Management of Colorectal Cancer Patients During The COVID-19 Pandemic: Triage and Treatment

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Abstract

Background

The outbreak of coronavirus disease-2019(COVID-19)cause significant difficulties to the treatment of oncological patients, including colorectal cancer(CRC) patients. Establishing new manage strategies and emergency triage system is urgent.

Methods

We collected the outpatients, inpatients and surgeries number and COVID-19 nucleic acid test results of Shanghai East Hospital from December 2019 to January 2020, and the changes during this period were analyzed.

Result

The number of outpatients, inpatients and surgeries all decreased significantly. Not a single case of COVID-19 infection occurred in Shanghai East Hospital in this period. The triage system and management strategy are shared here.

Conclusion

Our triage strategy can help reduce the infection rate of COVID-19 in hospital, and the management strategies of CRC can be used as a reference for clinicians.

Background

At present, colorectal cancer (CRC) is the second most common cancer in women and the third most common in men, accounting for approximately 10% of new malignant tumors and cancer-related deaths globally^[1]. The United States estimates over 140000 new CRC diagnoses in 2020, and more than 50000 deaths attributable to CRC. More than 2.2 million new cases and nearly 1.1 million colon cancer-related deaths are expected worldwide by 2030^[2,3]. Patients with oncologic conditions are frequently among the most vulnerable patient populations because of their heightened risk for opportunistic and other infections or medical complications. Active preparation of efficient and safe healthcare delivery for such patients is critical during the ongoing pandemic. Some experts suggest that during the COVID-19 pandemic, the chemotherapy regimen of oncological patients should be adjusted to avoid excessive immunosuppression ^[4].

In March 2020, the Ministry of Health in China issued COVID-19 pilot diagnosis and treatment guidelines, the “COVID-19 diagnosis and treatment Program (7th Edition)”^[5]. The guide provided information about

COVID-19 pathology and updated clinical manifestations, diagnostic criteria, treatment methods, and discharge criteria according to the clinical cases, compared to the 1st Edition issued in February 2020. Because this is a national level guide line, almost all clinical institutions in China localized and adopted these guidelines. Such institutions provide routine and ongoing patient care, including oncological patients' surgery and chemotherapy. This paper aims to share the experience and insights learned from one academic medical center during COVID-19 pandemic from China, including the hospital triage system, the treatment strategy of CRC, the important role of telemedicine in follow-up care and clinical consultation. This case may offer strategies for healthcare organizations to plan and deliver patient care during the COVID-19 pandemic.

Brief Introduction Of Covid-19

COVID-19 first appeared in December 2019, and was caused by a type of novel coronavirus, then labelled as "2019-new coronavirus (2019-nCoV)", and the disease named "coronavirus disease-2019(COVID-2019)by WHO^[6]. Later, the International Committee on Taxonomy of Viruses named 2019-nCoV "Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)^[7]. SARS-CoV-2 is mainly transmitted through droplets or direct contact among humans and people are generally susceptible to it, after infection, there is an 2–14 days incubation period after infection, on average 5 days^[8]. The basic reproductive rates (BCR) are 2.24–3.58^[9], and 2-6.47 in another report^[10], and during this incubation period the infected patient is also contagious^[9].

Fever is the primary manifestation after infection in most cases, but the initial clinical symptoms may also include cough, dyspnea, myalgia and fatigue, cephalgia or diarrhea, sore throat, rhinitis and, in some patients, prominent anosmia and dysgeusia^[11–14]. Patients with underlying conditions, such as cardiovascular disease, hypertension, obesity and diabetes mellitus, were recognized as individuals at high-risk for severe COVID-19.^[11, 15] Patients with severe COVID-19 routinely developed dyspnea^[12, 13]. Those who rapidly developed acute respiratory distress syndrome (ARDS) also clinically declined quickly, resulting in often fatal multi-organ failure.^[13] COVID-19 infection and mortality rates vary globally due to multifactorial reasons.

