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Research

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The Impact of COVID-19 on Gastric Cancer Surgery: A Single-center Retrospective Study Based on Real-world Data

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Abstract

Background: A respiratory epidemic defined as coronavirus disease 2019 (COVID-19) is becoming unstoppable and has been declared a pandemic. Patients with cancer are more likely to develop COVID-19. Based on our experience during the pandemic period, we propose some surgery strategies for gastric cancer patients under the COVID-19 situation.

Methods: We defined the 'COVID-19' period as occurring between 2020-01-20 and 2020-03-20. All the enrolled patients were divided into two groups, pre-COVID-19 group (PCG) and COVID-19 group (CG). A total of 109 patients with gastric cancer were enrolled in this study.

Results: The waiting times before admission increased by 4 days in CG(PCG:4.5 [IQR: 2, 7.8] vs. CG:8.0 [IQR: 2,20]; $P = 0.006$). More patients had performed chest CT scan besides abdominal CT before admission during COVID-19 period(PCG:22[32%]vs. CG:30[73%], $p=0.001$). After admission, during COVID period, the waiting time before surgery was longer(3[IQR: 2,5] vs. 7[IQR: 5,9]; $P < 0.001$),more laparoscopic surgery were performed(PCG: 51[75%] vs. CG: 38[92%], $p=0.021$), and hospital stay after surgery was longer (7[IQR: 6,8] vs.9[IQR:7,11] ; $P < 0.001$). The total cost of hospitalization increased during COVID period, (9.22[IQR:7.82,10.97] vs. 10.42[IQR:8.99,12.57]; $p=0.006$).

Conclusion: Since no data is available yet on the impact of COVID-19 on gastric cancer patients,our own experience with COVID-19 in gastric cancer surgery has hopefully provided an opportunity for colleagues to reflect on their own service and any contingency plans they have to tackle the crisis.

Keywords: gastric cancer; coronavirus disease 2019; COVID-19; retrospective analysis; real-world data.

Background

A respiratory epidemic defined as coronavirus disease 2019 (COVID-19) emerged in Wuhan city, Hubei Province, China in late December 2019. 41 patients were admitted to hospitals with an initial diagnosis of pneumonia of an unknown etiology, most of them had visited a local fish and wild animal market in November (1, 2). Then the spread of COVID-19 is becoming unstoppable and has been declared a pandemic. According to the Situation Report-77 of WHO (Data as of 6 April 2020), more than 1.2 million people have been infected all over the world (3).

Although most patients presented with symptoms such as fever, dry cough and dyspnea, the incidence of isolated or coexisting abdominal and gastrointestinal symptoms such as diarrhea, nausea, vomiting and abdominal discomfort were also common(4), which resulted in the implementation of stringent precautionary measures for patients and particularly hospital staff who were at greatest risk from the contaminated droplets and bodily fluids of the patients (5, 6).

Gastric cancer surgery is not a front-line subject in the fight against the COVID-19, however, in such a special situation, patients with cancer are more likely to develop COVID-19 (7, 8). As the virus can be transmitted by asymptomatic infectors, and it has been confirmed to be transmitted by droplets and contact (9), it is important to protect the safety of surgeons , nurses , patients and their families from infection (10). Based on our experience during the pandemic period, we propose some surgery strategies for gastric cancer patients under the COVID-19 situation.

Methods

Study Design and Patients

The General Surgery Department of our hospital serves as a final referral unit for a cluster of hospitals from other districts and provides specialist services for gastric cancer. On January 20, 2020, National Health Commission of the PRC announced that

pneumonia infected by the new coronavirus would be included in the management of the statutory infectious disease category B, but the prevention and control measures for the infectious disease were category .Since then we've applied intensified strategies and managements composed of three aspects of outpatients, inpatients and discharged patients, in case of COVID-19 infection On March 20, 2020,Beijing,the city our hospital locates, had no new local confirmed COVID-19 case for consecutive days, which was a milestone in the battle against the virus. Based on the above, we defined the 'COVID-19' period as occurring between 2020-01-20 and 2020-03-20. Data for this period was compared with a similar preceding 1-month period between 2020-12-20 and 2020-1-19 which we termed 'Pre-COVID-19'. Thus all the enrolled patients were divided into two groups, pre-COVID-19 group (PCG) and COVID-19 group (CG), based on which period they were admitted to our hospital.

All of the case series was approved by the Institutional Review Board of General Hospital of PLA. Inclusion criteria were as follows: (1) Gastric cancer patients were diagnosis based on pathological examination and all those clinical data were integral and available. (2) All the patients received surgery treatment. (3) Patients who received neoadjuvant chemotherapy (NACT) or underwent emergency surgery were excluded. A total of 109 patients with gastric cancer enrolled in this study were diagnosed according to The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for Gastric Cancer. Operations were performed by the same team of surgeons.

