5–22	0–33
Surgery				
Yes	2 (1.4%)	2 (2.9%)	14 (38.9%)	11 (35.5%)
No	143 (98.6%)	66 (97.1%)	22 (61.1%)	20 (64.5%)
Partial colectomy	2 (1.4%)	2 (2.9%)	5 (13.9%)	11 (35.5%)
Partial small intestinal resection	0 (0%)	0 (0%)	4 (11.1%)	20 (64.5%) 6 (19.4%)
Partial small intestinal and colon resection	0 (0%)	0 (0%)	5 (13.9%)	2 (6.5%) 3 (9.7%)
Disease extent				
E1	39 (26.9%)	14 (20.6%)		
E2	44 (30.3%)	14 (20.6%)		
E3	62 (42.8%)	40 (58.8%)		
Localization				
L1			12 (33.3%)	6 (19.4%)
L2			12 (33.3%)	8 (29.0%)
L3			11 (30.6%)	16 (51.7%)
L4			1 (2.8%)	0 (0%)
Sulfasalazine/mesalamine				
Yes	115 (79.3%)	50 (73.5%)	12 (33.3%)	2 (6.5%)
No	30 (20.7%)	18 (16.5%)	24 (66.7%)	29 (93.5%)
Oral/parenteral steroids				
Yes	4 (2.8%)	3 (4.4%)	0 (0%)	0 (0%)
No	141 (97.2%)	65 (95.6%)	36 (100%)	31 (100%)
Immunosuppressor				
Yes	3 (2.1%)	5 (7.4%)	3 (8.3%)	2 (6.5%)
No	142 (97.9%)	63 (92.6%)	33 (91.7%)	29 (93.5%)
Biologic (anti-TNF)				
Yes	2 (1.4%)	4 (5.9%)	9 (25%)	9 (25%)
No	143 (98.6%)	64 (94.1%)	25 (75%)	13 (41.9%)
Biologic (anti-integrin)				
Yes	2 (1.4%)	4 (5.9%)	4 (11.1%)	2 (6.5%)
No	143 (98.6%)	64 (94.1%)	32 (88.9%)	29 (93.5%)
Biologic (IL12/23 inhibitor)				
Yes	0 (0%)	0 (0%)	0 (0%)	1 (3.2%)
No	145 (100%)	68 (100%)	36 (100%)	30 (96.8%)
Other (traditional Chinese medicine treatment, probiotics, etc.)				
Yes	8 (55.2%)	2 (2.9%)	4 (11.1%)	4 (12.9%)

Table 1 (continued)

	UC ($n=213$)		CD ($n=67$)	
	Vaccinated group	**Unvaccinated group**	**Vaccinated group**	**Unvaccinated group**
No	137 (44.8%)	66 (97.1%)	32 (88.9%)	27 (87.1%)
Drug withdrawal				
Yes	15 (10.3%)	6 (8.8%)	2 (5.6%)	4 (12.9%)
No	130 (89.7%)	62 (91.2%)	34 (94.4%)	27 (87.1%)

Research showed that over one-third of patients with IBD expressed SARS-CoV-2 vaccine hesitancy. Vaccine safety and efficacy were the most common reasons [6]. In general, the disease activity of the subjects in this study was relatively low, and most patients were in a stable stage of the disease. Immunosuppressants or biological agents accounted for a smaller proportion of the population. All patients in this study received inactivated vaccines (Vero cells). This indicated that mild patients tended to be vaccinated. More data were needed on the impact of vaccination in patients with severe IBD.

There have been few studies on the effects of vaccination on disease activity in patients with IBD. Hadi et al. [5] found that there was no signal toward increased steroid need in vaccinated patients with IBD compared with unvaccinated patients with IBD [5]. Lev-Tzion et al. [7] found that the SARS-CoV-2 vaccine likely did not increase the risk of IBD exacerbation [7]. These results may increase the willingness to pursue SARS-CoV-2 vaccination in IBD patients. All the vaccines involved in these studies were mRNA vaccines, while the vaccines widely used in the Chinese population were inactivated vaccines (Vero cells). No studies have examined the effect of inactivated vaccines on disease activity in patients with IBD. Therefore, we conducted this prospective and multi-institution cohort study involving five large IBD centers in China, followed up for 6 months. Vaccinated and unvaccinated IBD patients in this study had similar baseline information, including demographic data, medication status, and baseline disease activity. Very few participants in this study described worsening IBD disease activity requiring a change or addition of medication during the follow-up. There was no significant difference in disease activity between the two groups during the follow-up, suggesting that vaccination against SARS-CoV-2 should not cause significant IBD exacerbations, consistent with the conclusion of previous studies [7].

A recent survey of gastroenterologists also indicated an almost universal agreement on recommending SARS-CoV-2 vaccination [1, 2]. There have been some concerns that patients with IBD, especially those using immunosuppressive medications, may be at risk of suboptimal vaccine response. Decreased seroconversion rates to other vaccines have been demonstrated in IBD patients treated with TNF inhibitors [8, 9]. Lower serologic response to the COVID-19 mRNA vaccine in patients with IBD treated with TNF inhibitors was showed recently [10, 11]. However, another research revealed that a second exposure to antigen, either by vaccination after infection, or a second dose of vaccine led to seroconversion in most patients [11]. Recent studies reported that the SARS-CoV-2 vaccine was equally effective in IBD patients and in the non-IBD population including those on TNF inhibitors and corticosteroids [7, 12–14].

Our study is limited by a lack of regional diversity, a small sample, mild baseline disease activity, and a short follow-up time. More work is needed to confirm these observations.

Table 2 The disease activity scores of UC patients

	Baseline	1 m	3 m	6 m
Disease activity score of the unvaccinated group *M*(IQR)	1(2.75)	1(2)	1(2)	1(2)
Disease activity score of the vaccinated group *M*(IQR)	1(2)	1(2)	1(2)	1(2)
Z	−0.224	−0.329	−0.386	−0.312
P	0.823	0.742	0.7	0.755

Table 3 The disease activity scores of CD patients

	Baseline	1 m	3 m	6 m
Disease activity score of the unvaccinated group *M*(IQR)	1(4)	1(3)	1(3)	1(3)
Disease activity score of the vaccinated group *M*(IQR)	2.5(3.75)	2.5(3.75)	3(2)	2(2)
Z	−0.551	−1.522	−1.617	−1.885
P	0.581	0.128	0.106	0.059

In conclusion, the SARS-CoV-2 vaccine is safe and well tolerated among individuals with IBD and has no adverse effect on disease activity. IBD patients should be recommended to receive the SARS-CoV-2 vaccine in time.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00384-023-04315-x.

Author contribution Mingjun Zhang: writing—original draft preparation; formal analysis. Qing Huang: methodology, formal analysis. Chenchen Shi: data curation, formal analysis. Yun Feng: data curation. Tianjiao Duan: data curation. Tianyu Lin: data curation. Yuanming Zhu: data curation. Guisheng Liu: data curation. Hongxia Li: data curation. Yulan Liu: conceptualization; writing—review and editing. Bo Jiang: conceptualization; writing—review and editing; supervision.

Data availability The data that support the findings of this study are available on request from the author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

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