How should colorectal surgeons practice during the COVID-19 epidemic? A retrospective single-center analysis based on real-world data from China

Colorectal surgery in COVID-19 epidemic

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Abstract

Background: The coronavirus disease 2019 is currently of global concern. Cancer patients are advised to stay at home in case of potential infection, which may cause delays of routine diagnosis and necessary treatment. How colorectal surgeons should manage this during the epidemic remains a big challenge.

Objective: To evaluate the feasibility of routine colorectal surgery during coronavirus disease 2019 and to offer some Chinese recommendations to colorectal surgeons throughout the world.

Methods: A total of 166 patients receiving colorectal surgery from 20th December 2019 to 20th March 2020 at Department of General Surgery in Chinese General Hospital of People’s Liberation Army were enrolled, and further divided into two groups based on before or after admission date of 20th January 2020. Clinicopathologic data such as hospital stay and economic data such as total costs were collected and analyzed retrospectively.

Results: Longer hospital stay, higher proportion of non-local patients and more hospitalization cost were found in the post-20 January group (special-time group) ($P < 0.001; P < 0.05; P < 0.05$ respectively). Apart from this, no difference existed with regard to baseline demographical data such as age, sex and height, as well as clinicopathological data such as previous history, surgery time, operation extent and TNM staging.

Conclusions: This real-world study indicated that performing colorectal surgery during coronavirus disease 2019 epidemic might be safe and feasible based on comprehensive screening and investigation. We have summarized several recommendations here, hoping to help surgeons from related departments across the world.

Key words: colorectal surgery; coronavirus disease 2019; retrospective analysis; real-world data
Introduction

Currently, the whole world is facing a big challenge of the novel virus pneumonia known as coronavirus disease 2019 (COVID-19) named officially by World Health Organization (WHO). Since it broke out in Wuhan, Hubei Province of China in late December 2019 initially as reported [1], the COVID-19 has caused hundreds of thousands of people to be infected and resulted in a heavy burden on the global economy. As a result of the rising numbers, verified person-to-person transmission and different health security capacities between countries [2-4], the WHO has already declared COVID-19 a Public Health Emergency of International Concern (PHEIC).

A nationwide analysis about cancer and COVID-19 in China revealed that patients infected with this virus were more likely to have a history of cancer and cancer patients had higher risks of COVID-19 and poorer outcomes from it [5]. Some researchers summarized that for cancer patients who were advised to stay at home during the global COVID-19 pandemic, potential risks existed for lacking early diagnosis, delaying of clinical therapy and further causing potential disease progression and poor prognosis [6]. Thus, we should pay more attention to those patients with cancer, especially the elderly as some reports have shown that older patients tend to have lower immune functions and worse COVID-19 outcomes [7, 8].

Researchers from Italy proposed that the COVID-19 epidemic could postpone outpatient visits, early test screening, oncological follow-up and endoscopy examination for patients with colorectal cancer (CRC) [9]. Delay of treatment for cancer was associated with decreasing survival years and increasing medical costs [10, 11]. Therefore, it’s vital to ensure colorectal surgery is performed safely and effectively during this special time. To date we’ve carried out several measures and put forward a Chinese expert consensus on surgical diagnosis and treatment strategies for CRC patients during COVID-19 epidemic [12]. In this retrospective study, we enrolled all those CRC patients receiving surgical treatment in our hospital around this COVID-19 outbreak period, collected and analyzed aspects such as safety and costs to conduct surgery for CRC. Meanwhile, we’ve introduced several precautions based on
real-world data and hope to exchange our learning experiences with intestinal surgeons around the world.

**Patients and Methods**

In Beijing, China, the first confirmed case of COVID-19 was officially announced by Beijing government on 20th January 2020, and the number of new cases reached zero on 20th March 2020. Thus, it was considered that the time of the epidemic situation was from 20th January 2020 to 20th March 2020, and we chose period from 20th December 2019 to 20th January 2020 as a control normal time in our study.

CRC patients hospitalized at General Surgery Department of Chinese PLA General Hospital (Beijing, China) from 20th December 2019 to 20th March 2020 were enrolled, and the inclusion criteria were as follows: (1) all patients received surgical treatment, including radical surgery for CRC and other non-radical surgery; (2) operations were all performed by experienced senior surgeons; (3) CRC patients were diagnosis based on pathological examination and all clinical data were integral and available. Patients who underwent emergency surgery were excluded. All patients signed informed consent before surgery and this study was approved by ethics committee of Chinese PLA General Hospital.

