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ORIGINAL ARTICLE

SARS-CoV-2 vaccination in patients with inflammatory bowel disease: A systemic review and meta-analysis

Kuan-Yi Sung[a,b,c], Tien-En Chang[a,b,c], Yen-Po Wang[a,b,c,d,*], Chun-Chi Lin[c,e], Chung-Yu Chang[b,c,f], Ming-Chih Hou[a,b,c], Ching-Liang Lu[a,b,c,d]

[a]Endoscopy Center for Diagnosis and Treatment, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [c]Department of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [d]Institute of Brain Science, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [e]Division of Colon and Rectum Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [f]Healthcare and Services Center, Taipei Veterans General Hospital, Taipei, Taiwan, ROC

Abstract

Background: In the coronavirus disease 2019 (COVID-19) pandemic, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccination has been effective in preventing COVID-19 infections and related mortality. The SARS-CoV-2 vaccination was also recommended by the international society for patients with inflammatory bowel disease (IBD). However, IBD patients were not recruited in prospective randomized clinical vaccine studies. To evaluate the efficacy and safety of SARS-CoV-2 vaccination in IBD patients, we conducted this systemic review and meta-analysis.

Methods: We systematically searched PubMed, Medline, and the Cochrane Library for studies published between January 1, 2019, and September 9, 2021. Studies written in English reported the efficacy, seroconversion (anti–SARS-CoV-2 anti-spike (S) antibody titer beyond the threshold) rate, and adverse events after the SARS-CoV-2 vaccination in IBD patients. We extracted the author, date, study design, country, types of SARS-CoV-2 vaccination, number of IBD patients receiving SARS-CoV-2 vaccinations, and study outcomes. Published data from the enrolled studies were pooled to determine effect estimates. The study protocol was registered in PROSPERO (CRD42021264993).

Results: We analyzed findings from 27 454 IBD patients who received SARS-CoV-2 vaccinations in 11 studies that met the inclusion criteria. The post–SARS-CoV-2 vaccination COVID-19 infection rate was comparable between the IBD patients and non-IBD patients (odds ratio [OR], 1.28 [95% CI, 0.96–1.71]) and higher in nonvaccinated IBD patients compared with vaccinated IBD patients (OR, 8.63 [95% CI, 5.44–13.37]). The adverse event rate, severe adverse events, and mortality after the SARS-CoV-2 vaccination were 69%, 3%, and 0%, respectively.

Conclusion: The SARS-CoV-2 vaccine is effective and tolerated in preventing COVID-19 infections in IBD patients. Over 98% of patients had seroconversion after receiving all doses of the SARS-CoV-2 vaccination, and the influence of biologics on vaccination was limited. The SARS-CoV-2 vaccination is recommended for IBD patients.

Keywords: Inflammatory bowel diseases; SARS-CoV-2; Vaccination

1. INTRODUCTION

The outbreak of a novel infectious disease, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China, in December 2019.[1] It quickly spread all over the world, led to the COVID-19 pandemic, and resulted in over 1 hundred million infections and millions of deaths.[2,3] A SARS-CoV-2 infection can cause gastrointestinal symptoms such as anorexia nausea, vomiting, diarrhea, abdominal pain, and abdominal discomfort, which may mimic disease exacerbation in patients with inflammatory bowel disease (IBD).[4,5] The SARS-CoV-2 virus receptor angiotensin-converting enzyme 2 is highly expressed in intestinal epithelial cells from the terminal ileum and, to a lesser extent, in the colon.[6] Intestinal inflammation and gut leakage may make IBD patients more vulnerable to a SARS-CoV-2 virus infection via the gastrointestinal tract. In the reported real-world data, the SARS-CoV-2 infection risk is comparable between IBD patients and the general population.[7–9] However, the risk of severe COVID-19 was higher in patients with ulcerative colitis[8] and those treated with steroids or 5-aminosalicyate.[7] Several societies have published recommendations, position statements, or expert opinions about SARS-CoV-2 virus prevention and management for IBD patients.[10–15]

*Address Correspondence. Dr. Yen-Po Wang, Endoscopy Center for Diagnosis and Treatment, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail address: ulnafu@gmail.com, ypwang@vghtpe.gov.tw (Y.-P. Wang).

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Shortly after the COVID-19 pandemic outbreak, vaccine development for SARS-CoV-2 virus prevention quickly started worldwide.[16] At least 6 kinds of vaccines were listed in the World Health Organization (WHO) emergency use listing, including mRNA-based vaccines (BNT162b2[17] and mRNA-1273[18]), adenovirus vector vaccines (AZD1222[19] and Ad26.COV2. S[20]), and inactivated vaccines (Vero cell[21] and CoronaVac[22]). These vaccines were proven to be effective in reducing symptomatic SARS-CoV-2 virus infections and preventing severe disease and death.[17–22] Theses SARS-CoV-2 vaccination were also effective in preventing severe disease and disease against the SARS-CoV-2 B.1.617.2 variant.[23] According to previously published recommendations in the prevention of SARS-CoV-2 infections in IBD patients, vaccination was suggested to be an effective method.[10–15] However, those suggestions were mainly based on previous experiences with other vaccinations. The risk of severe adverse events after vaccination, such as thromboembolism, anaphylactic shock, and myocarditis, was also unknown in IBD patients.[24] These recommendations and predicted efficacy according to previous clinical trials may not correspond to the real-world clinical practice of SARS-CoV-2 virus vaccinations for IBD patients. Therefore, we conducted this systemic review and meta-analysis to evaluate the efficacy and safety of SARS-CoV-2 vaccination in patients with IBD.

