Evaluating the burden of the COVID-19 pandemic on patients with colorectal cancer

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Received March 9, 2022; Accepted May 13, 2022

DOI: 10.3892/ol.2022.13383

Abstract. After the emergence of the coronavirus disease 2019 (COVID-19) pandemic, individuals needing medical help preferred to not go to the hospital to avoid the risk of severe acute respiratory syndrome coronavirus 2 infection. The present study investigated the influence of the COVID-19 pandemic on patients with colorectal cancer. Patients with colorectal cancer treated between January and December 2019 were classified as the pre-pandemic group (pre-group) and those treated between April 2020 and March 2021 as the post-pandemic group (pandemic group). The clinicopathologic features of patients who underwent surgery for colorectal cancer in the two groups were retrospectively compared. A total of 161 patients were enrolled: 79 In the pre-group and 82 in the pandemic group. Although no significant differences were observed in tumor location and surgical procedure between the two groups, circumferential lesions (P<0.001), colorectal stenting (P=0.016) and Stage IV classification (P=0.019) had a higher frequency in the pandemic group compared with the pre-group; additionally, surgical curability was significantly lower (P=0.036) in the pandemic group. The spread of COVID-19 has increased the incidence of patients with advanced colorectal cancer. To reduce this incidence, healthcare professionals should inform the general public not only about the risk of COVID-19, but also about the increased incidence of advanced colorectal cancer after the pandemic.

Introduction

The first case of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in December 2019 in Wuhan, China. The disease has since spread worldwide, with the World Health Organization declaring it a pandemic on March 11, 2020 (1). As of March 1, 2022, 462 million cases and 6.05 million deaths have been recorded worldwide, and there is a continuous increase in the number of infections (2). The first case of COVID-19 was reported in January 2020 in Japan, and the Japanese government declared a state of emergency according to the Act on the Special Measures against Pandemic Influenza and New Infectious Diseases Preparedness and Response on April 7, 2020. By the end of April 2021, Japan had declared a state of emergency three times. On March 1, 2022, the number of infected individuals was 5.86 million, with 26,000 deaths (3). Strict regulations such as lockdown have been in place worldwide to prevent the spread of infection. These regulations have also greatly affected social and economic functioning.

The COVID-19 pandemic has had a great impact on medical care. As gastrointestinal surgeons, we have also experienced the effect of COVID-19 in clinical practice. Several countries have taken precautionary measures, such as the discontinuation of primary colorectal cancer screening, which includes colonoscopy. At the same time, a large number of individuals are unwilling to go to a hospital to avoid the risk of SARS-CoV-2 infection. Under these circumstances, elective surgeries for colorectal cancer increased and the number of advanced cases decreased. Refraining from going outdoors, even for medical consultations, may help prevent the spread of SARS-CoV-2 infection. However, this may result in increased cancer-related mortality. In the present study, we aimed to investigate the severity of colorectal cancer in patients referred to our department before and after the COVID-19 outbreak, where the severity was measured in terms of cancer progression, metastasis, and remission.

Materials and methods

Patients who underwent elective and emergency surgery for colorectal cancer in our hospital between January 2019 and March 2021 were included in the study. We excluded patients who were treated between January and March 2020, which is the interval from the onset of the COVID-19 pandemic to the declaration of a state of emergency. Eligible patients were classified into two groups. The patients treated between January and December 2019 were classified as the COVID-19 pre-pandemic group (pre-group), and those treated between

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Key words: coronavirus disease 2019, severe acute respiratory syndrome coronavirus 2, pandemic, colorectal cancer

April 2020 and March 2021 were classified as the COVID-19 post-pandemic group (pandemic group). We retrospectively compared the clinicopathologic features of patients who underwent surgery for colorectal cancer in the two groups. To assess nutritional status, we evaluated the prognostic nutritional index (PNI), which combines the serum albumin (Alb) concentration and total peripheral blood lymphocyte count (TLC) and is calculated using the following formula: 10 x Alb (g/dl) +0.005 x TLC/mm^3 (4).