Since 20th January 2020, we’ve applied intensified strategies in case of COVID-19 infection, composed of three aspects of outpatient, inpatient, and discharged patient management. After 20th March 2020, the epidemic situation of COVID-19 began to stabilize, and hospital admissions gradually recovered. All the enrolled patients were divided into normal-time group (NTG) and special-time group (STG) based on hospitalization date. Clinical data were collected from those patients meeting inclusive and exclusive criteria above. Measurement data with normal distribution were presented as mean ± standard deviation (M ± SD) and analyzed via t test. Enumeration data were displayed as N (%) and analyzed using χ2 test. P < 0.05 was considered statistically significant, and all the statistical analyses were accomplished with IBM SPSS 23.0 (IBM, Armonk, New York, United States).
Results

Study population and baseline demographics

A total of 166 patients were enrolled, with 95 patients into NTG who were hospitalized before 20th January 2020 and the remaining 71 patients in the STG. Patients demographics for NTG and STG are shown in Table 1. The differences between NTG and STG were similar with regard to age, sex, height and weight ($P > 0.05$). The origin of patients between two groups showed a significant difference, with proportion of non-local patients of NTG significantly higher than that of STG ($P < 0.05$).

Clinicopathological data of all patients enrolled before or after 20th January

Preoperatively, patients had similar characteristics with respect to waiting time for hospitalization, imaging examinations of CT, MRI or PET/CT and colonoscopy, previous disease, major admission diagnosis and history of neoadjuvant chemotherapy (NACT) ($P > 0.05$). Compared to STG, patients in NTG had longer length of hospital stay before surgery ($P < 0.05$) (Table 2).

Intraoperatively, no statistically significant differences existed in terms of surgery time, operative method, resection extent, dissection of lymph nodes (LNs), combined organ resection or transfusion of blood ($P > 0.05$) (Table 3).

Postoperatively, there were no statistically significant differences for pathological diagnosis, TNM staging, complication including pneumonia and blood transfusion, as well as highest temperature, screening test, and reason for fever between the two groups ($P > 0.05$). Compared to NTG, patients of STG had more fever after surgery, longer length of postoperative stay and total stay ($P < 0.05$) (Table 4).

Health economics data of all patients enrolled before or after 20th January

We analyzed health economics data especially and results showed that patients of STG had higher costs of laboratory tests, anaesthesia, total hospitalization expenses, and other costs ($P < 0.05$). Other costs include beds, carers, diets and heating bills. Costs were similar concerning medicine, examination, treatment, surgery and medical consumables ($P > 0.05$). The results were shown in Table 5.
Discussion and Conclusion

According to the latest figures by the Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU)\textsuperscript{[13]}, there are more than 3,930,000 confirmed cases of COVID-19 throughout the world and over 270,000 deaths from it. Currently, the US with more than 1,280,000 confirmed cases and over 77,000 deaths, has already surpassed China and ranks first place among all the countries.

Colorectal cancer (CRC), one of the most common malignant tumors, has over 1.8 million new cases and more than 900,000 fatal cases every year, ranking third and second place globally for morbidity and mortality respectively, and in addition, there’s also a younger and increasing trend of CRC in China, which has raised concern both in China and across the world\textsuperscript{[14, 15]}. The outbreak of COVID-19 resulted in potential risks for cancer patients that delays of diagnosis and treatment might cause disease progression and survival shortening\textsuperscript{[6]}. How to run a colorectal surgery department effectively in this special time remains a big challenge.

In this study, during COVID-19 epidemic, non-local patients visiting our hospital decreased owing to strategies of traffic restriction and reducing movement of people. As Table 2 shows, preoperative examinations including CT, MRI and PET/CT were similar, with ongoing screening of patients with suspected symptoms, signs, temperatures and epidemiological (COVID exposure) history. Information about operations revealed that conducting surgery during COVID-19 is feasible. However, lengths of preoperative, postoperative and total hospital stay were all significantly longer and cost of hospitalization and treatment were notably higher, which was related to a three-day observation and isolation before operation. Fever after surgery occurred more often in STG patients, most of which were associated with stress response postoperatively, after comprehensive testing and investigation. And after further grouping and analyzing, postoperative fever conditions showed no statistically differences as shown in Table 4.

On behalf of Group of Colorectal Surgery, Society of Surgery, Chinese Medical association, our team drafted and published a Chinese expert consensus on surgical diagnosis and treatment strategies for CRC patients during COVID-19 epidemic\textsuperscript{[12]}. 

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We recommended several strategies, in order to not only accomplish the prevention and control of COVID-19 but also promote diagnosis and treatment for CRC safely and orderly, including three aspects of outpatient, inpatient and postoperative patient management. Flowchart of diagnosis and treatment for colorectal cancer patients during COVID-19 is shown in Figure 1.