2. METHODS

2.1. Search strategy and study selection

A systematic review and meta-analysis was executed according to the PRISMA-2020 statement.[25,26] This study was registered on PROSPERO (registration number CRD42021264993).

We performed systematic searches on September 9, 2021, using 3 databases, PubMed, Medline, and the Cochrane Library, for publications from January 1, 2019, to September 9, 2021. The search terms are detailed in Supplementary Table 1 http://links.lww.com/JCMA/A125. We used a combination of text words and subject headings in our search to find studies of IBD patients receiving SARS-CoV-2 vaccinations. Only articles written in English were included. Abstracts of the articles were reviewed independently by 2 authors (K.-Y.S. and T.-E.C.) first, with discrepancies resolved by a third author (Y.-P.W.). We included all studies that enrolled patients with IBD receiving the WHO-listed vaccines approved for emergency use as of September 9, 2021. At least one of the following outcomes needed to be available in the enrolled studies: efficacy of the vaccine, seroconversion rates after vaccination, or adverse events after vaccination. Seroconversion was defined as data beyond the threshold of the anti–SARS-CoV-2 spike (S) antibody as described previously.[27–29] We excluded reviews, editorials, recommendations or guidelines, studies that did not include IBD patients, and studies irrelevant to vaccination or vaccinations other than the SARS-CoV-2 vaccine.

2.2. Study outcomes

The primary outcome of interest was the efficacy of SARS-CoV-2 vaccination in IBD patients, including post–SARS-CoV-2 vaccination COVID-19 infections and mortality events in IBD patients. We also compared vaccination efficacy between IBD and non-IBD patients. The secondary outcome included the seroconversion rate and adverse events including adverse events, severe adverse events, and mortality after SARS-CoV-2 vaccination.

2.3. Data extraction and quality assessment

Data from the eligible studies were extracted from the articles and supplementary files http://links.lww.com/JCMA/A125. Extracted data include information on the first author's last name, the title of the article, year of publication, data source, countries where the study was conducted, study design, participant characteristics, vaccine types, previous biologics usage, and outcomes. For all eligible nonrandomized control trial studies, the Newcastle-Ottawa Scale was used to assess the risk of bias.[30]

2.4. Statistical analysis

All statistical analyses were performed using the RevMan Review Manager software, version 5.3.5 (The Cochrane Collaboration, Oxford, United Kingdom), and R software, version 4.1.0 (R Foundation for Statistical Computing, Vienna, Austria), with the metaphor package.[31] In this study, odds ratios (ORs) were generally used for analyzing discrete variables. The corresponding 95% CIs were used to compare the outcomes between the analyzed studies. The pooled effect size was considered statistically significant if a p value of <0.05 was reached. The I squared (I^2) statistic, which indicates the percentage of total variation and inconsistency across studies caused by heterogeneity, with a cutoff value of ≥50%, or the χ^2 test for Cochrane Q statistics with $p < 0.10$, indicated significant heterogeneity. If significant heterogeneity was found, a random-effects model was selected to analyze the pooled data.

3. RESULTS

3.1. Study selection and study characteristics

A total of 5983 citations were found in the searched databases. After review and selection, 11 studies that enrolled 27 454 vaccinated IBD patients were eligible for meta-analysis. The study selection process is shown in Fig. 1.

3.2. Study characteristics and quality

The characteristics of the 11 enrolled studies are listed in Table 1. Of the selected 11 studies, eight studies were conducted in the United States,[28,32–38] one study was conducted in the United Kingdom,[39] one study was conducted in Israel,[40] and one study was conducted in Germany.[41] Eight studies were performed prospectively, and three studies were performed retrospectively. mRNA vaccines, including the BNT162b2 and mRNA-1273 vaccines, were used in most studies, while the adenovirus vector vaccine AZD1222 was used in the UK study and the Ad26.COV2.S vaccine was used in a US study. Three studies focused on vaccination efficacy in preventing infections and mortality, seven studies focused on the seroconversion rate after vaccination, and three studies focused on adverse events after vaccination. The overall quality of the included studies is shown in Supplementary Table 2 http://links.lww.com/JCMA/A125. The Newcastle-Ottawa Scale yielded an average score of 7.2 stars (range, 6–9 stars; the highest quality studies are given nine stars).

3.3. Efficacy of the SARS-CoV-2 vaccine in patients with IBD

In the pooled analysis of three studies that included 31 140 IBD patients, the estimated infection rate after SARS-CoV-2 vaccination was 0.258% ([95% CI, 0.173–0.384] I^2 = 77%). In the pooled analysis of 2 studies that included 25 578 IBD patients, the estimated mortality rate due to SARS-CoV-2 after SARS-CoV-2 vaccination was 0.042% ([95% CI, 0.014–0.128] I^2 = 77%; **Fig. 2A**). The pooled OR for the SARS-CoV-2 infection rate after SARS-CoV-2 vaccination was comparable between the IBD patients and non-IBD patients (OR, 1.28 [95% CI, 0.96–1.71]; p = 0.09; I^2 = 0%; 2 studies; **Fig. 2B**). The risk of SARS-CoV-2 infection was significantly higher in nonvaccinated IBD patients than in vaccinated IBD patients (OR, 8.63 [95% CI, 5.44–13.37]; $p < 0.01$; 1 study; **Fig. 2C**).