Statistical analysis was performed using EZR (5) software, which is a modified version of the R commander, to perform statistical functions used in biostatistics. Univariate analysis was performed using the Mann-Whitney U test or chi-squared test. Statistical significance was set at $P<0.05$. Numerical values are expressed as median (range).

This study was approved by the Teikyo University Medical Research Ethics Committee (approval no. 20-049).

Results

A total of 161 patients were enrolled: 79 in the pre-group and 82 in the pandemic group. The results of the univariate analysis are shown in Tables I-III.

The two groups were similar in terms of sex, age, and American Society of Anesthesiologists Physical Status Classification (6). However, there were significantly more comorbidities (86.6 vs. 67.1%; P=0.005) and a higher tendency of the prevalence of heart disease (24.1 vs. 21.5%; P=0.082) in the pandemic group than in the pre-group. No significant differences were found in the prevalence of hypertension, respiratory disease, and cerebrovascular disease between the two groups. However, the prevalence of diabetes (32.9 vs. 14.6%; P=0.009) and high body mass index tended to be higher (22.8 kg/m^2 [14.1-33.3] vs. 22.1 kg/m^2 [14.0-41.2]; P=0.061) in the pre-group than in the pandemic group. As indicators of nutritional status, Alb (3.5 g/dl [1.5-4.8] vs. 3.7 g/dl [2.1-5.4]; P=0.030) and PNI (42.7 [18.6-55.2] vs. 44.7 [31.2-66.6]; P=0.033) were both significantly lower in the pandemic group than in the pre-group. In terms of tumor markers, the carcinoembryonic antigen levels were similar in both the groups, whereas carbohydrate antigen 19-9 tended to be higher in the pandemic group than in the pre-group (8.3 U/ml [2.0-15200] vs. 4.9 U/ml [2.0-708]; P=0.076).

No significant differences were found in tumor location, surgical procedure, and degree of lymph node dissection between the two groups. However, laparoscopic surgery was more frequently performed in the pre-group (P<0.001), whereas robotic surgery was more frequently performed in the pandemic group (P<0.001). Only one case (1.4%) in the pandemic group was converted to laparotomy. The operation time tended to be longer in the pandemic group than in the pre-group (294.5 min [43-1183] vs. 241 min [109-776]; P=0.083). However, no significant differences were observed in the amount of blood loss, perioperative blood transfusions, and postoperative complications between the two groups. Surgical curability was significantly improved in the pre-group than in the pandemic group (R0 91.1%/R1 0%/R2 8.9% vs. R0 76.8%/R1.2%/R2 22.0%; P=0.036). Further, primary resection was more frequent in the pre-group than in the pandemic group (98.7 vs. 87.8%; P=0.009), and the length of hospital stay tended to be longer in the pre-group than in the pandemic group (10 days (6-88) vs. 8 days [6-71]; P=0.054).

In terms of pathologic factors, the number of circumferential lesions was higher (42 cases [51.2%] vs. 17 cases [21.5%]; P<0.001) and colorectal stenting (13 cases [15.9%] vs. 3 cases [3.8%]; P=0.016) was more frequent in the pandemic group than in the pre-group. Trans-anal drainage tube placement was performed in only one case in the pandemic group. T4 cases tended to be more common (28 patients [34.1%] vs. 17 patients [21.5%]; P=0.082) and Stage IV cases were more frequent (23 patients [28%] vs. 10 patients [12.7%]; P=0.019) in the pandemic group than in the pre-group. No significant differences were found in lung metastasis and distant lymph node metastasis between the two groups. However, liver metastasis (P=0.098) and peritoneal dissemination (P=0.079) tended to be more frequent in the pandemic group than in the pre-group.