Methods

From December 2019 to February 2020, all patients who come to Shanghai East Hospital (without distinguishing between oncological patients and non-oncological patients) strictly follow the triage system established by the hospital. And be supervised and guided by professional nurses. We counted the number of all inpatients in the hospital during this period, as well as the surgeries. Separate statistics were collected on oncology department and gastrointestinal & Colorectal department. All in-patients are required to complete nucleic acid tests and the test result must be negative before being approved for hospitalization. Since February 2020, all healthcare workers undergo nucleic acid tests twice a month. Combined with the pre-COVID-19 guidelines for management of colorectal cancer, we have developed a

new management strategy that meets the conditions of the COVID-19 pandemic. All the statistics are displayed in the following table.

Table 1
Shanghai East Hospital, Tongji University School of Medicine: Overview of the overall out- and inpatient numbers, and surgeries numbers at the beginning of the COVID-19 pandemic.

Shanghai East Hospital		2020.02	2020.01	2019.12
Patients Number	Out-patient	42956	106385	119625
	In-patient	789	2977	3536
Surgeries	Non-emergency	196	856	1373
	emergency	32	74	92

Table 2
Department of Gastrointestinal & Colorectal Surgery: Overview of the overall out- and inpatient numbers, and surgeries numbers at the beginning of the COVID-19 pandemic.

Department of Gastrointestinal & Colorectal Surgery		2020.02	2020.01	2019.12
Patients Number	Out-patient	120	2228	2789
	In-patient	50	85	207
Surgeries	Non-emergency	23	63	133
	emergency	18	8	15

Table 3
Department of Oncology: Overview of the overall out- and inpatient numbers at the beginning of the COVID-19 pandemic.

Department of Oncology		2020.02	2020.01	2019.12
Patients Number	Out-patient	220	939	1323
	In-patient	25	104	118

Table 4
COVID-19 nucleic acid test: Overview of the inpatient numbers, colorectal cancer patient numbers and the nucleic acid test in February 2020.

COVID-19 nucleic acid test	Total	Positive	Negative	%Positive (infection rate)
In-Patients Number	789	0	789	0.00
Colorectal Cancer patients Number	50	0	50	0.00
Healthcare workers Number	3100	0	3100	0.00

Result

Compared with the situation before the outbreak, the number of outpatients, inpatients and surgeries all decreased significantly. The same change also can be seen in the department of Oncology and Gastrointestinal & Colorectal Surgery. At the beginning of the pandemic, not a single case of COVID-19 infection occurred among all inpatients and all health care workers.

The triage system and management strategies our institution established as follow.

1. Triage system for patients during COVID-19

To carry out medical work more safely and efficiently, a triage system was established (Fig. 1) by epidemiologists, respiratory experts and hospital managers at Shanghai East Hospital, a large general hospital affiliated to Tongji University with more than 1800 inpatient beds, located in Lujiazui, Shanghai, China. Experts combined clinical experience, mandated control measures of the government, and similar control measures was adopted in other hospitals around the country. Between January 2020 and January 2021, no cases of COVID-19 have been identified in Shanghai East Hospital.

This triage system applied to all clinical care. At an individual level, a limited number of persons, no visitors, and only one accompanying person was allowed with the patient. Each incoming patient including accompanying person was required to wear mask and underwent screening at the external hospital gate by checking temperature and scanning their national electronic permit QR code.

The national electronic permit QR code is designed by government, containing the necessary personal basic information like gender, age, address, as well as the health status voluntarily reported by the public on a daily basis. These data are associated with authoritative data from local Ministry of Health, including whether there are new and suspected cases in the area and any confirmed cases have arrived here within 14 days. Finally, all the data will go through comprehensive judgment to assess whether you may have been in contact with confirmed and suspected cases, and then a QR code will be created with color codes as a "risk hint". Red represents positive risk, or the individual has suspected/confirmed COVID-19, or had contact with a suspected/confirmed case within 14 days. Green represents no risk, or there are no symptoms potentially consistent with COVID-19 and no contact with a suspected/confirmed case within 14 days. A confirmed case is defined as an individual with a positive SARS-CoV-2 nucleic acid. A suspected case is defined as an individual who had contact with a confirmed case in 14 days or has symptoms potentially consistent with COVID-19 or with a positive SARS-CoV-2 antibody but has not been confirmed by nucleic acid detection.

