



The Effect of COVID-19 on the Management of Rectal Cancer

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Abstract

Background: Rectal cancer is a malignant tumor of the digestive tract, and as it is a widespread condition, it demands comprehensive research. At the time of writing this study, coronavirus disease 2019 (COVID-19) affliction rates are rising rapidly in Iran. Hence, this study attempts to evaluate the country's rectal cancer management during the pandemic.

Methods: A total of 83 patients were divided into two groups and were closely studied. The first group underwent rectal cancer surgery during a nine-month period in 2019, while the second group underwent the same process during the same amount of time in 2020. Demographic data, surgery, and outcomes after surgery were assessed and compared between the two groups. Data were analyzed by SPSS (statistical analyzer software, ver. 22).

Results: The age, weight, height, BMI, tumor size, and numbers of involved lymph nodes were not different between the two groups. The radiotherapy techniques were significantly different between the two groups ($P=0.012$). Neoadjuvant long-course chemoradiation therapy was changed to short-course radiation therapy during the pandemic, and hospital stay was significantly longer during the pandemic ($P=0.010$). There was no difference in the recurrence or overall survival between the two groups. Metastasis was seen in six patients in the 2019 group but was not observed in the 2020 group. The size of tumors was larger in the 2020 group, but this was statistically insignificant ($P=0.064$).

Conclusion: Cancer is a highly complicated and problematic disease, highlighting the importance of immediate diagnosis and treatment. However, during the COVID-19 pandemic, medical centers may need to take additional measures to protect their cancer patients.

Keywords: COVID-19, Rectal cancer, Shiraz, Iran

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Introduction

The number of people afflicted with coronavirus disease 2019 (COVID-19) is unfortunately still rising in many parts of the world (1-3). Among significant factors affecting the burden of the

pandemic are the capacity of healthcare systems in every country and the adopted policies and strategies in curbing the disease. In the harsh circumstances brought about by the pandemic, it stands to reason that countries protect their most vulnerable citizens. One group of highly susceptible people are cancer

patients. Early reports suggest that patients with cancer and COVID-19 need special medical care as their mortality and risk of severe complications after surgery are higher than patients without COVID-19 (4). In patients undergoing active oncologic therapy, cytotoxic chemotherapy leads to an increased risk for morbidity and mortality due to the weakening of the immune response, which results in patients being more susceptible to viral infections (4, 5).

Rectal cancer is a malignant tumor of the digestive tract, and as it is a widespread condition, it demands comprehensive research. Rectal cancer treatment requires various imaging studies and multiple referrals to multimodality therapy centers (radiotherapy, chemotherapy, and surgery). A high degree of assurance must be reached during the treatment process before the patients are dismissed from hospitals. Depending on the circumstances, the patients might require intensive care. In the case of surgical treatment, several follow-ups might be necessary. Upon receiving neoadjuvant therapy, patients suffer immune system deficiency, and their operation may be emergency or semi-emergency. Due to the prevalence of COVID-19 and the already perilous condition of these patients, time constraints and delays in treatment might lead to irreversible disease progression.

The pandemic has brought serious challenges to the diagnosis and management of rectal cancer patients. One particular problem is that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have been detected in the gastrointestinal and urinal tracts, with the potential transmission routes being of concern, especially in the diagnosis and treatment of rectal cancer. According to our knowledge, there are no fixed set of management policies regarding rectal cancer patients exposed to the pandemic. Various guidelines have been proposed by the medical centers, at times being contradictory. The following are some of the existing challenges listed: (i) lack of information about COVID-19, (ii) limitations in medical resources, (iii) fears of referring to medical centers due to the possibility of SARS-CoV-2 infection, and (iv) the need for neoadjuvant and adjuvant therapy (short course or long course). Prior to March 2020, our standard approach with regard to patients with locally advanced rectal cancer was neoadjuvant with long-course chemoradiation therapy (6-8).

In this paper, we decided to discuss the diagnosis and management plan of patients with rectal cancer in our referral center during the COVID-19 outbreak based on a new guideline, thereby providing a reference for clinical practitioners. We evaluated our rectal cancer management outcomes based on our proposed guideline during the nine months when the pandemic peaked in Iran (February to October 2020) and compared it against the previously established guideline for a similar period of time in 2019 before the COVID-19 pandemic.

Patients and Methods

The Ethics Committee of Shiraz University of Medical Sciences approved the protocol of this study (IR.SUMS.REC.1400.195). Clinical, laboratory, and radiological data were gathered from patients treated for rectal cancer according to the new guideline (Figure 1).

