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## CASE REPORT

# Lessons from the COVID-19 Pandemic: A New Paradigm in Treating Patients with Colorectal Cancer

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## Abstract

Starting in 2020 and continuing for 2 years thereafter, the COVID-19 pandemic has greatly affected routine clinical practice, particularly in treating patients with gastrointestinal cancer. Delay, postponement or refusal to continue multimodal treatment have increased the number of emergency cases, and consequently patient morbidity and mortality.

Many recommendations have been announced to guide the adaptation of clinical practice during and after the COVID-19 pandemic. Although early diagnosis and screening should proceed as usual before the pandemic, adjuvant treatment for patients with gastrointestinal cancer should be evaluated in the future. For example, during the pandemic, most recommendations state that adjuvant treatment for patients with colorectal cancer is still required, and many adaptations have been suggested according to local conditions.

In some instances, 6 months of adjuvant chemotherapy has been modified to an optional 3 month duration. A common challenge is that most patients remain unsure about the decreased chemotherapy duration, although many guidelines recommend this modified treatment strategy. Short term follow up has already indicated promising clinical outcomes of this modified adjuvant duration, but the long-term outcomes remain to be evaluated.

**Keywords:** colorectal cancer, COVID-19 pandemic, adjuvant treatment

## Introduction

Colorectal cancer, the most common cancer, affects the gastrointestinal tract and leads to increasing mortality each year. Screening and early diagnosis are critical to increasing favorable short- and long-term clinical outcomes, as well as long-term survival. Since early 2020, clinicians have faced many challenges in treating patients with gastrointestinal cancer, particularly those with colorectal cancer.<sup>1</sup>

No countries or health systems had clear prior recommendations applicable to the COVID-19 pandemic. Many guidelines were announced after the start of the pandemic, such as those from the European Society for Medical Oncology, and European Association for Endoscopic Surgeons, both of which recommend not to delay screening examinations or definitive treatment for colorectal cancer.<sup>2</sup> The greater the delay before the presentation of colorectal cancer, the greater the risk of emergency conditions.

The two most common signs and symptoms of colorectal cancer are intestinal obstruction (large bowel obstruction due to tumors) and closed loop obstruction, which can lead to intestinal perforation. As we reported in 2021, emergency cases of colorectal cancer increased during the pandemic, thereby increasing stoma creation, not only for temporary stoma, such as a diverting stoma or as a permanent stoma, because of the advanced condition of the colorectal cancer. In this case, a common problem was that most patients refused to continue multimodal treatment during the pandemic.<sup>1,3</sup>

Another recommendation during the pandemic has been a new strategy of providing adjuvant treatment for colorectal cancer after definitive surgery. There is no difference in the timing of starting adjuvant therapy: patients can receive the therapy 3–4 weeks after the surgery. Recommendations suggest modifying the interval of adjuvant chemotherapy. Before the pandemic, biweekly chemotherapy was the main recommendation for patients with colorectal cancer, to decrease locoregional recurrence. The most recent recommendation involves decreasing the duration of adjuvant treatment, by giving chemotherapy for only 3 months, to minimize contact between patients and healthcare teams. This study was aimed at evaluating the relevance of reducing the adjuvant chemotherapy to only 3 months for colorectal cancer treatment. Another question was whether this practice is safe and sufficient to control locoregional recurrence.

## Methods

This observational single center study during the COVID-19 pandemic was conducted in Surgery Department of Moewardi General Hospital, Indonesia, from 2020 to August 2022. Patients with colorectal cancer with R0 resection status were included in this study without age limitations. Patients receiving emergency surgery and elective resection were also included. Patients agreeing to 3 months of adjuvant chemotherapy were evaluated for short term clinical outcomes, evidence of chemotherapy interruption and loco-regional recurrence. Patients with evidence of disease recurrence

at early presentation were excluded from the study.

This observational study was conducted with a consecutive sampling technique, and all patients who meet the inclusion and exclusion criteria were evaluated.

Post chemotherapy evaluation was conducted through abdominal computerized tomography (CT) scanning and chest X-rays to evaluate locoregional and distant metastasis 6 months after the last cycle of adjuvant chemotherapy.

Locoregional recurrence was assessed on the basis of the data and radiology findings. The tumor site, type of chemotherapy regimen and TNM stage are reported.

This observational study was approved by the Health Research Ethic Committee of Moewardi General Hospital, Surakarta, Indonesia.

Ethical clearance number: 27/II/HREC/2020

## Results

Since the second wave of the COVID-19 pandemic, many limitations and challenges remain to be resolved by our health care system. Patients with gastrointestinal cancer have often had adjuvant therapy interrupted and postponed because of the pandemic. Chemotherapy cycles for colorectal cancer have also been interrupted, and most patients have not continued with multimodal treatment before and after definitive surgery. During this study, the starting time of the adjuvant chemotherapy, according to the current protocol and recommendations, was 3–4 weeks after the definitive surgery. We

reported 37 cases of colorectal cancer with pathology finding of adenocarcinoma of the colon and rectum. Both elective and emergency cases were included. The most common clinical presentation of emergency cases was total colonic obstruction due to rectal cancer or sigmoid cancer. Definitive surgery was performed through primary tumor resection, and both of them involved R0 resection.

The characteristics of the patients are presented in Table 1.