After initial screening, only the green QR code can enter the hospital, and the red will be advised to be isolated alone, if further SARS-CoV-2 nucleic acid test is positive, the patient will be escorted to a specific infectious disease hospital that specializes in treating COVID-19 patients. Upon entering the hospital, each patient underwent a comprehensive anamnestic interview with a practicing nurse on a designated floor, then separated from further departments. In-depth epidemiological history and clinical

manifestations were documented to exclude suspected cases, according to the official guiding classifications^[16] (Fig. 2).

If patients had unremarkable interviews with the nurse, they proceeded with their physician consultation appointment. However, patients with any remarkable items on their anamnestic interview (1 of the items of epidemiological history and any 2 clinical manifestations or no epidemiology history, but 3 clinical manifestations) were triaged for further etiological testing, including RT-PCR detection of SARS-CoV-2 nucleic acid, virus gene sequencing and antibody detection (Fig. 1).

For suspected cases presenting as acute emergency, like intestinal obstruction or intestinal perforation, the patient's condition was carefully evaluated and an immediate surgical treatment arranged in designated centers. In the whole process of triage system, clinical staff were with secondary personal protective equipment (PPE) (Table 5), which can effectively reduce the probability of body fluids and droplets contacting with the eyes and respiratory mucosa of clinical staff during examination, compared to the primary PPE.

Table 5

PPE is equipment include items such as safety helmets, gloves, eye protection, high-visibility clothing, safety footwear. It also includes respiratory protective equipment (RPE).

Primary PPE	Secondary PPE	Tertiary PPE
Overalls, isolation clothes, disposable hats and surgical mask, latex gloves.		
	overalls, isolation clothes, disposable hat, medical protective mask (N95 or above), latex gloves, goggles or protective mask, disposable shoe covers.	
		on the basis of secondary protection, add full facepiece mask and respiratory equipment

2. Management strategies of patients with CRC in our institution during COVID-19 pandemic

a) Evaluation

Prior to COVID-19, all CRC patients requiring surgery underwent a routine preoperative examination to evaluate their cardiopulmonary function and general physical condition. During the COVID-19 pandemic, examinations such as colonoscopy, biopsies, and radiological imaging (abdominal and pelvic CT/MRI, PET-CT) were limited as diagnostic/ evaluation tools and no longer used for CRC screening. If COVID-19 was neither suspected nor confirmed, then the preoperative evaluation (including circulatory system

function examination, respiratory system function examination, blood coagulation function test, etc.) remained unchanged. However, if COVID-19 was suspected, preoperative preparation was modified to include also a pulmonary spiral CT examination and SARS-CoV-2 test (nucleic acid and antibody detection). Invasive examinations like digital rectal examination, colonoscopy, and biopsies were carried out in a specific isolation room by clinical staff using tertiary PPE, and all the examinations were carried out under the guidance of an infectious disease specialist. Such supplemental protective measures were adopted because of previously published data about MERS that the virus can be transmitted by fecal-oral route^[17]. SARS-CoV-2 nucleic acid has also been detected in the feces of confirmed COVID-19 cases^[18, 19].

Multidisciplinary therapy meetings (MDT), already an essential component of routine oncological patient care, were maintained and even strengthened during COVID-19. MDT consists of discussing risks and benefits of various therapeutic options for an individual patient, drawing from the expertise of a variety of healthcare professionals, including, for example, department representatives from multiple specialties and disciplines such as general surgery, oncology, radiology, and radiotherapy. During the COVID-19 pandemic, MDT also involved specialists in respiratory medicine, epidemiology, and infectious disease. They provided expertise on patient risks in case of SARS-CoV-2 infection (e.g. lung reserve, preexisting organ damage).

b) Treatment and Management

The Department of Gastrointestinal & Colorectal Surgery at Shanghai East Hospital had previously established an evidence-based treatment strategy for patients with CRC prior to the COVID-19 pandemic. Because the pandemic introduced additional potential risks for patients undergoing treatment, modified treatment strategies were considered in addition to standard care. Here, an overview is provided to highlight these treatment modifications for patients with CRC during COVID-19.