A total of 83 patients were divided into two groups and closely studied. The first group underwent rectal cancer surgery during a nine-month period in 2019 (1st February to 31st October; pre-COVID-19 pandemic). The second group underwent the same process during the same amount of time in 2020 when the COVID-19 pandemic peaked in Iran. It is also noteworthy that the two groups were matched in terms of age and sex.

The multidisciplinary team (MDT) that proposed the new guideline was comprised of colorectal surgeons, oncologists, radiologists, pathologists, and intensive care unit (ICU) personnel in the Faghihi Hospital of Shiraz, Iran. Although the principles of tumor therapy remain unchanged, the details of the therapeutic methods may be different from the usual (short-term instead of long-term neoadjuvant radiotherapy). The follow-up of patients occurred in the first week, first month, third month, and the sixth month after surgery; the remaining follow-ups were scheduled yearly.

Demographic survey of patients, neoadjuvant (radiotherapy, chemotherapy, and its type), duration of completion of neoadjuvant therapy until surgery, type of surgery performed, length of hospital stay, need for intensive care, and 30-day mortality was assessed. Data of clinical follow-ups and online clinical consultation services were gathered. The data between the two groups were compared and analyzed.

Statistics

Data were analyzed by SPSS (statistical analyzer software, ver. 22). The chi-squared test was used for qualitative data, while the independent t-test was utilized to analyze quantitative data. P values < 0.05 suggested statistically significant results.

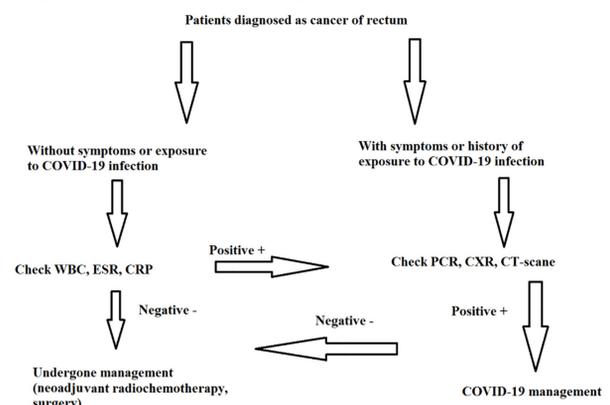


Figure 1: New guideline for the management of rectal cancer patients.

Results

The patients in the study had to follow the following protocol: if a patient showed any COVID-19 symptoms or was exposed to another symptomatic patient suspicious of COVID-19 during the 14 days preceding surgery, they should have their complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and SARS-CoV-2 polymerase chain reaction (PCR) assay checked to determine whether there is any SARS-CoV-2 infection. If they had no signs or symptoms, they

should check the CBC, ESR, and CRP to rule out COVID-19 before surgery.

In this study, there were 43 female and 40 male patients, 14 of whom have a family history of colon cancer and 5 of whom have a family history of rectum cancer. Recurrence in the 2020 group was observed in one patient, whereas this figure was two in the 2019 group. Metastasis was seen in six patients in the 2019 group while being non-existent in the 2020 group. The hospital stay was longer in the pandemic group ($P=0.010$, Table 1). The size of tumors was larger in the 2020 group; however, this

Table 1: Demographic and clinical data of patients in the two groups, showed by mean (SD)

Parameters		2020 (n=31)	2019 (n=52)	P value*
Age		52.35 (12.61)	55.75 (12.68)	0.240
Weight		69.61 (11.56)	72.11 (13.96)	0.403
BMI		25.30 (3.88)	26.05 (5.03)	0.476
Size of tumor		3.59 (2.45)	2.65 (1.88)	0.063
Hospital stay (days)		4.03 (1.81)	5.17 (1.94)	0.009*
Parameters	Groups	2020 (n, %)	2019 (n, %)	P value*
Sex	Female	16 (52%)	27 (52%)	0.978
	Male	15 (48%)	25 (48%)	
Family history of cancer	Colon	5 (16%)	9 (17%)	0.890
	Rectum	2 (6%)	3 (6%)	
Appearance of tumor	Diffuse	4 (13%)	5 (10%)	0.293
	Fungatin	6 (19%)	4 (8%)	
	polypoid	4 (13%)	3 (6%)	
	ulcerative	13 (42%)	31 (60%)	
Grading	Moderately differentiated	5 (16%)	3 (6%)	0.211
	Poorly differentiated	0 (0%)	2 (4%)	
	Well differentiated	23 (74%)	37 (71%)	
Type of surgery	A-P resection	7 (23%)	16 (32%)	0.412
	Low anterior resection	24 (77%)	36 (68%)	
Disease stage	I	9 (29%)	17 (33%)	0.844
	II A	7 (22%)	10 (19%)	
	III A	1 (3%)	1 (2%)	
	III B	8 (26%)	9 (17%)	
	III C	1 (3%)	4 (8%)	
	IV A	2 (6%)	2 (4%)	
M stage	M1a	2 (6%)	2 (4%)	0.467
	Mx	26 (84%)	40 (77%)	
N stage	N1a	4 (13%)	6 (11%)	0.520
	N1b	1 (3%)	3 (6%)	
	N1c	5 (16%)	2 (4%)	
	N2a	1 (3%)	2 (4%)	
	N2b	1 (3%)	3 (6%)	
	N0	16 (52%)	26 (50%)	
T stage	T1	2 (6%)	3 (6%)	0.630
	T2	9 (29%)	17 (33%)	
	T3	16 (52%)	18 (35%)	
	T4a	1 (3%)	3 (6%)	
	T4b	0 (0%)	1 (2%)	
	Pathologic complete response	Yes	2 (6%)	
Surgical technique	Laparoscopy	24 (77%)	40 (77%)	0.466
	Laparotomy	6 (19%)	7 (13%)	
	Conversion	1 (3%)	5 (10%)	
Radiotherapy technique	5	2 (6%)	15 (29%)	0.012*
	25	17 (55%)	19 (36%)	