Firstly, several tips for outpatient management should be addressed: (1) medical staff in outpatient must wear medical surgical mask or N95 mask, as well as disposable helmet, gloves and goggles, to protect them from potential infection; (2) appointment and triage protocols should be carried out through telephone, smartphone apps or internet service and patients visit the clinic based on reservation number and recommended time, to reduce crowds gathering and lower risks of cross infection; (3) for primary-care patients, triage nurses need to measure their temperature and investigate epidemiological history including travelling to Wuhan in Hubei Province and nearby cities, meeting with people who have been in those areas, and contact with confirmed or suspected cases within 14 days, as well as clinical manifestations including fever (≥ 37.3°C), fatigue and respiratory symptoms like coughing. For those with history of exposure or symptoms, the fever clinic screening had to be done first. Multidisciplinary team (MDT) meetings with doctors from General Surgery, Medical Oncology, Radiology, Radiotherapy, Respiratory and Epidemiology carried out via internet is recommended, for the sake of working out a personalized plan of diagnosis and treatment.

Secondly, perioperative management varies depending on type of surgical procedure. All hospitalized patients have to be isolated separately for at least 3 days, and only after all-round investigations of clinical symptoms and signs, laboratory test and imaging examinations, should operations be arranged. According to the latest version of the Standard of Diagnosis and Treatment of Colorectal Cancer in China\textsuperscript{[16]}, most CRC patients are diagnosed with advanced tumor. For cT\textsubscript{4} colon cancer, cT\textsubscript{3-4}/N\textsubscript{+} rectal cancer or CRC patients with resectable metastatic disease, NACT is recommended. FOLFOX and CapeOX both work for those CRC patients when given as NACT or adjuvant chemotherapy\textsuperscript{[17-19]}. We propose CapeOX as first choice during
COVID-19 epidemic, on account of its convenient method of taking oral medications for most of the time. Although neoadjuvant radiotherapy (NART) is proposed for rectal cancer patients, some research has showed that outcomes seemed not compromised without routine NART \(^{[20]}\). Thus, to some extent, NART could be postponed until COVID-19 epidemic ended. For CRC patients with unresectable metastasis, NACT plus bevacizumab or cetuximab is proposed \(^{[21]}\). Selective operation strategy is proposed for those CRC patients with locally advanced or metastatic disease. Limited endoscopic therapy should be performed for cT\(_1\)N\(_0\)M\(_0\) CRC patients, whereas limited operation should be done for cT\(_2-3\)N\(_0\)M\(_0\) colon cancer or cT\(_2\)N\(_0\)M\(_0\) rectal cancer patients.

Researchers from England put forward that no association existed between delay of treatment and survival of CRC patients, yet advised that for this issue, colon and rectum should be analyzed separately \(^{[22]}\). Heo and colleagues found that over 30 days of treatment delays was associated with poorer survival for rectum instead of colon cancer \(^{[23]}\). Moreover, waiting about 2 months after NACT and NART for rectal cancer didn’t increase response rate but adversely influenced morbidity from surgery \(^{[24]}\). Therefore, for advanced colon cancer patients, the watch and wait strategy (WWS) could be applied during COVID-19 epidemic. For advanced rectal tumors with demands of limited surgery, as well as other conditions such as hemorrhage, perforation and obstruction in need of emergency surgery, radical operations could be performed.

Thirdly, for postoperative management, the number of caregivers and visitors should be restricted and confined to fixed times for visiting. Further, mask wearing and temperature monitoring are mandatory for all personnel around the ward including medical staff, caregivers, visitors, and cleaners. For adjuvant therapy, a maximum of 60 days’ delay is acceptable \(^{[25]}\). After being discharged, an appropriate delay is recommended for patients who seek a review and recheck and media like telephone, WeChat or E-mails are preferred for postoperative consultations.

Experts in different areas have also summarized and shared management and working experiences \(^{[26-33]}\) including departments of intensive care unit (ICU), urology,
colorectal surgery, obstetrics, transplantation, oncology, and dermatology. Currently, some countries have suspended all non-urgent surgery during COVID-19 epidemic [34]. We believe that all should be cautious about COVID-19, although overcorrecting for the epidemic is inappropriate. The results of our single-center analysis showed that it’s safe to perform colorectal surgery during COVID-19, and what needs to be done careful assessment and screening comprehensively before admission, accepting a longer length of hospital stay and an increased cost.