Discussion

The present study showed the spread of COVID-19 has increased the incidence of patients with advanced colorectal cancer, and the number of patients who could not undergo primary resection increased. There have been several studies on increased medical costs, lack of medical resources, and increased number of inpatients and deaths resulting from the SARS-CoV-2 infection (7). However, only some have described the impact of COVID-19 on the delayed detection of colorectal cancer (8). A reason for the delayed detection might be a decrease in the use of cancer screening tests, such as fecal occult blood tests and colonoscopy. During the pandemic, some individuals refrained from visiting the hospital even if they have had symptoms, such as bloody stool, persistent diarrhea, and abdominal pain. This study indicated that health professionals should inform the general public not only about the risk of COVID-19 but also about the increased incidence of advanced colorectal cancer after the pandemic.

The increase in the number of COVID-19 cases has resulted in physical and mental stress among healthcare workers and a consequent decrease in the number of available hospital beds. Moreover, the COVID-19 pandemic has affected the timely diagnosis and treatment of colorectal cancer. During the COVID-19 pandemic, a decrease in the number of patients undergoing medical examinations, endoscopy, and surgery has been reported (9).

Although there was no decline in the number of colorectal cancer surgery cases per year, differences were observed in patient characteristics before and after the COVID-19 pandemic. In the present study, there was a higher incidence of advanced colorectal cancer in the pandemic group than in the pre-group, as indicated by circumferential lesions requiring colorectal stent placement and the rate of Stage IV diagnoses. Consequently, the number of patients who underwent curative resection was lower in the pandemic group than in the pre-group. Simultaneously, there was an increase in the number of patients who did not undergo resection for primary tumors. Although the long-term outcomes in the two groups are unclear at present, the pandemic group is expected to be far worse than the pre-group. In this study, we compared patients from each data collection period. Despite the small number of

Table I. Results of univariate analysis of patient clinical and demographic variables.

Variables	Pre-group (n=79)	Pandemic-group (n=82)	P-value
Sex[a]			
Male	50 (63.3)	46 (56.1)	0.422
Female	29 (36.7)	36 (43.9)	
Age (years)[b]	72 (36-101)	73 (44-98)	0.91
Body mass index (kg/m^2)[b]	22.8 (14.1-33.3)	22.1 (14.0-41.2)	0.061
ASA-PS[a]			0.485
Class 1	4 (5.1)	2 (2.4)	
Class 2	58 (73.4)	66 (80.5)	
Class 3	17 (21.5)	14 (17.1)	
Serum albumin level (g/dl)[b]	3.7 (2.1-5.4)	3.5 (1.5-4.8)	0.03
Prognostic nutritional index[b]	44.7 (31.2-66.6)	42.7 (18.6-55.2)	0.033
Comorbidity[a]			
Total	53 (67.1)	71 (86.6)	0.005
Diabetes	26 (32.9)	12 (14.6)	0.009
Hypertension	38 (48.1)	35 (42.7)	0.529
Heart disease	17 (21.5)	28 (34.1)	0.082
Respiratory disease	10 (12.7)	17 (20.7)	0.208
Cerebrovascular disease	4 (5.1)	10 (12.2)	0.161
CEA (ng/ml)[b]	4.2 (0.5-105)	4.1 (0.6-7150)	0.871
CA19-9 (U/ml)[b]	4.9 (2.0-708)	8.3 (2.0-15200)	0.076
Lesion location[a]			1
Cecum	2 (2.5)	8 (9.8)	
Ascending colon	22 (27.8)	15 (18.3)	
Transverse colon	9 (11.4)	5 (6.1)	
Descending colon	5 (6.3)	3 (3.7)	
Sigmoid colon	18 (22.8)	16 (19.5)	
Rectosigmoid	13 (16.5)	14 (17.1)	
Upper rectum	7 (8.9)	10 (12.2)	
Lower rectum	2 (2.5)	11 (13.4)	
Circumferential lesion[a]	17 (21.5)	42 (51.2)	<0.001
Colorectal stent[a]	3 (3.8)	13 (15.9)	0.016
Trans-anal drainage tube[a]	0	1 (1.2)	1

[a]n (%); [b]median (range). ASA-PS, American Society of Anesthesiologists Physical Status Classification; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9.

patients, significant differences were observed in clinicopathologic features between the two groups. These results cannot be overlooked.