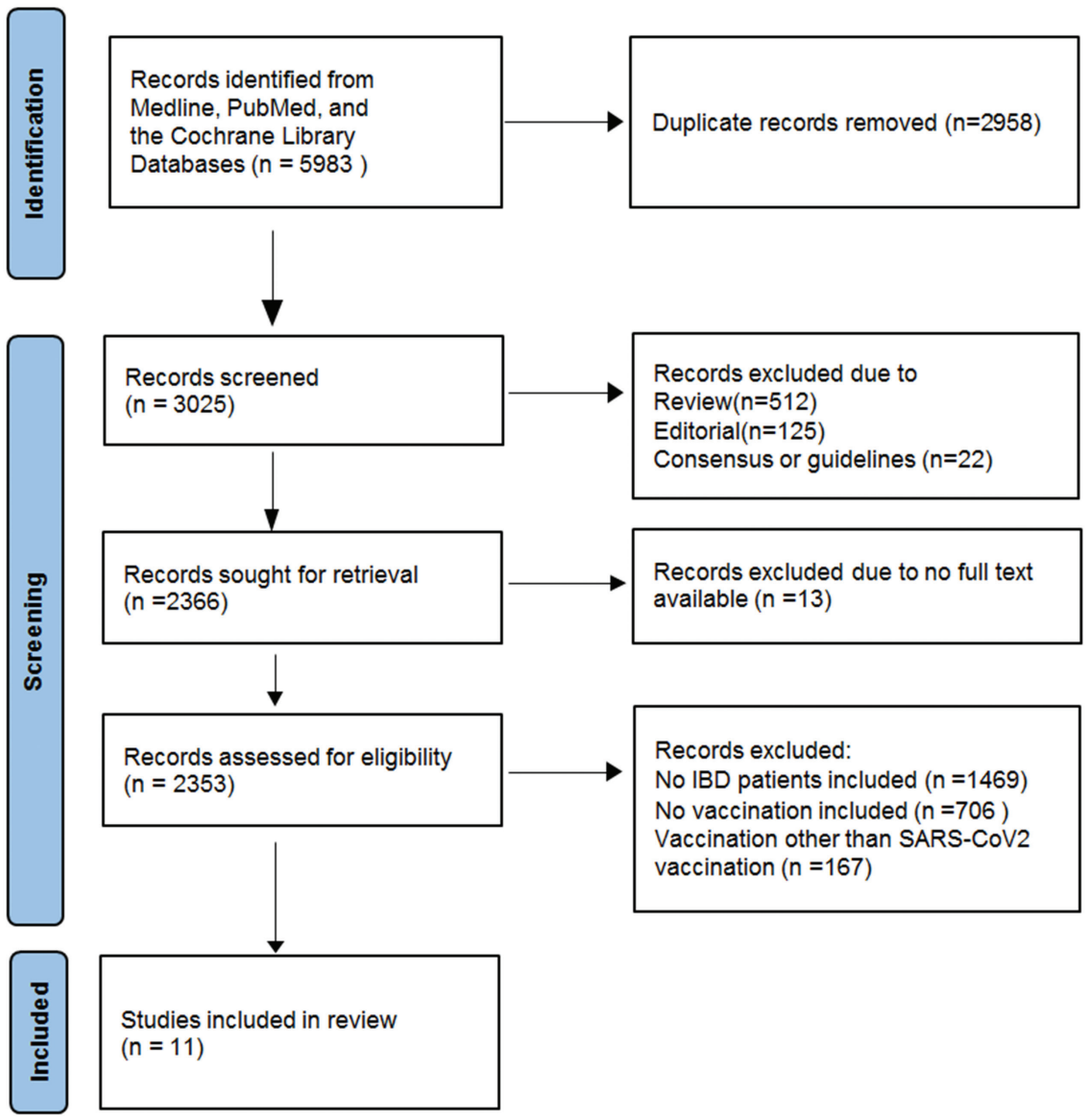

Fig. 1 Study selection flowchart. IBD = inflammatory bowel disease.

3.4. Seroconversion rate after SARS-CoV-2 vaccination in patients with IBD

In the pooled analysis of 1315 patients who received the first dose of a SARS-CoV-2 vaccine, the estimated seroconversion rate was 38% ([95% CI, 36%–41%] I^2 = 58%; 2 studies). Of 702 patients who received the scheduled second dose of a SARS-CoV-2 vaccine, the estimated seroconversion rate was 98% ([95% CI, 93%–100%] I^2 = 51%; 7 studies; **Fig. 3A**). The pooled analysis of the seroconversion rate was the highest in patients who received the full dose of the mRNA-1273 vaccine (99% [95% CI, 86%–100%]; I^2 = 0%), followed by the BNT162b2 vaccine (97% [95% CI, 87%–99%]; I^2 = 49%) and the Ad26.COV2.S vaccine (93% [95% CI, 65%–99%]; I^2 = 0%; **Fig. 3B**). We further compared the seroconversion rate between the different vaccines. The seroconversion rates between the mRNA-1273 and BNT162b2 vaccines were comparable (OR, 2.46 [95% CI, 0.91–6.65]; p = 0.08; I^2 = 58%; 3 studies; **Fig. 3C**). The seroconversion rate was significantly higher in patients who received the mRNA-1273 vaccine than in those who received the Ad26.COV2.S vaccine (OR, 38.37 [95% CI, 1.46–1007.51]; p = 0.03; 2 studies; **Fig. 3D**), and no statistically significant difference was found between patients who received the BNT162b2 vaccine and patients who received the Ad26.COV2.S vaccine (OR, 15.78 [95% CI, 0.91–273.45]; p = 0.06; 2 studies; **Fig. 3E**).