In this study, the results were based on analysis of real-world data from one single center, which might lead to some bias. In addition, COVID-19 in Beijing is not as severe as in some areas like USA, Italy, Spain, France or Wuhan in Hubei Province of China, and the public health resources, hygiene measures, populace obedience and some aspects vary in different regions, for which some of our recommendations might be impractical to imitate.

In conclusion, our study indicated that it might be safe and feasible to perform colorectal surgery during COVID-19 after implementing strategies to lower risks for patients and hospital staff. We do believe this epidemic will end soon after joint efforts, and hope that some of our recommendations would be helpful for experts from other countries.

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Competing interests

The authors declared no conflicts of interest.
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Table 1 Baseline demographical data of all patients enrolled

| Demographics           | NTG (N=95)   | STG (N=71)   | P     |
|------------------------|--------------|--------------|-------|
| Age (years)            | 60.34±11.30  | 59.77±12.35  | 0.757 |
| Sex                    |              |              | 0.216 |
| Male                   | 70           | 46           |       |
| Female                 | 25           | 25           |       |
| Height (cm)            | 167.96±7.35  | 167.54±8.70  | 0.735 |
| Weight (kg)            | 70.62±12.91  | 69.75±12.79  | 0.664 |
| Origin of patients     |              |              | 0.035*|
| Local                  | 11           | 17           |       |
| Nonlocal               | 84           | 54           |       |

NTG: normal time group; STG: special time group; M: mean; SD: standard deviation; N: number.

* P < 0.05, statistically different
| Clinicopathologic data | NTG (N=95) M ± SD or N (%) | STG (N=71) M ± SD or N (%) | P     |
|------------------------|-----------------------------|-----------------------------|-------|
| Admission waiting(day) | 7.95±13.97                  | 9.59±14.19                  | 0.470 |
| Previous history       |                             |                             | 0.801 |
| Yes                    | 53                          | 41                          |       |
| No                     | 42                          | 30                          |       |
| Major diagnosis        |                             |                             | 0.590 |
| Duodenal cancer        | 1                           | 1                           |       |
| Colon cancer           | 43                          | 33                          |       |
| Rectal cancer          | 42                          | 28                          |       |
| Interstitialoma        | 3                           | 1                           |       |
| Benign diseases        | 6                           | 6                           |       |
| Other                  | 0                           | 2                           |       |
| CT examination         |                             |                             | 0.158 |
| Plain                  | 9                           | 13                          |       |
| Enhanced               | 74                          | 53                          |       |
| None                   | 12                          | 5                           |       |
| MRI examination        |                             |                             | 0.374 |
| Plain                  | 2                           | 1                           |       |
| Enhanced               | 19                          | 12                          |       |
| None                   | 74                          | 58                          |       |
| PET/CT examination     |                             |                             | 0.467 |
| Yes                    | 14                          | 12                          |       |
| No                     | 81                          | 59                          |       |
| Enteroscope test       |                             |                             | 0.051 |
| Yes                    | 89                          | 60                          |       |
| No                     | 5                           | 10                          |       |
| History of NACT        |                             |                             | 0.739 |
|   | Yes | 2   | 1   |
|---|-----|-----|-----|
| No | 93  | 70  |     |

Hospital stay before surgery (day) 4.68±5.88 7.42±3.62 0.001*

NTG: normal time group; STG: special time group; M: mean; SD: standard deviation; N: number; CT: computed tomography; MRI: magnetic resonance imaging; PET/CT: positron emission tomography computed tomography; NACT: neoadjuvant chemotherapy.

* $P < 0.05$, statistically different
Table 3 Intraoperative clinicopathological data of all patients enrolled

| Clinicopathologic data                        | NTG (N=95) M ± SD or N (%) | STG (N=71) M ± SD or N (%) | P      |
|----------------------------------------------|-----------------------------|----------------------------|--------|
| Surgery time (min)                           | 157.79±60.51                | 167.45±83.58                | 0.389  |
| Operative method                             |                             |                            | 0.472  |
| Open                                         | 20                          | 10                         |        |
| Laparoscopic                                 | 70                          | 59                         |        |
| Conversion to open                           | 4                           | 2                          |        |
| Other                                        | 1                           | 0                          |        |
| Resection extent                             |                             |                            | 0.083  |
| Local/non-radical                            | 14                          | 4                          |        |
| Radical                                      | 80                          | 64                         |        |
| Extended radical                             | 1                           | 3                          |        |
| Dissection of LNs                            |                             |                            | 0.822  |
| D2                                           | 76                          | 56                         |        |
| D3                                           | 7                           | 7                          |        |
| Unclear                                      | 4                           | 4                          |        |
| None                                         | 8                           | 4                          |        |
| Combine organ resection                      |                             |                            | 0.420  |
| Yes                                          | 4                           | 6                          |        |
| No                                           | 91                          | 65                         |        |
| Transfusion of blood                         |                             |                            | 0.393  |
| Yes                                          | 6                           | 8                          |        |
| No                                           | 89                          | 63                         |        |