1. Neoadjuvant therapy (NAT)

On the background of COVID-19, it was important to consider applying NAC to CRC patients during the pandemic and not withhold this crucial therapeutic step, despite potentially increasing their infection risk. At present, the preoperative treatment for colon cancer is primarily neoadjuvant chemotherapy (NAC). NAC can eradicate occult micro-metastatic disease at an earlier time, improve tolerability and dose intensity to the chemotherapy drug, and assess the response to chemotherapy to guide adjuvant considerations. Preoperative chemical tumor reduction may lower the frequency of tumor cell shedding during surgery and increase R0 resection rates. NAC can also improve postoperative recovery by minimizing the extent of surgery. Previous studies have shown that NAC is safe and effective for some cT4 patients, and can improve the survival rate of patients^[20–23]. The National Comprehensive Cancer Network (NCCN) guidelines also emphasize NAC with folinic-acid, fluorouracil and oxaliplatin (FOLFOX) or capecitabine and oxaliplatin (CAPEOX) as a potential treatment for resectable cT4b colon cancer. And an American national cancer database analysis also suggested that the neoadjuvant radiotherapy (NAR)

could be considered as an alternative in locally advanced, cT4 colon cancer. But it should be considered on a case-by-case basis^[23]. Those who could receive the therapy in outpatient setting were preferred if they had no further major comorbidities, a Karnofsky score of 0 or 1 and younger than 65 years of age.

The application of radiotherapy in rectal cancer is more beneficial than in colon cancer. A large number of existing studies have shown that preoperative neoadjuvant chemoradiotherapy (NCR) for cT3-4 rectal cancer has significant benefits in reducing the local recurrence rate comparing to postoperative chemoradiotherapy, despite no significant difference in overall survival^[24–29]. Additionally, preoperative neoadjuvant chemoradiotherapy can reduce tumor size, increase the tumor resection rate and anus retention rate with very slight side effect^[30]. Both NCCN guidelines and European Society of Medical Oncology (ESMO) guidelines regard preoperative simultaneous radiotherapy and chemotherapy + TME surgery + adjuvant chemotherapy as the preferred treatment strategy for locally advanced cT3-4 rectal cancer. Therefore, in our department, we recommend that NAT should be applied in patients with locally advanced colon cancer in stage cT4 and rectal cancer in stage cT3-4 without significant risk of bleeding, obstruction and perforation. At present, clinical trials have proved that both FOLFOX regimen and CapeOX regimen have good efficacy in the treatment of locally advanced colon cancer^[22, 31]. And NCR can improve local control, anus retention rate and is associated with reduced toxicity compared to the postoperative chemoradiotherapy, despite the similar overall survival^[24–29].

During the COVID-19 pandemic, the CapeOX regimen was considered to be more suitable because of its convenience, as the patients spend less overall time in the healthcare institutional setting compared to the FOLFOX regimen and therefore potentially less exposure risk to COVID-19^[32]. We followed the current NCCN guidelines, in which it is permitted that the advanced rectal cancer is treated with radiotherapy, combined with oral capecitabine NAT, and whether surgical treatment should follow is to be evaluated 8 weeks later^[33]. For patients with primary liver metastasis of CRC, NAC can be considered first, after evaluation of patients' condition, resection of the primary focus combined with metastatic focus can be performed. When the metastatic focus cannot be removed, NAC combined with targeted drug therapy can be considered^[33]. We did not consider such option during the COVID-19 pandemics, since all surgical indications should be strictly controlled, and patients who meet the indications of NAT should choose selective surgery after NAT to reduce the risk of hospital related infection.

2. Endoscopic therapy

Endoscopic treatment is the first choice for early CRC patients (cT1N0M0) with a maximum diameter of the tumor is < 3 cm. After endoscopic resection, pathological examination must be performed, and the necessity for additional surgical treatment should be evaluated according to the pathological result.