Data Collection

The medical records of patients were collected and analyzed by our research team. We summarized the clinical, epidemiological, radiological ,laboratory characteristics from electronic medical records, including patient demographics and baseline characteristics(sex, age, body mass index, comorbidity, clinical TNM classification, pathological TNM classification, chemotherapy regimen , hemoglobin, neutrophil-to-lymphocyte

ratio,CEA,CA199,AFP,CA724),surgical procedure, operating time, estimated blood loss ,postoperative complications ,postoperative body temperature, waiting times for the admission ,length of postoperative hospital stay ,hospital costs etc.

Statistical Analysis

SPSS version 26.0 was used for statistical analysis. Normality assumption for all quantitative variables data was verified with the Shapiro-Wilk test. Data were expressed as mean \pm standard deviation ($\bar{x}\pm s$) for normal distribution variables.For the data that did not conform to the normal distribution, the median and interquartile range were used to express the measurement data ,and count data were expressed by frequency and percentage (%). Student t tests were applied to compare means for normally distributed variables and Mann-Whitney test for variables without normal distribution. Statistical analysis of count data using chi-square test or Fisher exact probability method.

Results

Study population and baseline demographics

Between December 20,2019 to March 20,2020,a total of 109 patients were enrolled in this study. For the 109 patients who underwent elective surgery,68 of them were enrolled into PCG and 41 were into CG(**Figure 1**). Patients demographics for PCG and CG were shown in **Table 1**. There was no difference between PCG and CG in age, sex, Body mass index ($P > 0.05$).

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

Pre-COVID-19, admissions to the gastric unit totaled 68 cases over the 1-month period. During COVID-19, 2-months period, the total dropped by 30% to 41 admissions. In contrast, the waiting times before admission increased by 4 days (PCG:4.5 [IQR: 2, 7.8] vs. CG:8.0 [IQR: 2,20]; $P = 0.006$) .The proportion of local patients in

PCG is lower than in CG (3 [4%] vs. 16 [39%]; $P < 0.001$). More patients had performed chest CT scan besides abdominal CT before admission during COVID-19 period (PCG:22[32%] vs. CG:30[73%], $p=0.001$). The granulolymphatic ratio in CG was lower than in PCG, (2.83 ± 3.21 vs. 1.90 ± 1.08 ; $p=0.03$). **(Table 2)**

After admission, during COVID-19 period, the waiting time before surgery was longer (3[IQR: 2,5] vs. 7[IQR: 5,9]; $P < 0.001$), more laparoscopic surgery were performed (PCG: 51[75%] vs. CG: 38[92%], $p=0.021$), and hospital stay after surgery was longer (7[IQR: 6,8] vs. 9[IQR:7,11] ; $P < 0.001$). There was no statistical difference in surgical time, pathological diagnosis, TNM staging, complication including pneumonia and blood transfusion, as well as highest temperature, screening test and reason for fever between two groups ($P > 0.05$). **(Table 3-4)**

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

The total cost of hospitalization increased during COVID period, (9.22[IQR:7.82,10.97] vs. 10.42[IQR:8.99,12.57]; $p=0.006$), Medicine cost, treatment cost and other aspects including beds, cares, diets etc. were higher in GC($p > 0.05$).

The results were shown in **Table 5**.

Discussion

The COVID-19 outbreak alerted us the importance of infection control measures for pandemic diseases. Successful implementation of infection control required strict management of inpatients during this period. Due to disease consumption, malnutrition, coupled with chemotherapy , gastric cancer patients may be immunocompromised, which leads to more susceptible to COVID-19 (4, 8). Therefore, we suggest that all outpatients should be triaged before admission to reduce the possibility of exposure in hospital. Making personalized diagnosis and treatment plans for gastric cancer patients by multidisciplinary team (MDT) are essential (11, 12). departments and staff members of MDT include: general surgery, oncology, radiology, radiotherapy, respiratory medicine, and infectious disease experts. It is recommended that patients

should have completed gastroscopy, pathological examinations and imaging examinations (abdominal, pelvic CT or MRI, including PET-CT if necessary) at the local hospital before visiting our clinic. The MDT clinic comprehensively evaluates the gastric cancer patients based on clinical symptoms, pathological classification, imaging staging, and other examination, which resulted in precisely determination of the cTNM stage.