**Table 1. Patient Characteristics**

Data	n	%
<b>Tumor site</b>		
Ascending Colon	4	11
Transverse Colon	2	5
Descending Colon	6	16
Sigmoid Colon	10	27
Rectum	15	41
<b>TNM Staging</b>		
Stage III	20	54
Stage IV	17	46
<b>Chemotherapy Regimen</b>		
FOLFOX	15	40
5FU + Leucovorine	22	60
<b>Recurrence</b>		
Locoregional	-	
Distant Metastasis	-	

During this study, by using the same chemotherapy interval protocol as that before the pandemic, we found no chemotherapy interruption and no major adverse effects of chemotherapy related symptoms after the administration of this adjuvant therapy. Radiologic evaluation was performed 6 months after the last cycle of adjuvant chemotherapy. Abdominal CT scans and chest X-rays indicated no local recurrence or distant metastasis in short term clinical evaluation.

### Discussion

Colorectal cancer is the third most common cancer worldwide. A total of 1,880,000 new cases have been estimated to occur each year, and more than 900,000 people have colorectal tumor associated mortality. Surgery is the gold standard treatment for resectable colorectal cancer. In the United States, a 4-month delay in colon cancer surgery has been estimated to result in an additional 10,043 stage I–III deaths associated with tumors over the past 5 years. Several studies have shown that patients with colorectal cancer are at elevated risk of contracting COVID-19 with high severity, and have suggested that patients with colorectal cancer should delay surgical treatment for as many as 3 months of diagnosis.<sup>4</sup>

According to some early data suggesting that patients with colorectal cancer are at elevated risk of COVID-19-associated infection, a severe course, and morbidity and mortality, definitive resection has been suggested to be postponed for patients with colorectal cancer to within 3 months after

diagnosis.<sup>5</sup> In addition, some gastrointestinal cancer societies have supported low-risk strategies, such as construction of a diverting stoma rather than primary anastomosis after surgical resection, to minimize the risk of potentially life-threatening complications, such as bowel anastomosis leakage.<sup>6</sup>

The use of minimally invasive techniques, such as laparoscopic approaches, has been highly controversial during the COVID-19 era. Although the laparoscopic approach has well-known advantages over conventional open surgery for many abdominal diseases, the Intercollegiate General Surgery Guidance in the UK has suggested avoiding laparoscopy except in selected cases during the COVID-19 endemic.<sup>7</sup> This statement has been based on the hypothesis of increased risk of virus aerosolization when electrosurgical devices are used, although no evidence of COVID-19 emission and transmission during laparoscopic surgery has been reported. With universal precautions and protective devices, any technique chosen will have its own advantages. By following current recommendations, in the local conditions of our health center, the feasibility and safety procedures were the same.<sup>8</sup>

To date, the potential implications of the changes proposed to cancer management pathways during the COVID-19 pandemic on the prognosis of cancer patients remain debated and poorly understood. Postponing surgery after the pandemic or using other treatment modalities has been challenged by inconsistent results in studies published before the COVID-19 pandemic assessing

survival according to different delay times for definitive surgical resection.<sup>9,10</sup>

Earlier in the pandemic, most recommendations suggested continuing adjuvant chemotherapy by using oral capecitabine for three weekly interval. In our country, particularly in our center, we were unable to control the continuation of this oral chemotherapy, because many patients directly stopped the medication if they experienced gastrointestinal symptoms associated with oral capecitabine, without seeking medical consultation. However, under these pandemic conditions, modified chemotherapy duration and intervals might be preferred methods.

The established recommendations for adjuvant colorectal cancer chemotherapy suggest biweekly treatments for 6 months for better control of local recurrence and distant metastasis. In many centers in our country, data regarding the use of modified chemotherapy durations and intervals are lacking, although these practices are currently followed in many hospitals.<sup>11</sup> The most common challenges come not only from the patients given this adjuvant treatment but also from the physicians providing multimodal treatment.<sup>12</sup> The results of this observational study indicated the feasibility of shortening the adjuvant chemotherapy duration to only 3 months. For this shorter regimen, compared with standard practice, the surveillance follow up did not differ, and comparable short term clinical outcomes were observed; the findings indicated the safety of this shorter chemotherapy regimen, which provided an

additional benefit of decreased adverse effects.<sup>12,13</sup>

This study has several limitations. First, we found no local recurrence in resectable and R0 resection cases. A further study including both post operative resection types is needed to generalize whether this new paradigm could be applied in the evidence of macro or microscopic residual tumors. Multimodal treatment of this condition is highly challenging, and many controversies remain to be resolved by long-term clinical follow up. However, local recommendations could be accepted for each health center, on the basis of local data and the condition of colorectal cancer cases.<sup>14,15</sup>

The rationale for this new paradigm in treating patients with colorectal cancer is modifying or reducing adjuvant chemotherapy duration; decreasing the contact between patients and health care providers; and diminishing the adverse effects of chemotherapy.<sup>16</sup> Another aspect is socio-economic factors pertaining to the national health insurance in Indonesia, a developing country. A shortage in fluoropyrimidine, the most common regimen that we used, could occur in the future if the use of this regimen controlled. Therefore, our efforts to reduce fluoropyrimidine use might affect the overall national health system.

### Conclusion

The COVID-19 pandemic has greatly affected our strategy in treating patients with gastrointestinal cancer, particularly colorectal cancer. Many adaptations could be applied

according to the local conditions at each healthcare center. Controversies still remain regarding whether which one has a better one to be applied, but on the basis of our

short term clinical outcomes, a modified 3 month chemotherapy regimen achieved reliable loco-regional control and therefore was feasible.

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**Author Contribution**

Budhi Ida Bagus contributed to the conception, design and interpretation of data, and is responsible for the content of this manuscript.

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**Informed Consent**

Patients were informed of the purpose of this case study, and provided permission for the use of clinical information, such as clinical findings during the operation and radiological examination findings, in the publication.

**Ethical Approval**

This case study was approved by the Health Research Ethics Committee of Moewardi General Hospital, Surakarta, Indonesia.

Ethical clearance number: 27/II/HREC/2020

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