There are two possible reasons for the increase in the number of patients with advanced colorectal cancer after the COVID-19 pandemic. The first is a reduction in colorectal cancer screening. In several countries, colorectal cancer screening has been discontinued, resulting in a significant reduction in the detection rate of colorectal cancer of up to 86% (9). In the United States, the US Surgeon General advised hospitals to delay non-urgent procedures and suspend lower gastrointestinal endoscopy for colorectal cancer screening and surveillance, which effectively reduced the number of endoscopies by 92% (10). Although this may help prevent SARS-CoV-2 infections, it may lead to the delayed detection of colorectal cancer. In the current circumstances, lesions that can usually be diagnosed at an early stage might be diagnosed at a more advanced stage.

The second reason is avoiding hospital visits due to the fear of contracting COVID-19. In the pandemic group, a large number of patients delayed a hospital visit even after symptom onset. In fact, of the 13 patients who had undergone colorectal stent placement in the pandemic group, nine delayed making a medical appointment for more than a month to avoid the risk of SARS-CoV-2 infection. Nutritional status indicators, such as serum Alb level and PNI, were significantly lower in the pandemic group than in the pre-group, indicating that patients with more advanced colorectal cancer who visited our

Table II. Results of univariate analysis of patient clinicopathological variables.

Variables	Pre-group (n=79)	Pandemic-group (n=82)	P-value
Surgical approach[a]			<0.001
Laparotomy	5 (6.3)	13 (15.8)	
Laparoscopic surgery	70 (88.6)	44 (54.3)	
Robotic surgery	4 (5.1)	25 (30.9)	
Conversion to laparotomy[a]	0	1 (1.4)	0.486
Surgical procedures[a]			1
Ileocecal resection	18 (22.8)	16 (19.5)	
Right hemicolectomy	10 (12.7)	10 (12.2)	
Transverse colectomy	2 (2.5)	0	
Left hemicolectomy	2 (2.5)	2 (2.4)	
Descending colectomy	6 (7.6)	1 (1.2)	
Sigmoidectomy	14 (17.7)	15 (18.3)	
High anterior resection	14 (17.7)	9 (11)	
Low anterior resection	8 (10.1)	10 (12.2)	
Hartmann	2 (2.5)	3 (3.7)	
Abdominoperineal resection of the rectum	1 (1.3)	5 (6.1)	
Total pelvic exenteration	0	1 (1.2)	
Total colectomy	1 (1.3)	0	
Stoma	1	10 (12.2)	
Resection of the primary lesion[a]	78 (98.7)	72 (87.8)	0.009
Dissection[a]			0.737
D1	2 (2.5)	3 (4.2)	
D2	12 (15.2)	13 (18.1)	
D3	65 (82.3)	56 (77.8)	
Surgical curability[a]			0.036
R0	72 (91.1)	63 (76.8)	
R1	0	1 (1.2)	
R2	7 (8.9)	18 (22.0)	

[a]n (%).

department during the COVID-19 pandemic were suffering from undernutrition. Our results are consistent with those of previous studies (11-13).

These reasons were not specific to colorectal cancer. The results of the present study were similar to those of the studies reported on other cancers. For example, the decrease in screening and hospitalization has resulted in delayed diagnoses and an increased incidence of distant metastasis in gastric cancer (14,15). We hypothesize that it is important to balance the treatment and prevention of COVID-19 with sufficient cancer screening and treatment, regardless of the cancer type.

Contrary to our hypotheses there was no difference in the number of colorectal cancer surgery cases between the two groups. We hypothesize that this can be attributed to the fact that the patients could not visit other hospitals in the same area. Although our hospital could provide cancer care as usual due to the low number of patients with COVID-19, there were several public hospitals in the vicinity that were struggling to provide cancer care because of the burden of providing COVID-19 care. The number of colorectal cancer surgery cases did not exceptionally reduce in our hospital as we took on patients from such hospitals.