EMR or ESD are suggested for patients with early-stage gastric cancer lesions ≤ 2 cm in diameter without associated ulcer formation (cTis or cT1a). Surgery is the primary treatment option for cT1b patients. And patients with histologically confirmed gastric adenocarcinoma of cT2 to cT4a were suggested to receive perioperative chemotherapy. This shunt method allows patients to receive appropriate treatment, while reducing the number of hospitalized patients during the pandemic and reducing the risk of infection. Especially for patients who have finished neoadjuvant chemotherapy in several month later, they could benefit from avoiding the peak of the pandemic. However, for resectable gastric cancer patients with anemia, refusal of neoadjuvant chemotherapy, or low granulolymphatic ratio, delaying the time of radical surgery will not benefit the patient. Therefore, timely surgery might be a better choice. During the 'COVID-19' period, we recommend chest CT and new coronavirus nucleic acid tests to rule out patients with new coronary pneumonia and suspicious infection, which explains the longer waiting time before admission and higher chest CT scan rates in CG compared to PCG. In addition, the provinces were relatively isolated during the pandemic, therefore, compared with PCG, the proportion of local patients in CG had increased.

After admission, patients were isolated in separated single-room wards without contact to surgeons or nurses, which helps us to observe whether they manifested elevated temperature or symptoms suspicious for COVID-19. If the patients did not had a fever of over 37.3°C or other symptoms associated to pneumonia for 3 days since admission, the surgery would then be performed. During the pandemic, routine

surgery should be based on the principles of safety and efficiency, with the main purpose of reducing the incidence of postoperative complications and accelerating the patient's recovery and discharge(12, 13). Therefore, it is necessary to avoid performing surgery beyond authoritative guidelines, including oversized lymph node dissections with uncertain effects and complex digestive tract reconstruction methods. Attention should be paid to clear anatomy and accurate operation during surgery to reduce the risk of bleeding during and after surgery due to the tight blood source in the blood bank during the pandemic period, which could decrease unexpected blood transfusion treatment.

Enhanced Recovery After Surgery(ERAS) pathway was initially established by Henrik Kehlet (14) in colorectal surgery, Since then the idea has gradually been accepted .However, the first ERAS guideline for gastric cancer were published in 2014, and most evidence of it based on western countries. Lacking of gastric cancer ERAS protocol appropriate to Chinese conditions hampered us from accepting it at the first time. However, in recent years we are gradually conducting clinical trials on ERAS for gastric cancer. In the light of COVID- 19 pandemic, ERAS for gastric cancer patients demonstrated considerable advantages since it could reduce the patient's surgical stress response, postoperative complications, and shorten the length of hospital stay, thereby reducing the chance of nosocomial infection. While, the total hospital stay of patients in CG was longer than that in PCG, which seems ERAS was not applied to patients in CG. However, considering that during the COVID-19 period, patients had to remove the stitches in outpatient clinics and local hospitals since discharged, which would increase the risk of unnecessary viral infections, It was better to stay longer in our department until stitches were removed. In addition, other ERAS procedures in the two periods were almost analogous.

After surgery, If the patient had fever of unknown cause, appropriate ward isolation measures should be taken and postoperative blood routine, C-reactive protein, procalcitonin, chest CT, and new coronavirus nucleic acid tests are necessary.

Perioperative chemotherapy has significantly increased survival in patients with locoregional resectable gastric cancer. Capecitabine combined with Oxaliplatin or S-1 (SOX or XELOX) , has been applied as one of the standard perioperative chemotherapy strategy for patients with advanced gastric cancer in Chinese population (15-18). The preoperative chemotherapy schedules were composed of Oxaliplatin (130 mg/m² intravenously on day 1 every 3 weeks), combined with S-1 (40/50/60 mg orally twice daily for 14 days followed by 7 days off ,The does depends on surface area: < 1.25 m² /1.25–1.5 m² /> 1.5 m²)(SOX)or Capecitabine (1000 mg/m² twice daily for 14 days followed by 7 days off) (XELOX). Patients were admitted to day-care ward for intravenous injection of Oxaliplatin every 3 weeks, which shorten patient exposure time in hospital due to surgical treatment and reduce the risk of cross infection. The radical gastrectomy surgery would be performed in 4 weeks after 2–4 cycles neoadjuvant chemotherapy, at that time, the peak of the pandemic might pass.

Conclusions

In conclusion, no data is available yet on the impact of COVID-19 (if any) on gastric cancer patients. The full impact of COVID-19 on surgery is still unknown, since its effects on global economics, politics, hospital management, health strategy and personnel may only become evident in the long term. Our own experience with COVID-19 in gastric cancer surgery has hopefully provided an opportunity for colleagues to reflect on their own service and any contingency plans they have to tackle the crisis.