3.5. Seroconversion rate after SARS-CoV-2 vaccination in patients with IBD receiving biologics

In the meta-analysis of the seroconversion rate after SARS-CoV-2 vaccination, no statistically significant difference was found between patients taking anti–tumor necrosis factor (TNF) alpha agents and vedolizumab (OR, 3.04 [95% CI, 0.52–17.70]; p=0.22; 4 studies; I^2 = 2%; **Fig. 4**).

3.6. Adverse events after SARS-CoV-2 vaccination in patients with IBD

The adverse event rate after SARS-CoV-2 vaccination was 69% ([95% CI, 53%–81%] 2 studies; I^2 = 78%). Approximately 3% of the 5844 patients experienced severe adverse events ([95%

Table 1

Summary of the included studies

Study	Study design	Data Source	Country	Participants	Medication status	Age, y; mean (SD)	Male, n (%)	Types of vaccines	Primary outcome	Secondary outcome
Kennedy et al[39]	Prospective	(CLARITY) IBD multicenter cohort study	United Kingdom	1293 vaccinated IBD patients	Continued current medications	43.8	653/50.7[a]	BNT162b2, AZD1222	Antibody titer after the first vaccine dose[b]	Seroconversion rates after two vaccine doses
Khan and Mahmud[32]	Retrospective	National Veterans Health Administration database	United States	7321 vaccinated IBD patients/7376 unvaccinated IBD patients	Continued current medications	71	6777/92.6	BNT162b2, mRNA-1273	SARS-CoV-2 infection	Severe SARS-CoV-2 infection or all-cause mortality
Wong et al[28]	Prospective	Mount Sinai Therapeutic Infusion Center, Mount Sinai Hospital	United States	48 vaccinated IBD patients	Continued current medications	49, 20.2	23/48	BNT162b2, mRNA-1273	Antibody titer[c]	-
Botwin et al[33]	Prospective	Nationwide (Corale-IBD) registry database	United States	246 vaccinated IBD patients	Continued current medications	47.4, 15.5	86/36.2	BNT162b2, mRNA-1273	Adverse events	-
Hadi et al[34]	Retrospective	TriNetX research network database	United States	5562 vaccinated IBD patients/859017 vaccinated non-IBD patients	Continued current medications	57.3, 17.5	2299/41.33	BNT162b2, mRNA-1273	SARS-CoV-2 infection	Adverse events
Ben-Tov et al[40]	Retrospective	MHS database	Israel	12 231 vaccinated IBD patients/36 254 vaccinated non-IBD patients	Continued current medications	47, 17	6124/50.1	BNT162b2	SARS-CoV-2 infection 7 d after vaccination	SARS-CoV-2 infection 14 d after vaccination
Dailey et al[35]	Prospective	Ambulatory infusion center	United States	33 vaccinated IBD patients	Continued current medications	13	NA	BNT162b2, mRNA-1273, Ad26.COV2.S	Antibody titer[d]	-
Kappelman et al[36]	Prospective	Single center (University of North Carolina at Chapel Hill)	United States	317 vaccinated IBD patients	Continued current medications	50.9, 16.7	79/25	BNT162b2, mRNA-1273	Total seroconversion rate	Seroconversion rate for different immunosuppressants
Simon et al[41]	Prospective	Multicenter DZI	Germany	84 IMIDs[d]; patients: 8 vaccinated IBD patients	Continued current medications	53.7, 17.0	29/34.5	BNT162b2	Seroconversion rate in immune-mediated inflammatory disease patient	-
Deepak et al[37]	Prospective	Multicenter COVaRiPAD study	United States	133 adults with CIDs/42 vaccinated IBD patients	Continued current medications	45.5, 16.0	34/25.6	BNT162b2, mRNA-1273	Seroconversion rate in patients with chronic inflammatory diseases	Seroconversion rate for different immunosuppressants
Pozdnyakova et al[38]	Prospective	Multicenter CORALE-IBD study group	United States	353 vaccinated IBD patients	Continued current medications	51	134/38	BNT162b2mRNA-1273, Ad26.COV2.S	Seroconversion rate for different vaccine	-

CID = chronic inflammatory disease; CLARITY = ImpaCt of bioLogic therApy on saRs-cov-2 Infection and immunity; CORALE-IBD = Coronavirus Risk Associations and Longitudinal Evaluation-IBD; COVaRiPAD = COVID-19 Vaccine Responses in Patients With Autoimmune Diseases; DZI = Deutsche Zentrum fuer Immuntherapie; IBD = inflammatory bowel disease; IMID = immune-mediated inflammatory disease; MHS = Maccabi Healthcare Services; NA = not available; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2.

[a]Five patients' sex data missing.

[b]Roche Elecsys Anti-SARS-CoV-2 spike (S) immunoassay alongside the nucleocapsid (N) immunoassay and anti–SARS-CoV- 2 anti-spike (S) protein receptor-binding protein antibody titer.

[c]Anti–SARS-CoV-2 anti-spike (S) protein receptor-binding protein antibody titer.

[d]Immune-mediated inflammatory diseases.