For patients with CRC complicated with obstruction, an emergency surgery rarely achieves a R0 resection. Moreover, intestinal wall edema and poor intestinal preparation increases the difficulty of operation, so endoscopic stent implantation was considered. There is no significant difference in 3-year disease-free survival rate and overall survival rate between endoscopic stent implantation and emergency surgery,

even though it has a higher recurrence rate^[34]. It has been reported that emergency colonic stent implantation has shorter operation time, hospital stay and lower infection rate than emergency operation^[35]. As a bridge to surgery, stent implantation achieve the effect of decompression for emergency colon cancer patients with obstruction, thus improve anastomosis rate, avoid neostomy, reduce short-term complications, and improve the long-term survival^[36, 37]. Colonic stent implantation followed by surgery or NAC has been proved to be safe and effective^[38, 39]. Preoperative comorbidity is associated with poor prognosis in postoperative cancer patients^[40] and considering the impact of COVID-19 on the function of lung, heart, liver, kidney and gastrointestinal^[41–43], colonic stent implantation is a relatively safe and effective choice for these emergency patients, especially for the confirmed and suspected cases of COVID-19.

3. Surgical treatment

Stage cT2-3 colon cancer and stage cT2 rectal cancer are indications for radical surgery. If COVID-19 is excluded, then the operation could be carried out in accordance with Chinese Society of Clinical Oncology (CSCO), NCCN or ESMO guideline. During the COVID-19 pandemic, our modified treatment recommend that extended lymph node dissection and complex digestive tract reconstruction should be avoided as much as possible, and new surgical methods and relevant clinical trials should be delayed^[44]. The purpose is to shorten the length of stay and reduce possible complications (fever, anastomotic leakage, abdominal infection, etc.).

CRC patients accompanied bleeding, perforation or obstruction, emergency surgery should be carried out in time. Then the operation is performed in a negative pressure room which is optimal protection to surgeon^[45]. Repeatedly emphasized, the surgeons and anesthesiologists must be in tertiary PPE. For patients with ultra-low rectal cancer, ileostomy is an effective measure to reduce the possibility of postoperative anastomotic leakage, which can lead to pelvic infection, fever.

4. Postoperative management

Patients with negative testing for COVID-19 during preoperative evaluation received usual postoperative management, including short-term observation in the postoperative ward, nutritional support, and vital sign monitoring. In addition to usual management, during the COVID-19 pandemic, postoperative monitoring also included more frequent body temperature checks and respiratory symptom monitoring. If a temperature greater than 37.3°C occurred, clinical staff would check the patient's respiratory symptoms while wearing secondary PPE, recheck the patient's blood indicators, including blood cell analysis, inflammation indicators, urinalysis, chest x-ray and arterial oxygen saturation. If physical examination and these tests did not rule out pneumonia or other typical postoperative etiologies of fever, chest CT examination was pursued. Furthermore, if fever and respiratory symptoms are present together, then protocols for COVID-19 suspected cases were applied. These include a single isolation room, frequent body temperature monitoring and oxygen inhalation. Once SARS-CoV-2 nucleic acid test is confirmed (within several hours), the patient is then transferred to another special designed infectious hospital

designed for collecting all the COVID-19 patients, meanwhile postoperative management is carried out in there. Visitors were not permitted during the postoperative period during the COVID-19 pandemic.

5. Application of Telemedicine in Shanghai East Hospital during the COVID-19 pandemic

The outbreak of COVID-19 caused great pressure on the traditional medical system. Thus, remote work for healthcare professionals become much more important and frequent. For example, nutrition education and stoma management for almost all CRC patients after operation have been transferred to an online form. During the COVID-19 pandemic, doctors at Shanghai East Hospital adjusted the time spent on patient care using telemedicine. After the outbreak, oncologists spend 4 hours per week on teleconsultation (2 hours before the outbreak) and gastrointestinal & colorectal surgeons spend five hours per week (2 hours before the outbreak). Another important task of telemedicine is tele-training. After the outbreak, oncologists take 1 hour per week to complete this task (0.5 hours before the outbreak) and gastrointestinal & colorectal surgeons spend 2 hours per week (0.5 hours before the outbreak). The time adjustment of telemedicine is not limited to oncology and gastrointestinal surgery, other departments have also made appropriate adjustments according to the needs.