*Pearson chi-square test was displayed.

was not statistically significant ($P=0.064$). The rate of pathologic complete response to neoadjuvant therapy was 6% in the 2020 group and 21% in the 2019 group. Notably, 77% of surgical techniques in both groups were laparoscopy (Table 1). Radiotherapy techniques (short-term/long-term) were different between the two groups ($P=0.012$). The number of patients in the 2020 and 2019 groups varied in terms of lymphatic invasion (3 vs. 5, respectively), neuronal invasion (3 vs. 8, respectively), and vascular invasion (3 vs. 5, respectively).

Discussion

The pandemic has brought serious challenges to the diagnosis and management of rectal cancer patients, leading to the cancellation of many surgeries, especially elective ones. Depending on the circumstances, the patients might require oxygen support and immediate transfer to the intensive care unit; however, such conventional procedures might run into difficulties during the pandemic.

In the case that surgical treatment takes place, several follow-ups might be necessary. Upon receiving neoadjuvant therapy, patients suffer immune system deficiency, and their operation may be emergency or semi-emergency. Due to the prevalence of COVID-19 and the already perilous condition of these patients, time constraints and delays in treatment might lead to irreversible disease progression.

In the COVID-19 pandemic, short-course radiation therapy seems to be a well-validated alternative that helps a greater number of potentially curable patients. While our long-course chemoradiation comprised a five-week radiotherapy course and an eight-week lag time before surgery, due to the pandemic it had to be substituted by a short course of chemoradiotherapy consisting of two weeks of radiation and an eight-week lag time. Radiotherapy in the 2020 group was significantly less according to oncology guidelines during the pandemic ($P=0.012$).

According to our results, the size of tumors was larger in the 2020 group (probably due to the patients delaying their treatments during the pandemic), but this was not statistically significant ($P=0.064$). Also, the hospital stay was longer in the pandemic group ($P=0.010$, Table 1). The staging of the cancer was not significantly different between the two groups.

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More than 32% of patients in the 2020 group were diagnosed with stage III, while this figure was approximately 27% in the other group. More than 50% of patients were diagnosed with the T3 stage in the 2020 group, whereas only 35% of patients in the other group were diagnosed as such (Table 1).

The results of the study suggest that many patients are afraid to visit medical centers for their treatment. On the other hand, patients with both cancer and COVID-19 have twice the mortality rate of those who only have cancer (9, 10). However, further research is required to confirm the findings.

Another reason for the delays in the treatment of patients could be related to the compliance with special protocols during the COVID-19 pandemic. These difficulties may include a lack of vacant beds and facilities (CT-scan, MRI) due to the oddly high number of patients during the pandemic, leading to delays in diagnosis and treatment.

Suggestions could be made concerning additional policy changes during the pandemic. The multidisciplinary team (MDT) could utilize virtual platforms for their decision-making meetings. The study also recommends that cancer patients afflicted with COVID-19 immediately start the latter's treatment to reduce their cancer treatment delay.

Conclusion

Cancer is a highly complicated and problematic disease, which stresses the importance of immediate diagnosis and treatment; however, during the COVID-19 pandemic, medical centers may need to take additional measures to protect their cancer patients. For patients to be treated in lower stages and with less progression, we highly recommend that treatments like radiotherapy, chemotherapy, and surgery be performed promptly according to the proposed guideline for rectal cancer management during the COVID-19 pandemic.

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Conflicts of interests: None declared.

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