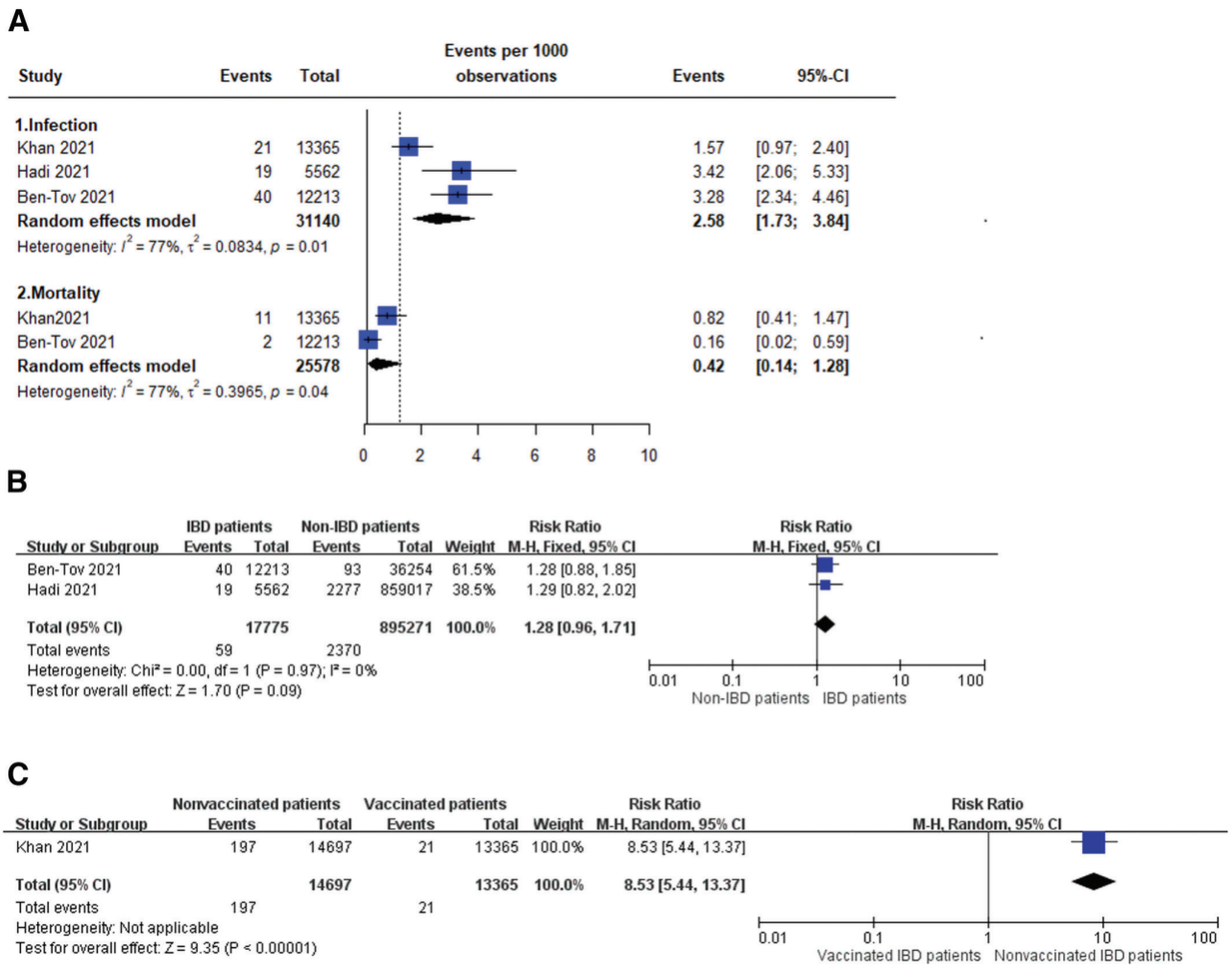

Fig. 2 Forrest plot of efficacy of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccinations in patients with inflammatory bowel disease (IBD). A, The efficacy of SARS-CoV-2 vaccinations on infection and mortality in patients with IBD. B, Post-SARS-CoV-2 vaccination coronavirus disease 2019 (COVID-19) infections between IBD and non-IBD patients. C, COVID-19 infection rates between vaccinated IBD patients and unvaccinated IBD patients. M-H = Mantel-Haenszel method.

CI, 1%–10%] I^2 = 95%; 3 studies), and no mortality after SARS-CoV-2 vaccination in IBD patients was reported (**Fig. 5**).

4. DISCUSSION

This is the first comprehensive systemic review and meta-analysis evaluating SARS-CoV-2 vaccination in IBD patients. SARS-CoV-2 vaccination was effective in preventing SARS-CoV-2 infections and related mortality in IBD patients. The seroconversion rate was modest 14 days after the first dose of a vaccine and high 14 days after the second dose of a vaccine. The seroconversion rate was high among IBD patients who completed vaccination with the BNT162b2, mRNA-1273, and AZD1222 vaccines but relatively lower in patients who received the Ad26.COV2.S vaccine. In patients receiving treatment with biologics, the serologic response rate 14 days after receiving the first dose of a vaccine was relatively low in patients receiving anti-TNF alpha agents compared with patients receiving vedolizumab but was comparable 14 days after the second dose of a vaccine. The majority of patients had adverse events after vaccination, including fatigue/malaise, headache/dizziness, fever/chills, and gastrointestinal symptoms, while only a few patients had severe adverse events. No vaccine-related mortality was reported in IBD patients.

