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Impact of COVID-19 infection during the postoperative period in patients who underwent gastrointestinal surgery: a retrospective study

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Purpose: The coronavirus disease 2019 (COVID-19) pandemic has led to significant global casualties. This study examines the postoperative impact of COVID-19 on patients who underwent gastrointestinal surgery, considering their heightened vulnerability to infections and increased morbidity and mortality risk.
Methods: This retrospective observational study was conducted at a tertiary center and patients who underwent gastrointestinal surgery between January 2022 and February 2023 were included. Postoperative COVID-19 infection was defined as the detection of severe acute respiratory syndrome coronavirus 2 RNA by RT-PCR within 14 days after surgery. Propensity score matching was performed including age, sex, American Society of Anesthesiology physical status classification, and emergency operation between the COVID-19-negative (–) and -positive (+) groups.
Results: Following 1:2 propensity score matching, 21 COVID-19(+) and 42 COVID-19(–) patients were included in the study. In the COVID-19(+) group, the postoperative complication rate was significantly higher (52.4% *vs*. 23.8%, P = 0.023). Mechanical ventilator requirement, intensive care unit (ICU) admission, and readmission rate did not significantly differ between the 2 groups. The median length of ICU (19 days *vs*. 4 days, P < 0.001) and hospital stay (18 *vs*. 8 days, P = 0.015) were significantly longer in the COVID-19(+) group. Patients with COVID-19 had a 2.4 times higher relative risk (RR) of major complications than patients without COVID-19 (RR, 2.37; 95% confidence interval, 1.254–4.467; P = 0.015).
Conclusion: COVID-19 infection during the postoperative period in gastrointestinal surgery may have adverse outcomes which may increase the risk of major complications. Preoperative COVID-19 screening and protocols for COVID-19 prevention in surgical patients should be maintained.
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Key Words: COVID-19, Digestive system surgical procedures, Postoperative period, Postoperative complications

INTRODUCTION

Since early 2020, the coronavirus disease 2019 (COVID-19) pandemic, which causes severe acute respiratory syndrome, has spread worldwide, resulting in numerous severe morbidities and mortalities [1,2]. On March 11, 2020, the World Health Organization declared the COVID-19 outbreak a pandemic. In South Korea, the government relocated medical resources, focused on managing COVID-19-infected patients and suspended or postponed nonessential or elective surgeries.

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Although the pandemic has been declared to be under control, we are still experiencing intermittent, small-scale outbreaks, and a resurgence is possible [3].

Patients undergoing surgery are at a higher risk of COVID-19 infection, related complications, and mortality due to the immunosuppressive response associated with surgical inflammation [4,5]. Studies have reported an increased risk of complications and mortality among surgical patients infected with COVID-19 during the pandemic [6-8]. A study conducted by the COVIDSurg group reported that patients undergoing surgery with COVID-19 infection had a 30-day mortality rate of up to 24% and was accompanied by pulmonary complications in over 50% of cases [9]. Other studies have shown that surgical patients infected with COVID-19 have a three-fold higher incidence of severe surgical complications and a nine-fold higher mortality rate than noninfected patients [10].

Respiratory disease in patients undergoing intestinal resection surgery is a well-known factor that negatively affects surgical outcomes [11], and the formation of thromboembolisms related to COVID-19 may also affect anastomotic sites [12]. Therefore, the increased occurrence of respiratory complications due to COVID-19 may be detrimental to the surgical outcomes of patients undergoing intestinal resection surgery. This study investigated the impact of postoperative COVID-19 infection on surgical outcomes in patients undergoing gastrointestinal (GI) surgery during the COVID-19 pandemic when the omicron variant is mainly prevalent.

METHODS

Ethics statement

This study was approved by the Institutional Review Board of Korea University Anam Hospital (No. 2023AN0307), and the study protocol conformed to the tenets of the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study.

