COVID-19 pandemic: Impacts on diagnosis and treatment of colorectal cancer

Le Trinh Ngoc An, Tran Duc Huy, Le Minh Triet, Pham Ngoc Truong Vinh, Ung Van Viet, Hoang Danh Tan, Nguyen Huu Thinh

University of Medicine and Pharmacy at HCMC

Corresponding author:
Tran Duc Huy
University of Medicine and Pharmacy at HCMC
217 Hong Bang, Ward 11, District 5, Ho Chi Minh City
Mobile: +84909873773
Email: huy.td@umc.edu.vn

Abstract

Introduction: Since its first strike in 2019, the highly contagious Sars-Cov-2 virus has not only directly caused millions of deaths in Vietnam but also indirectly affected many other diseases such as colorectal cancer. In order to clarify this statement, this study was conducted to investigate the difference in disease stage, curative rate of colorectal cancer before and after the Covid-19 outbreak.

Patients and Methods: A retrospective study was conducted at Univercity Medical Center, Ho Chi Minh city. Data on cancer stage, surgical methods, and rate of preoperative and postoperative complications were collected from patients treated at the hospital in two stages: group A including patients from February to April 2021 (before applying social distancing) and group B including patients from September to November 2011 (when applying social distancing).

Results: When comparing 201 patients in group A and 150 patients in group B, the results showed that the clinical characteristics of the two groups were identical. However, the percentage of cancer that had metastasized at the time of diagnosis was significantly higher in group B than in group A (32% vs 21.4%, p = 0.025), leading to a decrease of radical cure rate in group B (44.7% versus 69.1%, p < 0.001). Particularly for rectal cancer, the rate of advanced tumors (stage T3 CRM+ or T4) in group B was higher than in group A (77.2% vs 58.1%, p = 0.026).

Conclusion: In general, not only directly threatening peoples health, the Covid-19 pandemic also delayed the diagnosis of colorectal cancer due to the influence of distancing regulation and the patient's psychological fear, thereby affecting patients prognosis.

Keywords: Covid-19, Sars-Cov-2 virus, colorectal cancer, advanced stage cancer.

Introduction

The appearance of the Sars-Cov-2 virus in 2019 has become an unforgettable milestone for mankind. With its high contagiousness and rapid spread, the number of infections in December 2021 has reached 346 million worldwide and 2.11 million in Vietnam [1]. According to data from the World Health Organization, the virus has killed 36,000 people in Vietnam [1]. Facing that situation, in order to control the pandemic, a series of policies to limit the spread have been issued: countries close their borders, provinces are isolated from provinces, people are forced to stay at home. However, the above policies have inadvertently hindered people's access to medical care, causing delays in diagnosis and treatment of chronic diseases, cancer, etc. Colorectal cancer is not an exception. Despite having the best prognosis among digestive cancers and high treatability when diagnosed early, colorectal cancer has been indirectly and negatively affected by the Covid-19 pandemic situation in Vietnam.

Patients and methods

To clarify the above statement, we retrospectively reviewed colorectal cancer patients who came for examination and treatment at University Medical Center of Ho Chi Minh city during the pandemic period. The research subjects were newly diagnosed colorectal cancer patients, whom divided into 2 groups: group A included patients who were examined and treated from February to April 2021 (before social distancing), group B included patients who were examined and treated from September to November 2021 (after the end of social distancing). The study sample did not include patients who were still on treatment at the time of this study and patients with recurrent colorectal cancer.

Upon admission, patients laboratory tests were performed according to the hospital's diagnostic process, then multidisciplinary consultation meetings were done to assess the cancer staging and decide on the treatment plan.

All patient information was collected from the hospital's electronic medical record. In addition to the basic information of the patient such as age, sex, medical history, surgical history, etc., the information that was of interest to the research team to conduct a comparison between the two groups included: history of Covid-19 infection, characteristics of cancer such as stage of disease (TNM), hospitalization situation, symptoms onset, duration of symptoms, methods of treatment , complications before and after surgery. The collected data were processed using SPSS 25 software.