NTG: normal time group; STG: special time group; M: mean; SD: standard deviation; N: number; LNs: lymph nodes

* P < 0.05, statistically different
Table 4 Postoperative clinicopathological data of all patients enrolled

| Clinicopathologic data | NTG (N=95) M ± SD or N (%) | STG (N=71) M ± SD or N (%) | P    |
|------------------------|-----------------------------|-----------------------------|------|
| Pathological diagnosis |                             |                             | 0.370|
| Primary disease        | 93                          | 62                          |      |
| Metastatic disease     | 2                           | 3                           |      |
| TNM staging            |                             |                             | 0.241|
| Stage I                | 13                          | 9                           |      |
| Stage II               | 22                          | 28                          |      |
| Stage III              | 41                          | 24                          |      |
| Stage IV               | 11                          | 5                           |      |
| Benign disease         | 8                           | 5                           |      |
| Complication           |                             |                             | 0.996|
| Yes                    | 4                           | 3                           |      |
| No                     | 91                          | 68                          |      |
| Fever (≥37.3°C)        |                             |                             | 0.006*|
| Yes                    | 27                          | 35                          |      |
| No                     | 68                          | 36                          |      |
| Highest temperature (°C)|                             |                             | 0.119|
| <37.3                  | 68                          | 36                          |      |
| 37.3-38.5              | 21                          | 25                          |      |
| >38.5                  | 6                           | 10                          |      |
| Screening examination  |                             |                             | 0.192|
| BRE                    | 10                          | 12                          |      |
| BRE+CRP                | 17                          | 17                          |      |
| BRE+CRP+X ray+CT       | 0                           | 1                           |      |
| ~+Fistulography        | 0                           | 1                           |      |
| None                   | 68                          | 40                          |      |
| Reason of fever        |                             |                             | 0.106|

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| Condition                          | NTG (N=74) | STG (N=96) | P-value |
|-----------------------------------|------------|------------|---------|
| Abdominal infection               | 7          | 3          |         |
| Pulmonary infection                | 0          | 1          |         |
| Incision infection                 | 1          | 0          |         |
| Anastomotic leakage                | 0          | 2          |         |
| Other                              | 18         | 24         |         |
| Unclear                            | 1          | 1          |         |
| None                               | 68         | 40         |         |
| Transfusion of blood               |            |            | 0.253   |
| Yes                                | 3          | 6          |         |
| No                                 | 92         | 65         |         |
| Hospital stay after surgery (day)  | 7.02±3.80  | 9.00±3.78  | 0.001*  |
| Total hospital stays (day)         | 11.78±7.43 | 16.70±5.80 | 0.000*  |

NTG: normal time group; STG: special time group; M: mean; SD: standard deviation; N: number; BRE: blood routine examination; CRP: C-reactive protein; CT: computed tomography

* P < 0.05, statistically different
| Health economics data | NTG (N=95) | STG (N=71) | P       |
|-----------------------|------------|------------|---------|
|                       | M ± SD or N (%) | M ± SD or N (%) |         |
| Medicine              | 2.40±1.00  | 2.66±1.18  | 0.126   |
| Laboratory test       | 1.04±0.33  | 1.17±0.40  | 0.022*  |
| Examination           | 0.10±0.23  | 0.11±0.17  | 0.847   |
| Treatment             | 0.60±1.02  | 0.69±1.10  | 0.581   |
| Surgery               | 0.44±0.11  | 0.47±0.12  | 0.054   |
| Anesthesia            | 0.19±0.06  | 0.21±0.07  | 0.037*  |
| Consumables           | 2.90±0.89  | 3.15±0.95  | 0.082   |
| Others                | 0.32±0.46  | 0.45±0.18  | 0.021*  |
| Total costs           | 7.99±2.51  | 8.91±2.47  | 0.020*  |

NTG: normal time group; STG: special time group; M: mean; SD: standard deviation; N: number; RMB: Renminbi.

* P < 0.05, statistically different
Figure 1 Flowchart of diagnosis and treatment for colorectal cancer patients during COVID-19

Abbreviations: MDT, multiple disciplinary treatment; CRC, colorectal cancer; RC, rectal cancer; CC, colon cancer; WWS, watch and wait strategy; NAT, neoadjuvant therapy.