Study population

This retrospective observational study was conducted at a tertiary center. The medical records of patients who underwent GI surgery between January 2022 and February 2023, when the coronavirus omicron variant was mainly prevalent were consecutively reviewed. Patients who had undergone elective or emergency GI resection or primary repair with or without anastomosis were eligible for inclusion. Patients with confirmed COVID-19 infection before surgery and those who underwent multiple major organ resections, cytoreductive surgery, or hyperthermic intraperitoneal chemotherapy (HIPEC) were excluded from the analysis.

COVID-19 diagnosis

COVID-19 was diagnosed based on quantitative real-time RT-PCR results for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA detection in patients with no history of COVID-19 infection within the past 3 months. The samples were collected using nasopharyngeal swabs. Postoperative COVID-19 was defined as an infection in patients with COVID-19 within 14 days after surgery.

Institutional protocols

All patients scheduled for surgery and their accompanying caregivers underwent RT-PCR tests within 3 days before admission and completed a questionnaire regarding the presence of COVID-19 symptoms (fever, dry cough, sore throat, rhinorrhea, tiredness, aches, pain, diarrhea, nausea, loss of olfaction, and/or taste). The RT-PCR test was performed either at a local institution in the patient's region of residence or at the hospital where the study was conducted. Admission and surgery were permitted only if there were no symptoms or history of contact with COVID-19-infected patients and the RT-PCR test confirmed a negative result. If a patient scheduled for surgery exhibited COVID-19-related symptoms or tested positive, surgery was postponed for at least 2 weeks, following the guidelines of the institutional infection control unit. All patients admitted to the emergency department underwent RT-PCR tests, and in cases requiring emergency surgery, rapid antigen tests were performed to obtain COVID-19 results quickly. If confirmed negative, the patients were transferred to the operating room. If tested positive, the patient was transferred to a dedicated COVID-19 facility; if transfer was not possible, the surgery was performed in a negative pressure operating room where all healthcare personnel wore level 4 protective equipment.

During hospitalization, an RT-PCR test was performed if the patient developed new symptoms related to COVID-19 or had a history of contact with a confirmed COVID-19-positive patient. Patients with confirmed COVID-19 were placed in negative pressure rooms for cohort isolation for 7 days. If a patient is diagnosed with COVID-19 while admitted to the intensive care unit (ICU), they have not stayed in the ICU for isolation purposes once their condition has sufficiently improved to allow transfer to a general ward. Instead, if their condition allows for transfer to a general ward, they have been transferred to a negative pressure room. If a patient has sufficiently recovered to allow for discharge, arrangements have been made for the patient to be discharged during the isolation period, allowing for self-isolation. They underwent antiviral therapy and prophylaxis for thrombosis with low-molecular-weight heparin according to the COVID-19 treatment guidelines recommended by the National Institutes of Health in collaboration with the Department of Infectious Disease [13].

Statistical analysis

Quantitative variables are expressed as median values with interquartile ranges, and categorical variables are presented as numbers and frequencies. We used the chi-square test to compare the proportions of categorical variables, and the t-test or Mann-Whitney U-test, depending on the data distribution, was used for continuous variables. Nearest-neighbor propensity score matching was performed between the COVID-19 positive (+) and COVID-19 negative (–) groups to reduce the effects of confounding factors, including age, sex, American Society of Anesthesiology (ASA) physical status (PS) classification, and emergency operation. A propensity score was calculated from the logistic equation for each predicted probability, and propensity score matching was performed using a 1:2 method without replacement, using the closest propensity scores. Only patients matched for propensity scores were included in the analysis. We used a Cox proportional regression model to compute relative risks (RRs) with 95% confidence intervals (CIs) for 30-day mortality, major complications, respiratory morbidity, and respiratory mortality. The primary outcome measure was the incidence of major complications. Statistical significance was established using a two-sided test with a

Table 1. Clinical characteristics of total patients and comparison of COVID-19-negative and -positive groups before and after 1:2 propensity score matching