In the present study, the pandemic group had longer operation times. We inferred that this may be a direct result of the introduction of robotic rectal cancer surgery in 2020 and the increased use of robotic surgery in the pandemic group.

Although a higher number of laparotomy cases were observed in the pandemic group than in the pre-group, colostomy cases without primary resection were grouped under laparotomy. Of the 13 patients with laparotomy in the pandemic group, eight underwent colostomy without primary resection. With the exception of these eight cases, the pandemic group comprised five laparotomies (6.7%), 44 laparoscopies (59.4%), and 25 robotic-assisted surgeries (33.8%). The rate of laparotomy in the pandemic group was equivalent to 6.3% of that in the pre-group. Surgical smoke has been reported to contain viruses and carcinogens. Considering the risk of SARS-CoV-2 infection, Chadi *et al* (16) recommended the combined use of

Table III. Results of univariate analysis of patient clinicopathological variables.

Variables	Pre-group (n=79)	Pandemic-group (n=82)	P-value
Operation time (min)[a]	241 (109-776)	294.5 (43-1183)	0.083
Laparotomy	156 (109-341)	149 (43-605)	
Laparoscopic surgery	241 (130-532)	281 (138-490)	
Robotic surgery	549 (365-776)	382 (236-1183)	
Blood loss (ml)[a]	20 (0-994)	19 (0-2361)	0.588
Blood transfusion[b]	6 (7.6)	11 (13.4)	0.307
Postoperative hospital stay (day)[a]	10 (6-88)	8 (6-71)	0.054
Complication[b]	10 (12.7)	9 (11)	0.81
Pneumonia	1 (1.3)	0	0.491
Intestinal obstruction	4 (5.1)	2 (2.4)	0.437
Surgical site infection	2 (2.5)	2 (2.4)	1
Stage[b]			0.09
I	17 (21.5)	17 (20.7)	
II	29 (36.7)	26 (31.7)	
III	23 (29.1)	16 (19.5)	
IV	10 (12.7)	23 (28)	
Stage IV case[b]	10 (12.7)	23 (28)	0.019
Liver metastasis	5 (6.3)	13 (15.8)	0.098
Lung metastasis	4 (5.1)	9 (11.1)	0.247
Peritoneal dissemination	3 (3.8)	10 (12.3)	0.079
Distant lymph node metastasis	3 (3.9)	3 (3.7)	1
T factor[b]			0.359
T1	11 (14)	10 (12.2)	
T2	10 (12.7)	9 (11)	
T3	41 (51.9)	35 (42.7)	
T4	17 (21.5)	28 (34.1)	
T4 case[b]	17 (21.5)	28 (34.1)	0.082

[a]median (range); [b]n (%).

laparoscopic surgery and flue gas equipment. At our hospital, laparoscopic and robotic surgeries are the first treatment options for colorectal cancer. Surgeries are performed using Air Seal® while considering the risk of infection. Furthermore, the use of flue gas prolonged the operation time in the pandemic group.

This study has several limitations. First, this was a single-center study with a small study population. Results may vary between institutions and would be more conclusive if they are obtained from a larger dataset. Thus, a large-scale study involving multiple institutions is expected in the future. The second limitation is the short length of follow-up; we only investigated the short-term outcomes in this study. The long-term outcomes should be clarified in future studies.

Our findings indicate that the COVID-19 pandemic has led to an increase in the number of patients with advanced colorectal cancer. In such situations, especially in the gastroenterological field, the general public should be advised to prevent the further increase in the number of cases with more advanced colorectal cancer.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

JT and HK conceptualized and designed the present study, collected and interpreted data and drafted the manuscript. YS, AK and FS analyzed the data, generated figures and tables and drafted the manuscript. KY, DF conceived the study and revised the manuscript. FM and KT conceptualized and designed the present study, and confirm the authenticity of

all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

This study was approved by the Teikyo University Medical Research Ethics Committee (approval no. 20-049) and performed according to the Declaration of Helsinki (1996). Written informed consent was obtained from all individual participants included in the study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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