The summarization of the recommendations for SARS-CoV-2 vaccinations in IBD patients from international societies are listed in Table 2. SARS-CoV-2 vaccination is strongly recommended for IBD patients from all societies. Inactivated vaccines were suggested by most societies according to previous vaccination experiences with other diseases.[42,43] If a live-attenuated SARS-CoV-2 vaccine is inevitable, at least 8 weeks after cessation of immunosuppressant is recommended.[14] In our meta-analysis, SARS-CoV-2 vaccination with mRNA-based and adenovirus vector vaccines was proven to be effective in preventing SARS-CoV-2 infection and related mortality, which supported suggestions from international societies. However, the seroconversion rate after a Ad26.COV2.S vaccination was relatively lower than that after an mRNA-based vaccine. This may be related to the limited number of patients who received the Ad26.COV2.S vaccine included in this study. Follow-up of IBD patients who received the Ad26.COV2.S vaccination may help with further clarification.

In patients receiving immunosuppressants, current recommendations suggest that immunosuppressants may result in

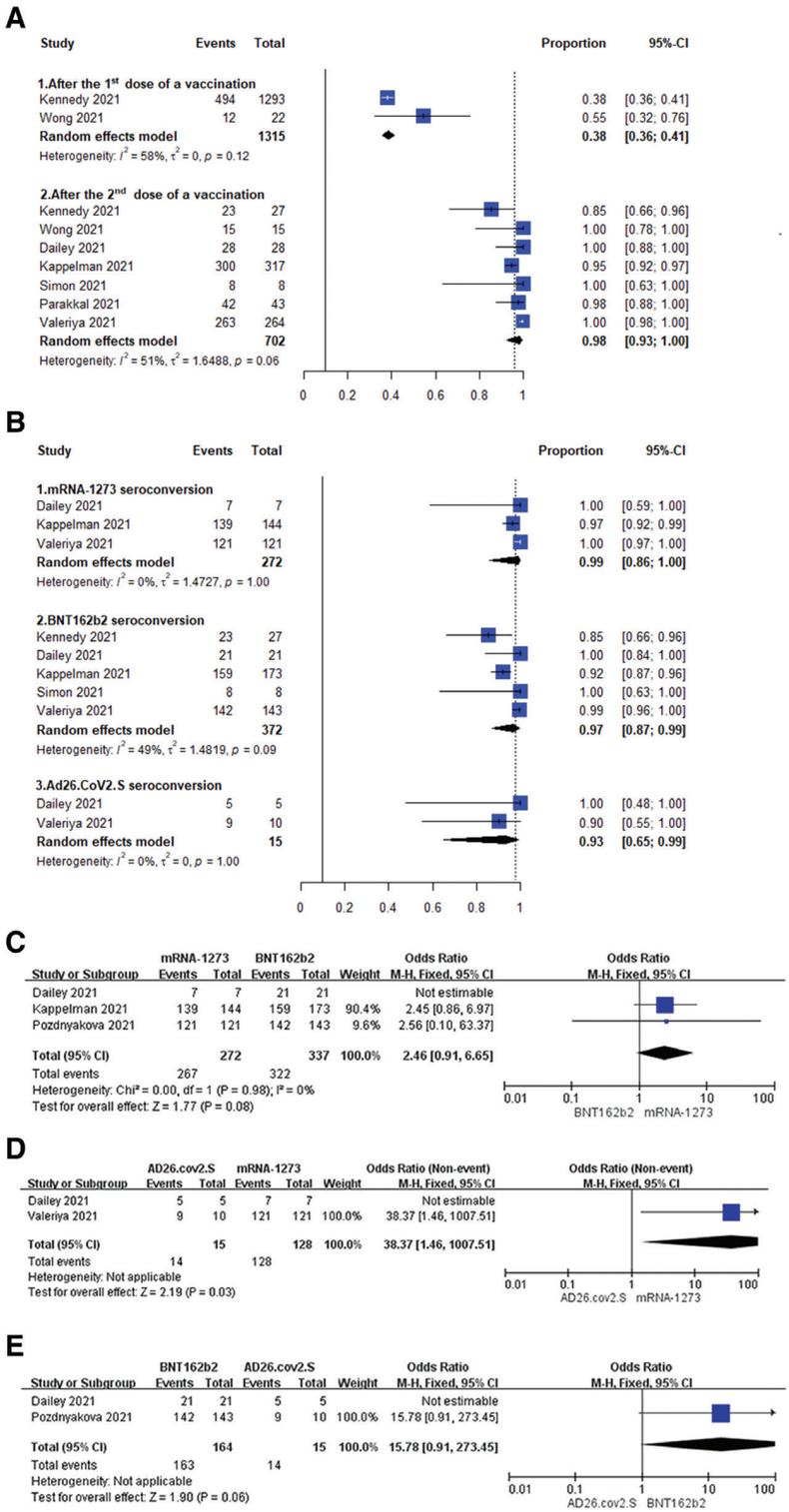

Fig. 3 Forest plot of seroconversion rate in patients with inflammatory bowel disease (IBD) patients taking different severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) vaccines. A, The seroconversion rate after the first and second doses of two scheduled doses for SARS-CoV-2 vaccination in IBD patients. B, The seroconversion rate after complete SARS-CoV-2 vaccination with different vaccines in IBD patients. C, The seroconversion rate after complete SARS-CoV-2 vaccination with the mRNA-1273 vaccine compared with the BNT162b2 vaccine in IBD patients. D, The seroconversion rate after complete SARS-CoV-2 vaccination with the mRNA-1273 vaccine compared with the Ad26.COV2. S vaccine in IBD patients. E, The seroconversion rate after complete SARS-CoV-2 vaccination with the BNT162b2 vaccine compared with the Ad26.COV2. S vaccine in IBD patients. The seroconversion rate was estimated by the proportion of patients with anti–SARS-CoV-2 anti-spike (S) antibody titers beyond the threshold. M-H = Mantel-Haenszel method.