Characteristic	Before matching			After matching		
	COVID-19(+) group	COVID-19(–) group	P-value	COVID-19(+) group	COVID-19(–) group	P-value
No. of patients	21	904		21	42	
Sex			0.11			0.41
Male	12 (57.1)	360 (39.8)		12 (57.1)	29 (69.0)	
Female	9 (42.9)	544 (60.2)		9 (42.9)	13 (31.0)	
Age (yr)	73 (64 – 81)	65 (53 – 75)	0.001	73 (64 – 81)	77 (67 – 81)	0.96
ASA PS classification			0.004			0.19
I, II	6 (28.6)	562 (62.2)		6 (28.6)	6 (14.3)	
≥III	15 (71.4)	342 (37.8)		15 (71.4)	36 (85.7)	
Comorbidity						
Hypertension	12 (57.1)	413 (45.7)	0.30	12 (57.1)	31 (73.8)	0.25
Diabetes mellitus	3 (14.3)	179 (19.8)	0.50	3 (14.3)	15 (35.7)	0.14
Respiratory	2 (9.5)	73 (8.1)	0.88	2 (9.5)	13 (31.0)	0.07
Cardiovascular	8 (38.1)	75 (8.3)	0.013	8 (38.1)	15 (35.7)	>0.99
Neurological	5 (23.8)	46 (5.1)	0.06	5 (23.8)	10 (23.8)	>0.99
Diagnosis			0.014			0.42
Malignancy	9 (42.9)	559 (61.8)		9 (42.9)	25 (59.5)	
Benign	0 (0)	178 (19.7)		0 (0)	0 (0)	
Bowel perforation or obstruction, malignancy	5 (23.8)	73 (8.1)		5 (23.8)	6 (14.3)	
Bowel perforation or obstruction, benign	7 (33.3)	94 (10.4)		7 (33.3)	11 (26.2)	
Emergency surgery	11 (52.4)	127 (14.0)	0.003	11 (52.4)	15 (35.7)	0.28
Operation			0.008			0.43
Gastrectomy	5 (23.8)	317 (35.1)		5 (23.8)	6 (14.3)	
Colectomy	4 (19.0)	330 (36.5)		4 (19.0)	16 (38.1)	
Low anterior resection	5 (23.8)	136 (15.0)		5 (23.8)	10 (23.8)	
Hartmann operation or abdominoperineal resection	3 (14.3)	31 (3.4)		3 (14.3)	2 (4.8)	
Small bowel resection	2 (9.5)	68 (7.5)		2 (9.5)	2 (4.8)	
Primary repair for perforation	2 (9.5)	22 (2.4)		2 (9.5)	6 (14.3)	
Stoma formation	5 (23.8)	104 (11.5)	0.21	5 (23.8)	10 (23.8)	0.63
Surgical approach			0.003			0.053
Open	12 (57.1)	176 (19.5)		12 (57.1)	12 (28.6)	
Minimally invasive	9 (42.9)	728 (80.5)		9 (42.9)	30 (71.4)	
COVID-19 symptoms (+)	14 (66.7)	NA		14 (66.7)	NA	
Antiviral therapy for COVID-19	11 (52.4)	NA		11 (52.4)	NA	
Timing of COVID-19 infection	4 (0–10.5)	NA		4 (0–10.5)	NA	

Values are presented as number only, number (%), or median (interquartile range).
COVID-19, coronavirus disease 2019; IQR, interquartile range; ASA, American Society of Anesthesiology; PS, physical status; NA, not applicable.

P-value of <0.05. All statistical analyses were performed using IBM SPSS Statistics ver. 25.0 (IBM Corp.) and R ver. 4.1.2 (R Project for Statistical Computing).