Ethics approval and consent to participate

All of the case series was approved by the Institutional Review Board of General Hospital of PLA(S2020-003-01). The need to obtain informed consent was waived because of its retrospective nature. In our hospital, every patient have right to refuse the use of their record at any time.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declared no competing interests.

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Authors' contributions

XHD and SYX conceived the analysis. YXL, CZH and YCL extracted all data. YFW, PYZ and XLX undertook and refined the inclusion process. YXL, CZH and YCL co-wrote the paper. YXL, YCL and YFW undertook the statistical analyses. All authors contributed to and revised the final manuscript.

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Table 1. Baseline demographical data of all patients enrolled

Demographics	PCG (N=68)	CG (N=41)	<i>P</i>
	M ± SD or N (%)	M ± SD or N (%)	
Age (years)	59.60±11.04	58.41±10.27	0.578
Sex			0.583
Male	45	25	
Female	23	16	
BMI	24.37±3.68	23.30±2.91	0.099
Origin of patients			0.000*
Local patients	3	16	
Other provinces	65	25	

PCG: pre-COVID-19 group; CG: COVID-19 group; M: mean; SD: standard deviation; N: number.

* $P < 0.05$, statistically different

Table 2. Preoperative clinicopathological data of all patients enrolled

Clinicopathologic data	PCG(N=68) M(IQR)orN (%)	CG (N=41) M(IQR)orN (%)	<i>P</i>
Admission waiting(day)	4.5 (2-7.75)	8.0 (2-20)	0.006*
Operation waiting(day)	3(2-5)	7(5-9)	0.000*
Comorbidity			0.144
Yes	46	22	
No	22	19	
Tumor marker			
CEA	2.12	1.85	0.298
AFP	2.85	3.01	0.771
CA199	9.70	9.63	0.883
CA724	2.03	2.13	0.863
Clinical TNM stage			0.112
I	17	4	
II	18	14	
III	30	23	
IV	3	0	
NLR	1.78(1.80-2.60)	1.63(1.24-2.23)	0.423
Hemoglobin	138.50(119.25-148.75)	143.00(119.50-151.00)	0.726
Chest CT scan			0.000*
Yes	24	30	
No	44	11	

PCG: pre-COVID-19 group; CG: COVID-19 group;NLR: Neutrophilto-Lymphocyte ratio CT: computed tomography; c; N: number.

* $P < 0.05$, statistically different

Table 3. Intraoperative clinicopathological data of all patients enrolled

Clinicopathologic data	PCG (N=68)	CG (N=41)	<i>P</i>
	M ± SD or N (%)	M ± SD or N (%)	
Surgery time (min)	184.74 ± 44.36	195.00 ± 57.49	0.298
Estimated blood loss (ml)#	100 (50-137)	100 (50-150)	0.569
Operative method			0.021*
Open	17	3	
Laparoscopic	51	38	
Combine organ resection			0.000*
Yes	1	0	
No	67	41	
Transfusion of blood			0.172
Yes	4	6	
No	64	35	

PCG: pre-COVID-19 group; CG: COVID-19 group; M: mean; SD: standard deviation; N: number. # M: median; IQR: inter-quartile range

* $P < 0.05$, statistically different

Table 4. Postoperative clinicopathological data of all patients enrolled

Clinicopathologic data	PCG(N=68)	CG (N=41)	<i>P</i>
	M(IQR)orN (%)	M(IQR)orN (%)	
Pathological TNM staging			0.394
I	18	8	
II	18	10	
III	29	23	
IV	3	0	
Complications			0.081
Yes	6	0	
No	62	41	
Postoperative fever			0.379
Yes	29	14	
No	39	27	
Highest temperature (°C)			0.587
<37.3	39	27	
37.3-38.5	22	12	
>38.5	7	2	
Screening examination			0.012*
None	16	2	
BRE+CRP	8	4	
BRE+CRP+CT	4	5	
Nucleic acid test	0	2	
Reason of fever			0.423
Abdominal infection	1	0	
Pulmonary infection	1	0	
Incision infection	4	0	
Anastomotic leakage	1	0	
Unclear	17	11	

None	5	3	
Transfusion of blood			0.422
Yes	3	4	
No	65	37	
Postoperative hospital stay (day)	7 (6-8)	9 (7-11)	0.000*
Total hospital stay (day)	11 (9-13)	15 (13-19)	0.000*

PCG: pre-COVID-19 group; CG: COVID-19 group; BRE: blood routine examination; CRP: C-reactive protein; CT: computed tomography; Postoperative fever ($\geq 37.3^{\circ}\text{C}$)
M: median; IQR: inter-quartile range; N: number.