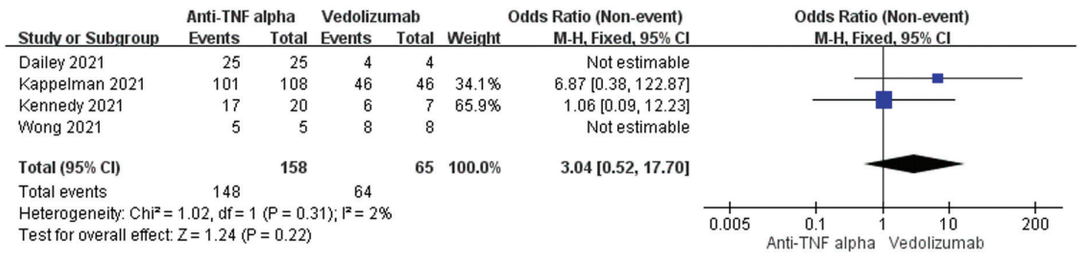

Fig. 4 Forest plot of the seroconversion rate in inflammatory bowel disease patients using anti–tumor necrosis factor alpha (TNFα) and vedolizumab. The seroconversion rate was estimated by the proportion of patients with anti–severe acute respiratory syndrome coronavirus-2 anti-spike (S) antibody titers beyond the threshold. M-H = Mantel-Haenszel method.

lower efficacy of protection from the vaccine. In patients with other autoimmune diseases, the seroconversion rate after SARS-CoV-2 vaccination was significantly lower than that in the control group,[44,45] especially in patients using rituximab and mycophenolate.[45,46] In contrast, our meta-analysis showed that for patients who had received full doses of the vaccine, a high percentage of seroconversion (98%) was achieved, and the influence of immunosuppressants on vaccination efficacy was unlikely and minimal if it existed. The seroconversion rate was also high among biologics users after full doses of the vaccines. Since the risk of severe COVID-19 infection was higher in IBD patients receiving steroids and 5-aminosalicylic acid treatment, vaccination for IBD patients taking immunosuppressants is highly suggested. Furthermore, the anti-SARS-CoV-2 spike (S) antibody was found to decrease 8 weeks after the second dose of a vaccine,[38] and a booster vaccination may be considered during follow-up or in patients without seroconversion after the second dose of a vaccine. It has been proven that a third dose booster vaccination increases the seroconversion rate for patients who have received solid organ transplants and had low antibody titers after the second dose of vaccination. To prevent the wide spread of the COVID-19 Delta variant, the Israeli government announced a third dose booster of SARS-CoV-2 vaccines for all individuals aged 12 years and over,[47] and the UK government announced a third dose booster SARS-CoV-2 vaccination for individuals aged 12 years and over with severe immunosuppression, including patients taking Janus kinase inhibitors, T-cell costimulation modulators, monoclonal TNF inhibitors, soluble TNF receptors, interleukin (IL)-6 receptor inhibitors, IL-17 inhibitors, IL 12/23 inhibitors, IL 23 inhibitors, high-dose or long-term moderate corticosteroids, and immunomodulators in proximity to their second dose of a SARS-CoV-2 vaccine.[48]