RESULTS

Clinical characteristics

We reviewed the data of 1,473 patients who underwent GI surgery. After excluding 4 patients with preoperative COVID-19 infections and 554 patients who underwent multiple major organ resections, cytoreductive surgery, or HIPEC, 925 patients were included in our study. Among them, 21 (2.3%) were infected with COVID-19. The 21 propensity-score-matched COVID-19(+) and 42 COVID-19(–) patients were compared. Table 1 presents the clinical characteristics of patients according to COVID-19 status after propensity score matching. In the COVID-19(–) group, 73.8% had malignancy, and 40% underwent surgery due to intestinal perforation or obstruction. In the COVID-19(+) group, 66.7% had malignancy and 57.1% underwent surgery due to intestinal perforation or obstruction. There were no significant differences in clinical characteristics between the 2 groups. Both groups had a high proportion of ASA PS grades of III or higher, 71% and 86%, in the COVID-19(+) and COVID-19(–) groups, respectively. Emergency surgery was performed in 52% of the COVID-19(+) group and 36% of the COVID-19(–) group. Although there was no statistically significant difference in the underlying comorbidities, the COVID-19(–) group had a much higher proportion of patients with respiratory disease (31% *vs.* 9.5%, P = 0.07). In the COVID-19(+) group, open surgeries were more frequently performed than minimally invasive surgeries, compared to the COVID-19(–) group (57% *vs.* 28.6%, P = 0.053). The 2 groups did not differ in the surgical procedure and stoma formation rates (23.8 %). Among patients with COVID-19, 66.7% had COVID-19-related symptoms, and 52.4% received antiviral therapy. The median timing of COVID-19 infection was postoperative day 4.

Postoperative outcomes

Table 2 summarizes the postoperative patient outcomes. The postoperative complication rate was significantly higher in the COVID-19(+) group than in the COVID-19(–) group (52.4% *vs.* 23.8%, P = 0.023). The COVID-19(+) group had a significantly higher proportion of major complications of Clavien-Dindo classification III or higher (38.1% *vs.* 11.9%, P = 0.015). Details of the postoperative complications are shown in Fig. 1. In the COVID-19(–) group, there were no cases of anastomotic leakage, while in the COVID-19(+) group, anastomotic leakage occurred in 14.3% of the patients (3 of 21). Pneumonia occurred in 2 patients (9.5%) in the COVID-19(+) group and in 2 patients (4.8%) in the COVID-19(–) group.

No differences were observed in terms of respiratory morbidities, including O_2 (47.6% in the COVID-19(+) group and 38.1% in the COVID-19(–) group, P = 0.48) and mechanical ventilator requirement (23.8% in the COVID-19(+) group and 16.7% in the COVID-19(–) group, P = 0.77). There was no difference in the 30-day mortality between the 2 groups (2 of 42 [4.8%] in the COVID-19(–) group and 1 of 21 [4.8%] in the COVID-19(+) group). Respiratory mortality occurred in 1 patient with COVID-19 infection, while in the COVID-19(–) group, 2 patients died, with cancer progression being the cause of death.

The ICU admission and readmission rates did not differ significantly between the 2 groups. However, compared to patients without COVID-19, those with COVID-19 had considerably longer ICU (19 days *vs.* 4 days, P < 0.001) and hospital stays (18 days *vs.* 8 days, P = 0.015).

In the RR analyses, patients with COVID-19 had a 2.4 times higher risk of major complications than patients without COVID-19 (RR, 2.37; 95% CI, 1.254–4.467; P = 0.015) (Table 3).

Table 2. Postoperative outcomes of patients according to COVID-19 infection

Variable	Total (n = 63)	COVID-19(+) group (n = 21)	COVID-19(–) group (n = 42)	P-value
Postoperative complications, CD grade	21 (33.3)	11 (52.4)	10 (23.8)	0.023
I, II	8 (12.7)	3 (14.3)	5 (11.9)	0.82
≥III	13 (20.6)	8 (38.1)	5 (11.9)	0.015
Mechanical ventilator requirement	12 (46.2)	5 (23.8)	7 (16.7)	0.77
Respiratory morbidity	26 (41.3)	10 (47.6)	16 (38.1)	0.48
Respiratory mortality	1 (1.6)	1 (4.8)	0 (0)	0.16
30-Day mortality	3 (4.8)	1 (4.8)	2 (4.8)	0.98
ICU admission rate	19 (30.2)	6 (28.6)	13 (31.0)	0.85
Length of ICU stay (day)	4 (2–11)	19 (9–27)	4 (2–5)	<0.001
Hospital stays (day)	11 (7–24)	18 (8–28)	8 (7–14)	0.015
Readmission	4 (6.3)	2 (9.5)	2 (4.8)	0.47

Values are presented as number (%) or median (interquartile range).
COVID-19, coronavirus disease 2019; CD, Clavien-Dindo classification; ICU, intensive care unit.