Results

Retrospectively, group A had 201 patients and group B had 150 patients who met the sampling criteria. The epidemiological characteristics of the two groups were quite similar with the average age of group A being 61.81 ± 14.23 and those of group B being 60.19 12.25, the male : female ratio was roughly 1 : 1. The distribution of cancer was also quite similar between the two groups, with the two most common cancer location were sigmoid colon and rectum (Figure 1).
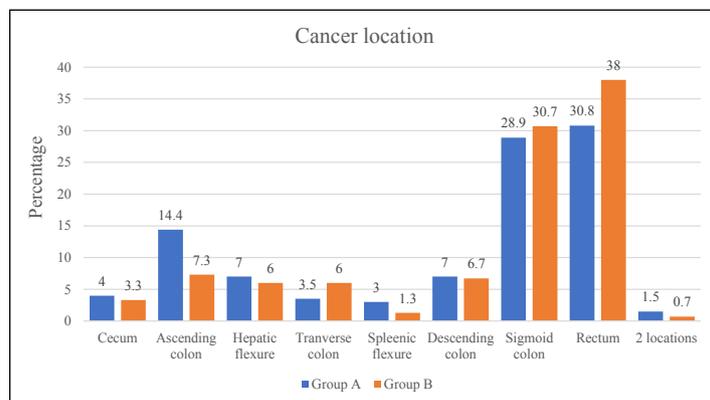

Figure 1. Colorectal cancer location distribution

Regarding hospital admission, about one-third of patients were admitted to the emergency department (33.3% in group A and 36.7% in group B). The mean duration of symptoms in group B was 9.65 weeks, longer than in group A (7.59 weeks), but this difference was not statistically significant. At the same time, the rate of cancer with preoperative complications was higher in group B than in group A (34% versus 26.4%). More specifically, the rates of two common complications of colorectal cancer, partial bowel obstruction and peritumoral abscess, were higher in group B than in group A (Table 1). Cancer stage was the key factor of interest in this study and is presented in Table 2.

Table 1. Colorectal cancer complications

Complications	Group A	Group B	p
None	73,5%	66%	0,121
Peritumoral abscess	1,5%	4,7%	0,077
Partial bowel obstruction	14,4%	21,3%	0,091
Complete bowel obstruction	6,5%	6%	0,858
Fistula	1,5%	0,7%	0,471
Perforation	2%	1,3%	0,639
Intussusception	1%	0%	0,509

Table 2. Colorectal cancer stages

TNM (AJCC 8th)		Group A (%)	Group B (%)
T stage	Tis	0,4	0
	T1	4,5	2,6
	T2	1	4
	T3	29,9	23,4
	T4a	40,3	49,3
	T4b	23,9	20,7
N stage	N0	39,3	37,3
	N1	20,9	14,7
	N2	39,8	48
M stage	M0	78,6	68
	M1	21,4	32

The results showed that the majority of patients were diagnosed when the tumor was locally advanced (T3 or higher). Using the Pearson Chi-square test, the rate of locally advanced cancer and the rate of lymph node metastasis were not statistically significant between the two groups. However, patients in group B had more distant metastases than patients in group A (32% vs 21.4%, p = 0.025), even if small nodules in the liver or lung with diameter smaller than 10 mm were considered to be M0. Regarding treatment, statistics from the study sample showed that the rate of radical surgery in group B (44.7%) was lower than in group A (69.1%) with statistical significance (p<0.001). Other factors related to treatment such as the rate of colostomy, hospital length of stay, postoperative length of stay were not statistically different between the two groups (Table 3).

Table 3. Colostomy rate, mean hospital length of stay, mean postoperative length of stay

	Group A	Group B	p
Colostomy rate	20,4%	24,7%	0,387
Mean hospital length of stay	9,75	10,23	0,358
Mean postoperative length of stay	6,8	7,08	0,353

In the study sample, 6 cases in group A had complications after surgery, including 1 case of partial bowel obstruction due to adhesions, 4 cases of incisional infection and 1 case of anastomosis leak, whom underwent second surgery. In group B, there was 1 case of anastomosis bleeding. In this case, hemostasis was achieved through endoscopic clipping.

When further analyze the rectal cancer subgroup, there was a difference in tumor stage between the two groups. The proportion of patients with locally advanced tumors (T3 CRM + or higher) in group B was statistically significantly higher than in group A (table 4). In addition, although the rates of lymph node and distant metastasis were also higher in group B than in group A, the comparison test of the two rates did not show a statistically difference (table

4). In terms of treatment, similar to the survey on the whole study sample, the rate of radical surgery in group B (40.4%) was lower than in group A (56.5%), with an odds ratio OR = 1,916. In addition, corresponding to more locally advanced rectal cancer in group B than in group A, the proportion of patients requiring neo-adjuvant treatment in group B was higher than group A (32.6% versus 21.6%)), however, the chi-squared test did not show that this difference was statistically significant.