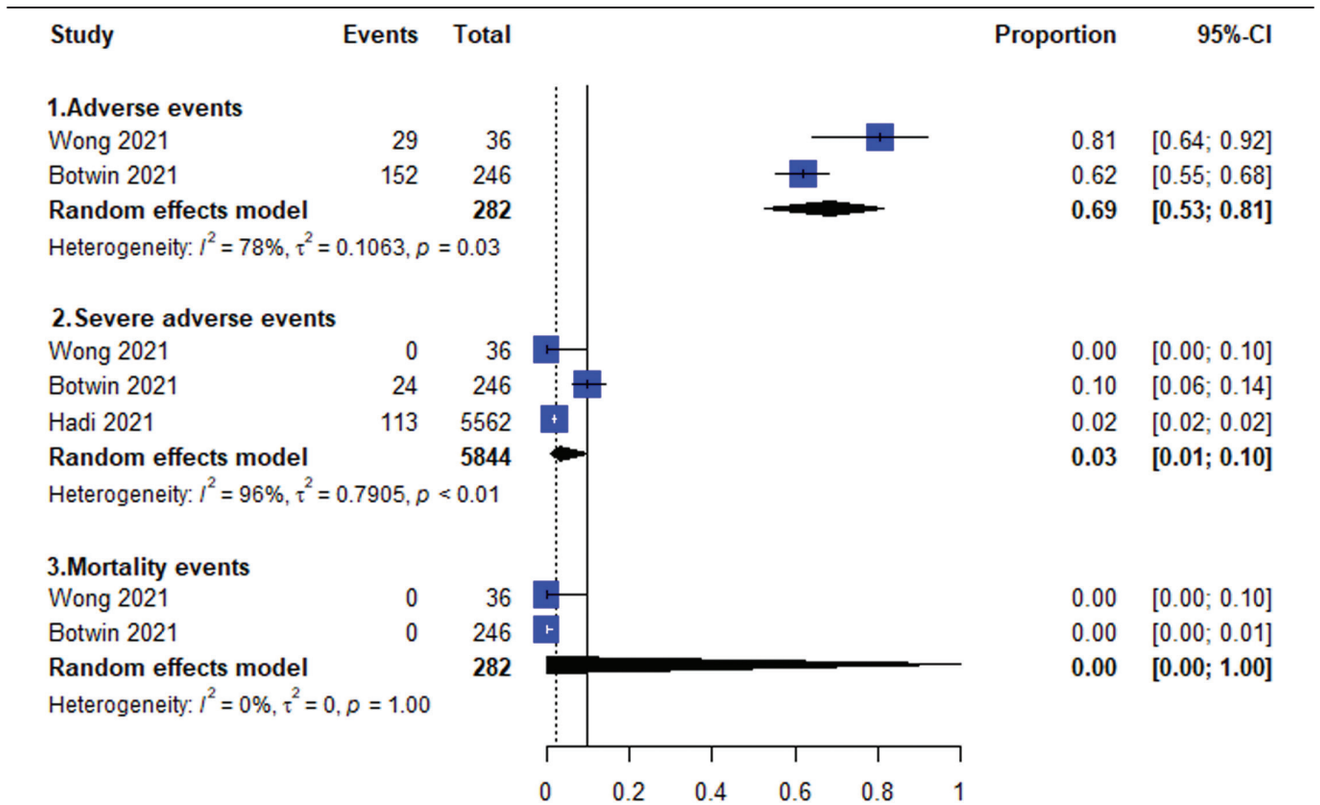

Fig. 5 Forest plot of the adverse events, severe adverse events, and mortality events after the severe acute respiratory syndrome coronavirus-2 vaccination in patients with inflammatory bowel disease.

Table 2

Guidelines or recommendations for vaccination in IBD patients

Question	UK BSG[13]	IOIBD[14,15]	Canada[11,14]	Poland[15]	Brazil[10]	IMIDs study group[12]
I. Should IBD patients receive COVID-19 vaccinations?	Recommended	Recommended	Recommended	Recommended	Recommended	Recommended
II. What kinds of vaccines are recommended for IBD patients?	Approved vaccines	Inactivated vaccines	Inactivated vaccines	Inactivated vaccines	Inactivated vaccines	Brazil approved vaccine
III. What kinds of vaccines are not recommended for IBD patients?	NA	Live virus vaccines	Live virus vaccines	Live virus vaccines	NA	NA
IV. Is the efficacy of a SARS-CoV-2 vaccination the same for patients with and without IBD?	NA	Same efficacy	Same efficacy	NA	NA	NA
V. Should IBD patients postpone or pause their biologic and immunosuppressants to get vaccinated?	Inactivated SARS-CoV-2 vaccines	NA	No	No	No	No
	Live-attenuated SARS-CoV-2 vaccines	NA	Postpone if immunosuppressants in 8 wk	Postpone if immunosuppressive therapy equivalent to ≥20 mg or 2 mg/kg/d of prednisone	NA	NA
VI. Is vaccination administration influenced by disease activity?	NA	No	No	Remission before vaccine administration	NA	No
VII. Is the efficacy of a SARS-CoV-2 vaccination the same for patients with and without IBD?	NA	Same efficacy	Same efficacy	NA	NA	NA
VIII. Is there any safety concern regarding SARS-CoV-2 vaccination for IBD patients?	No	No	No	No	No	No

COVID-19 = coronavirus disease 2019; IBD = inflammatory bowel disease; IMID = immune-mediated inflammatory diseases; IOIBD = International Organization for the Study of Inflammatory Bowel Disease; NA = not available; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; UK BSG = United Kingdom British Society of Gastroenterology.

Whether the third dose boosters of the SARS-CoV-2 vaccine are mandatory for all IBD patients or IBD patients with low antibody titers warrants further study.

Regarding the safety of SARS-CoV-2 vaccination, most of the recommendations suggest that SARS-CoV-2 vaccination should be performed for all IBD patients irrespective of disease activity, except the recommendations of the Polish Society of Gastroenterology, which suggested that SARS-CoV-2 vaccination should be considered for IBD patients in remission only.[15] No other safety considerations specified for IBD patients were suggested. In IBD patients receiving SARS-CoV-2 vaccinations, approximately 70% of patients experienced adverse events, similar to the general population. Only a few severe adverse events were encountered, while no mortality events related to SARS-CoV-2 vaccination were reported. This corresponded to the sound safety profile of previous inactivated vaccines for IBD patients.[49,50] For patients with other autoimmune diseases, the safety of the SARS-CoV-2 vaccine was also good, with few severe adverse events.[44,51]

Several limitations exist in this systematic review and meta-analysis. First, only cohort studies were included in this review. However, many cohort studies were prospectively conducted that limited the risk of reporting bias. Second, there was heterogeneity or data paucity in respect to type of vaccine (Adeno vector virus or mRNA based), the timing of seroconversion measurement, and previous COVID-19 exposure history, which may influence the seroconversion. High seroconversion rate observed on IBD patients receiving full doses of vaccination limited these potential influences. Third, the durability of the seroconversion after SARS-CoV-2 vaccination was unknown that long-term follow-up studies on vaccination efficacy are recommended. Finally, no enrolled study was conducted in Eastern Asia that the ethnic influences on vaccination efficacy and safety can't be evaluated in this study. Further Asian studies are also warranted.

In conclusion, the SARS-CoV-2 vaccination is effective in preventing COVID-19 infections in IBD patients, with few severe adverse events. Most patients experienced seroconversion after receiving a complete dose of a SARS-CoV-2 vaccination, and the influence of biologics on vaccination was limited. The need for vaccine boosters among IBD patients is worth researching further. SARS-CoV-2 vaccination is suggested for IBD patients.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A125.

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