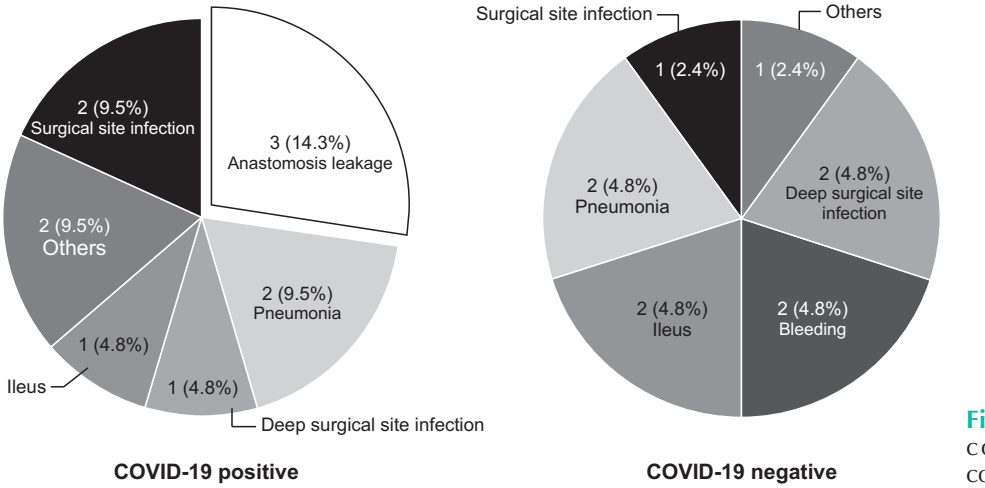

Fig. 1. Details of postoperative complications. COVID-19, coronavirus disease 2019.

Table 3. Relative risk of 30-day mortality and major complications according to COVID-19 infection

Variable	COVID-19(+) group (n = 21)	COVID-19(–) group (n = 42)	Relative risk (95% CI)	P-value
30-day mortality	1	2	1.00 (0.194–5.154)	>0.99
Major complications[a)]	8	5	2.37 (1.254–4.467)	0.015
Respiratory mortality	1	0	3.10 (2.161–4.446)	0.15

COVID-19, coronavirus disease 2019; CI, confidence interval.
[a)]Clavien-Dindo classification of ≥III.

DISCUSSION

This study showed that postoperative COVID-19 infection had a hazardous effect on patients who underwent GI surgery, with longer hospital and ICU stays, and were at a higher risk of serious complications.