We obtained the relevant data of outpatients, inpatients and operations in Shanghai East Hospital at the beginning of the COVID-19 pandemic (Table 2). These results show that after the outbreak, the number of outpatients, inpatients and surgical patients decreased significantly. It means that a considerable number of patients did not get medical assistance in time, so in order to provide more medical support for patients, telemedicine played an important role. Meanwhile telemedicine has the advantage of reducing medical costs and increasing the availability of medical resources^[46], thus is widely used for patients who need continuous treatment, such as diabetes and oncologic diseases^[46–49]. It can be believed that during the COVID-19, the role of telemedicine will become more and more prominent.

Discussion

The present case study suggests that such healthcare delivery modifications can help to resume oncologic care effectively during the COVID-19 pandemic. COVID-19 triage protocols, treatment modifications for patients with CRC at high risk for COVID-19 related complications, and use of telemedicine to continue providing care were key strategies in this case study for continuing care. Ensuring timely and effective healthcare delivery during the COVID-19 pandemic, especially for medically at-risk populations like patients with CRC, has been challenging for many health systems. To address these concerns, Shanghai East Hospital developed and adopted a triage system to continue providing care to patients with CRC. Modifications to care included in-person care with protocols to mitigate COVID-19 spread or remote care using telemedicine.

Limitations of this report include generalizability, given that the case study provides the experience and data from only one region or hospital. Unique hospital and health system factors may reduce

reproducibility. Adaptation and adoption of similar triage measures in other hospital systems may offer additional support to the effectiveness of Shanghai East Hospital's approach. Further longitudinal evaluation of clinical and health system outcomes as a result of healthcare delivery modifications during the pandemic would be valuable.

Conclusions

Cancer patients are more vulnerable to COVID-19 due to immunosuppression caused by chemotherapy [50, 51]. The fact that no cases of infection in our hospital in the early stage of the pandemic also shows that our triage strategy is effective. The coexistence of COVID-19 and cancer may increase the complexity of treatment and care management. Drawing from Chinese guidance on pandemic prevention and control, as well as CSCO, NCCN and ESMO guidelines, neoadjuvant radiotherapy and chemotherapy, endoscopic treatment, and surgical treatment could still continue for patients with CRC during the pandemic at our institution. Managing oncological patients during the pandemic nevertheless remains challenging, although seems more manageable with multidisciplinary, protocolized approaches that also integrate new technologies like telemedicine into healthcare delivery. Lessons learned from the Shanghai East Hospital experience may be informative for cancer care teams elsewhere.

List Of Abbreviations

Colorectal Cancer (CRC)

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)

Basic reproductive rates (BCR)

Respiratory distress syndrome (ARDS)

personal protective equipment (PPE)

Multidisciplinary therapy meetings (MDT)

Neoadjuvant therapy (NAT)

Neoadjuvant chemotherapy (NAC)

National Comprehensive Cancer Network (NCCN)

Folinic-acid, fluorouracil and oxaliplatin (FOLFOX)

Capecitabine and oxaliplatin (CAPEOX)

Neoadjuvant radiotherapy (NAR)

Neoadjuvant chemoradiotherapy (NCR)

European Society of Medical Oncology (ESMO)

Chinese Society of Clinical Oncology (CSCO)

Declarations

Ethics approval and consent to participate: The study was conducted according to the guidelines of the Declaration of China, and approved by the Institutional Review Board of Shanghai East Hospital

Consent for publication: Not applicable

Availability of data and materials: The datasets generated and analysed during the current study are not publicly available due these are the internal data information of Shanghai East Hospital but are available from the corresponding author on reasonable request.

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Figures

Figure 1

A flow chart of a patient from admission screening to treatment.

Figure 2

the in-depth epidemiological history and clinical manifestations