Table 4. Rectal cancer stages

Stage	Group A (n = 62)	Group B (n = 57)	p
T stage			
Locally advanced (T3 CRM+)	58,1%	77,2%	0,026
N stage			
N +	64,5%	77,2%	0,129
M stage			
M1	17,7%	24,6%	0,362

Discussion

The impact of the Covid-19 pandemic on colorectal cancer has been mentioned a lot in studies around the world. These impacts come from indirect ways through disease prevention policies, changes in health care policies rather than direct effects of Sars-Cov-2 virus on the pathogenesis of colorectal cancer. Indeed, so far there have been no reports on the change of colorectal cancer clinical characteristics or postoperative complications related to the Covid-19 pandemic. Even with the Covid vaccine, despite the reported risk of thrombosis after vaccination [2], there is no evidence to date that the Covid vaccine is related to the course or outcome of colorectal cancer treatment. Therefore, our study also does not focus on this area.

Instead, when looking back at the changes in society and health policy, it is possible to see why the pandemic has negatively affected colorectal cancer. With a strong ability to spread along with a high proportion of patients requiring respiratory support

and intensive care, the burden of the pandemic on the public health system requires a structural redistribution of the industry. A series of specialized care facilities for infected people were established and hospitals were converted, leading to a decrease in resources for treating other diseases in general and colorectal cancer in particular. In addition, the policies of social distancing and isolation of Fx subjects further hinder access to medical services which are already very limited. Therefore, it is not surprising that cancer screening has dropped dramatically. Figures from the NHS (National health service) in the UK show that as of April 2021, the number of colonoscopy cases is 92% lower than the average number per month in 2019 [3]. Similarly, a meta-analysis reported reported that the average decline in colonoscopy from 55 countries was 85% [4]. This leads to a decrease in the number of new cases diagnosed each year. A systematic analysis of 43 studies showed a reduction in the number of newly diagnosed cases in the UK from 43.1 to 62%5-7, in Italy from 11.9 to 46.6%8.9 and in Hong Kong Kong is 37% [10].

From the above data, the inevitable consequence is missed diagnosis and delay in diagnosis. The Morris study in the UK estimated there were 3500 missed cases of colorectal cancer between April and October 20203. Also in the UK, studies showed an increase in late diagnosis rates. In addition, the circumstances of admission and the stage of the disease at the time of diagnosis also vary. Results from studies in multiple countries have shown an increase in emergency hospital admissions (Table 5) and hospitalizations for colonic obstruction. However, through our study, there was no difference in the rate of emergency hospital admission before and after applying social distancing. The reason is probably because the cancer screening program in Vietnam is still limited, leading to a high rate of colorectal cancer patients hospitalized in emergency situations and less affected by social distancing measures. Regarding the stage of cancer, patients in group B in our study come to the doctor when the

disease is also more advanced. More specifically, there was an increase in the rate of distant metastases after the introduction of social distancing. When compared with the study results of the authors in the UK, an increase in the rate of stage T4 tumors in 2020 compared to 2018 - 2019 (34.5% vs 27.1%, p = 0,03) [11], the difference in results shows the heavy impact of the Covid-19 pandemic on the colorectal cancer situation in Vietnam. In Western countries, the Covid pandemic only increased the invasiveness of the tumor. According to Suárez's study, it is estimated that 3 months late diagnosis and the change from stage I to stage II will cause 88 more deaths per month, 6 months late diagnosis and treatment will cause 349 more deaths each month with a 29% decrease in survival rate [12]. In our country, while the majority of colorectal cancer patients are diagnosed at an advanced stage (stage III), the discharge of Sars-Cov-2 virus has increased the rate of stage IV cancer, taking away the opportunity for radical treatment and affecting the patient's survival prognosis.

Table 5. Emergency admission rate

Studies	Emergency admission rate		p
	Before pandemic	After pandemic	
Spain[12]	3,6%	12,1%	0,048
UK[11]	28,6%	36%	0,03
Japan[13]	18,2%	38,7%	< 0,05

As for rectal cancer, our study showed an increase in the local progression of the tumor, leading to an increase in the number of patients requiring neoadjuvant treatment. However, perhaps because the sample size was not large enough, the difference in the rate of neo-adjuvant treatment before and after the pandemic was not statistically significant. First of all, the need for neo-adjuvant treatment increases the patient's treatment costs and places an additional burden on the health insurance budget that has been severely damaged due to the cost of Covid treatment. Not only that, the change of rectal tumor

stage also affects the patient's prognosis because the local invasion of the rectal tumor is an important prognostic factor of local recurrence and disease-free survival time. Thus, in the long run, the patient will have to face the risk of re-surgery, the risk of permanent colostomy, the risk of intraoperative and postoperative complications as well as the cost of neo-adjuvant treatment.