Consistent with our findings, several studies on COVID-19 in surgical patients have reported a significant association between COVID-19 and a higher risk of complications. A matched cohort study conducted in Italy reported that postoperative complications were significantly higher in patients with COVID-19 (odds ratio [OR], 4.98; 95% CI, 1.84–16.07), and 30-day mortality was also significantly higher in patients with COVID-19 compared with those without COVID-19 (OR, 9.5; 95% CI, 1.77–96.53) [10]. In an American study, patients with COVID-19 infection presented a higher risk of severe complications (57.1% *vs.* 14.3%, P = 0.006), ICU admission (36.1% *vs.* 16.4%, P = 0.004), and mortality (16.7% *vs.* 1.4%, P < 0.001) [7]. In our series, anastomotic leakage occurred in 3 patients infected with COVID-19 (14.3%), despite no difference in the stoma formation rate between the 2 groups. Several nationwide studies conducted during the pandemic have reported no significant differences in perioperative outcomes after colorectal cancer surgery. However, there was a 2-fold increase in the incidence of stoma formation compared to the prepandemic period [14-17]. Coronaviruses affect the GI tract [18,19]. Many COVID-19 patients have experienced GI symptoms such as nausea, vomiting, diarrhea, and abdominal pain [20]. Some studies have confirmed intestinal damage caused by COVID-19 through autopsies and biopsies, with significant numbers of plasma cells and lymphocytes infiltrating the lamina propria [21,22]. Acute hemorrhagic colitis and intestinal ischemia caused by thromboembolism have been reported [12,23,24]. The proposed mechanism for causing intestinal damage includes high expression of angiotensin-converting enzyme 2 in enterocytes, which makes them highly susceptible to SARS-CoV-2 infection or the cytokine storm associated with systemic inflammatory reactions and multi-organ dysfunction [25-27]. Such intestinal damage could potentially affect the anastomosis after GI surgery.

In contrast to previous research findings, where a significantly higher rate of pulmonary complications was observed in surgical patients with COVID-19 [9,10,28], no differences were observed between the 2 groups in our study population. This could be attributed to the high prevalence of underlying respiratory conditions in the COVID-19(–) group (31% *vs.* 9.5%, P = 0.07), which led to a higher respiratory morbidity rate of 38%. The omicron variant, characterized by high transmissibility but often presenting with asymptomatic or mild symptoms [29], may not have influenced the incidence of respiratory morbidity rate. However, there was only one case of respiratory mortality in patients with COVID-19, and the

COVID-19(+) group had a significantly longer ICU stay because of prolonged mechanical ventilator weaning (19 days *vs.* 4 days, $P < 0.001$). This suggests that the COVID-19(+) group had more severe respiratory morbidity.

Our study had some limitations. First, since this was a retrospective, single-center study, there may be inherent selection bias, although we attempted to control for known confounders using adjusted analysis. Second, this small cohort study focused on patients who underwent GI surgery, including those clinically destined to have poor outcomes. In these cases, surgeries were performed despite restrictions on nonessential and elective surgeries during the pandemic, as the patients had severe or emergent diseases and underlying comorbidities. Consequently, the severity of patient status was higher, and there were more complications and longer ICU, or hospital stays than in the prepandemic period. When transferring patients from the ICU to the general ward, the possibility of a 1–2 day delay due to the unavailability of negative pressure rooms cannot be excluded. It should be taken into consideration when interpreting the results. The increased ICU stay due to this reason could not be confirmed through medical records; however, it would not have exceeded 1–2 days according to institutional policies. Furthermore, the severity of COVID-19 symptoms could not be assessed by reviewing medical records. According to epidemiological data, most COVID-19-infected patients are asymptomatic [30], and the presence of severe COVID-19 symptoms or accompanying complications can have an impact on morbidity and mortality. We cannot exclude the influence of underreported symptoms and severe patient status. Despite these limitations, we focused on the impact of COVID-19 on GI surgical outcomes in a matched population. Our findings indicate that COVID-19 is associated with poor surgical outcomes. Therefore, we recommend postponing GI surgery whenever possible in patients with COVID-19.

With the COVID-19 pandemic now under control, we have returned to performing elective surgeries as part of our routine. However, we still adhere to the COVID-19 screening protocols before elective and emergent surgeries. The global pandemic status will continue to change, and medical guidelines may evolve accordingly. Nevertheless, sporadic small-scale outbreaks persist, and considering the potential for adverse surgical outcomes in COVID-19 patients, COVID-19 screening and efforts to prevent infection before elective GI surgery must be maintained.

In conclusion, postoperative COVID-19 infection has been shown to increase the risk of major complications, including anastomotic leakage, prolonged hospital, and extended ICU stay in patients undergoing GI surgery. Hence, we strongly recommend continuing preoperative COVID-19 screening and adhering to COVID-19 infection prevention measures to optimize surgical outcomes.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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