* $P < 0.05$, statistically different

Table 5. Health economics data of all patients enrolled

Health economics data (10,000 RMB)	PCG(N=68) M(IQR)	CG (N=41) M(IQR)	<i>P</i>
Medicine	2.51(1.79-3.27)	2.89(2.29-4.30)	0.002*
Examination	0.05(0.03-0.09)	0.06(0.05-0.08)	0.051
Laboratory test	0.83 (0.68-1.06)	1.00(0.76-1.18)	0.078
Treatment	7.99(6.59-9.66)	9.00(7.59-11.09)	0.024*
Surgery	0.46(0.45-0.47)	0.47(0.40-0.47)	0.527
Anesthesia	0.20(0.18-0.23)	0.22(0.19-0.23)	0.131
Consumables	3.94(3.55-4.50)	4.45(3.45-5.45)	0.140
Others	0.26(0.21-0.34)	0.47(0.36-0.54)	0.000*
Total costs	9.23(7.82-10.97)	10.42(8.99-12.57)	0.006*

PCG: pre-COVID-19 group; CG: COVID-19 group; M: median; IQR: inter-quartile range.

* $P < 0.05$, statistically different

Figure legend

Figure1. Flow diagram of patient inclusion.

Figures

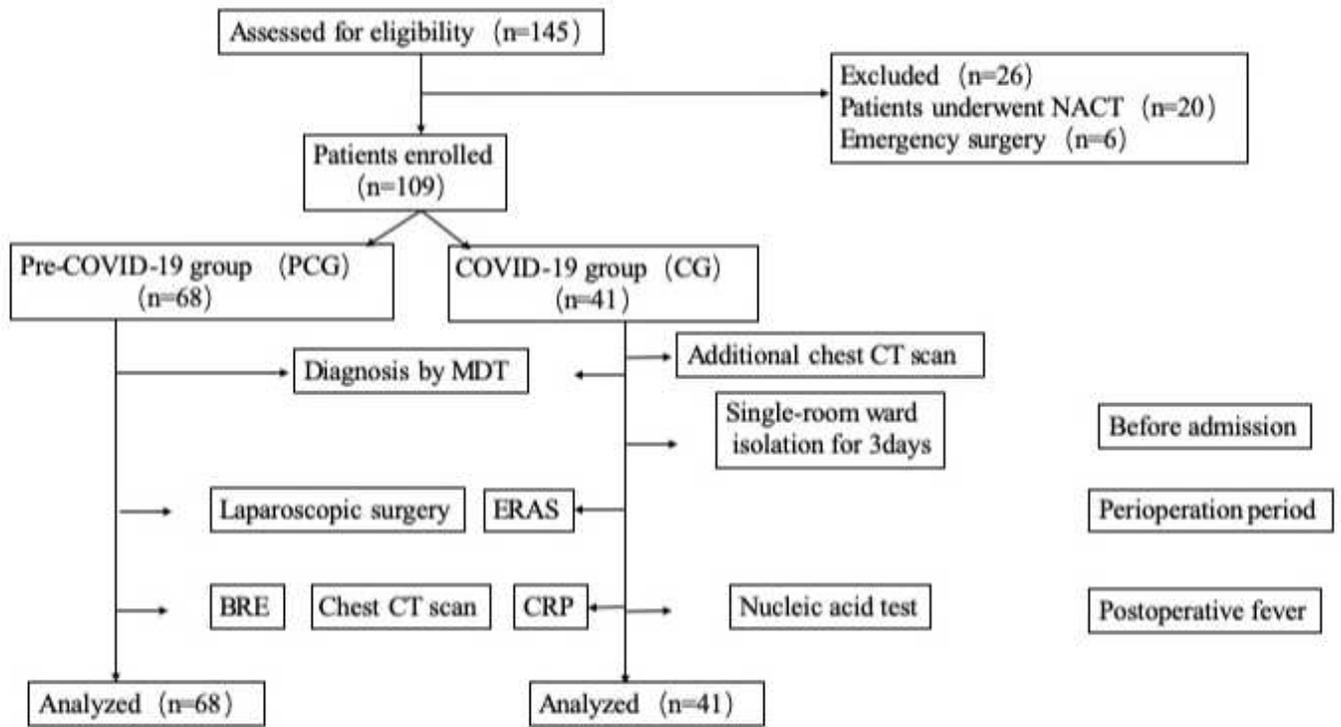


Figure 1

Flow diagram of patient inclusion.