Conclusion

With its worldwide influence, the Covid-19 pandemic has negatively impacted humanity in many ways. Although there is no evidence to show a direct link between Sars-Cov-2 and the progression of colorectal cancer, pandemic prevention and control policies in critical times have severely affected the population whom inflicted with this malignancy. Delays in diagnosis and treatment, on the one hand worsened the patient's prognosis, and on the other hand increased the treatment costs for patients and society as a whole. Fortunately, so far, the pandemic situation has been controlled when herd immunity is achieved, access to health services and cancer screening programs have gradually returned to normal. It is interesting to learn from the recent global pandemic and to prepare a more appropriate plan when responding to contangious diseases that may appear in the future.

References

1. WHO Coronavirus (COVID-19) Dashboard. https://covid19.who.int

2. Bilotta C, Perrone G, Adelfio V, et al. COVID-19 Vaccine-Related Thrombosis: A Systematic Review and Exploratory Analysis. Front Immunol. 2021;12:729251. doi:10.3389/fimmu.2021.729251

3. Morris EJA, Goldacre R, Spata E, et al. Impact of the COVID-19 pandemic on the detection and management of colorectal cancer in England: a population-based study. Lancet Gastroenterol Hepatol. Mar 2021;6(3):199-208. doi:10.1016/s2468-1253(21)00005-4

4. Mazidimoradi A, Hadavandsiri F, Momenimovahed

Z, Salehiniya H. Impact of the COVID-19 Pandemic on Colorectal Cancer Diagnosis and Treatment: a Systematic Review. Journal of Gastrointestinal Cancer. 2021/11/29 2021;doi:10.1007/s12029-021-00752-5

5. Abdellatif M, Salama Y, Alhammali T, Eltweri AM. Impact of COVID-19 on colorectal cancer early diagnosis pathway: retrospective cohort study. British Journal of Surgery. 2021;108(4):e146-e147. doi:10.1093/bjs/znaa122

6. De Vincentiis L, Carr RA, Mariani MP, Ferrara G. Cancer diagnostic rates during the 2020 'lockdown', due to COVID-19 pandemic, compared with the 2018-2019: an audit study from cellular pathology. J Clin Pathol. Mar 2021;74(3):187-189. doi:10.1136/jclinpath-2020-206833

7. London JW, Fazio-Eynullayeva E, Palchuk MB, Sankey P, McNair C. Effects of the COVID-19 Pandemic on Cancer-Related Patient Encounters. JCO Clin Cancer Inform. Jul 2020;4:657-665. doi:10.1200/cci.20.00068

8. Brito M, Laranjo A, Sabino J, Oliveira C, Mocanu I, Fonseca J. Digestive Oncology in the COVID-19 Pandemic Era. GE Port J Gastroenterol. Mar 22 2021;579(5):1-8. doi:10.1159/000514784

9. Ferrara G, De Vincentiis L, Ambrosini-Spaltro A, et al. Cancer Diagnostic Delay in Northern and Central Italy During the 2020 Lockdown Due to the Coronavirus Disease 2019 Pandemic. Am J Clin Pathol. Jan 4 2021;155(1):64-68. doi:10.1093/ajcp/aqaa177

10. Lui TKL, Leung K, Guo CG, Tsui VWM, Wu JT, Leung WK. Impacts of the Coronavirus 2019 Pandemic on Gastrointestinal Endoscopy Volume and Diagnosis of Gastric and Colorectal Cancers: A Population-Based Study. Gastroenterology. Sep 2020;159(3):1164-1166. e3. doi:10.1053/j.gastro.2020.05.037

11. Shinkwin M, Silva L, Vogel I, et al. COVID-19 and the emergency presentation of colorectal cancer. Colorectal Dis. Aug 2021;23(8):2014-2019. doi:10.1111/codi.15662

12. Suárez J, Mata E, Guerra A, et al. Impact of the COVID-19 pandemic during Spain's state of emergency on the diagnosis of colorectal cancer. J Surg Oncol. Jan 2021;123(1):32-36. doi:10.1002/jso.26263

13. Mizuno R, Ganeko R, Takeuchi G, et al. The number of obstructive colorectal cancers in Japan has increased during the COVID-19 pandemic: A retrospective single-center cohort study. Ann Med Surg (Lond). Dec 2020;60:675-679. doi:10.1016/j.amsu.2020.11.087