An Expert Opinion Regarding the Management of Lower Gastrointestinal Cancers During COVID-19 Outbreak in Iran: A Brief Report

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Received: 16 Oct. 2020; Accepted: 21 Apr. 2021

Abstract- Lower gastrointestinal cancer patients, like other immunosuppressed patients, are vulnerable to develop more severe infections. Iran is one of the countries with a high incidence of COVID-19, and some modifications are needed to adjust international protocols to deal with this pandemic. Therefore, our cancer institute has implemented some changes in the current treatment guidelines. In each specialty, all members agreed to choose the minimal intervention. The members know that some recommendations may interfere with the routine best-practice recommendations and decrease the quality measures in the patient's outcome. Therefore, these recommendations are valid just in the epidemic COVID-19 situation in the country. According to the consensus of colorectal and cancer surgery professors, if a patient is a new case of rectal cancer, he or she should be referred to undergo neoadjuvant chemoradiotherapy. But if the patient comes eight to twelve weeks after receiving chemoradiotherapy in accordance with the COVID-19 epidemic phase, it may be possible to delay surgery. A stent can be implanted in a patient with rectal cancer who presents with obstructive symptoms, and surgery can be postponed until resolving the crisis of the COVID-19 epidemic or its downward trend. For colon cancer, we will request a thoracic spiral CT scan. If there was no evidence of pulmonary involvement with COVID-19, the patient would undergo open surgery considering the patient's health and protection tips.

Acta Med Iran 2021;59(5):249-252.

Keywords: Lower gastrointestinal cancers; Coronavirus disease 2019 (COVID-19); Outbreak

Introduction

In March 2020, the World Health Organization declared the novel Coronavirus Disease 2019 (COVID-19) infection a pandemic (1,2). Although all individuals are susceptible to infection, the mortality rate is significantly higher in patients with older age, immunosuppressed status, or severe comorbid diseases, most notably cancer (3,4). Following the report of two deaths of COVID-19 in Qom city by the Ministry of Health of Iran on February 19, 2020, and the announcement of the epidemic of COVID-19, making the decision about whether to perform surgery on cancer patients was challenging. The coincidence of the New Year holidays with the COVID19 disease epidemic complicated the situation more than before.

On the other hand, there is not enough evidence to make a conclusive association between cancer and COVID-19 (5,6). Lower gastrointestinal cancers are one of the common cancers in patients with treatment ranging from surgery, systemic chemotherapy, and radiation therapy. These patients face a higher likelihood of exposure to the virus due to their frequent visits to medical and imaging centers. Furthermore, the immune

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suppression associated with most cancer-directed therapies confers a greater risk of serious complications and mortality from infection with COVID-19 (7,8). As the pandemic continued, the national health system of the country was increasingly engaged in the management of this critical and potentially life-threatening infection. On the other hand, medical centers admit patients who show more severe presentation of COVID-19. Therefore, the risk of involvement of patients referred for other diseases is increased. According to official statistics, Iran is in a critical situation as a result of the outbreak. Until the first of July 2020, there was nearly 11000 mortality and over 230 thousand confirmed patients with Covid-19 infection in Iran (9). Iranian Cancer Institute, affiliated with Tehran University of Medical Sciences, as the oldest institute for cancer diagnosis, research, and treatment in Iran, decided to make changes in lower gastrointestinal cancer surgeries. In this manuscript, we recommend our modifications in the approved lower gastrointestinal cancers guidelines to reduce the frequency of hospital visits for lower gastrointestinal cancer patients as the outbreak continues. The new guidelines will allow us to save the limited health care resources only for urgencies and emergencies and, more importantly, to protect our vulnerable patients against COVID-19. A large group of Iranian medical physicians involved in the care of cancer patients in large academic centers has contributed to this project through a virtual discussion platform.

Materials and Methods

This was an expert consensus study. First, some questions were selected on hot topics regarding lower gastrointestinal cancer management in the Covid-19 outbreak. These questions were then discussed in small groups of experts (4-5 well-known faculty members of the Cancer Institute, TUMS) before the main group discussion. Questions were refined and edited.

Secondly, some experts (15 persons in each session) from three main medical universities (IUMS, TUMS, SHUMS) were invited to discuss the aforementioned questions. These experts were well-known faculty members in the fields of oncosurgery, radiation oncology, colorectal surgery, hematology and oncology, and gastroenterology. Questions were discussed one by one in 2-3 hour sessions to reach a conclusion. Questions included “What are measures to prevent and control infection in healthcare providers and patients?” “How to screen lower GI cancer in the covid-19 outbreak?”, What is the role of neoadjuvant chemoradiotherapy in lower GI cancer in the outbreak? “When to consider a surgical intervention for lower GI cancers?”, What to do in the case of complete bowel obstruction?”, “What is the role of prophylactic antiviral therapy for COVID-19 in cancer patients?”. Questions were discussed each in a session to reach a consensus.

The discussions were done through a “WhatsApp” group considering the titles and the latest news about COVID19. The admin of the group (first author) asked the members to comment on each title by direct questions and case presentations. Also, some items were added according to Frequently Asked Questions (FAQ) banks and databases asked by patients and health care professionals. Finally, the outcome of each session was refined and compiled according to the available guidelines and manuscripts published recently.

Discussion

A) Infection prevention and control

To diminish the spread of the novel Coronavirus (COVID-19), health care professionals should engage in rigorous handwashing and advise their patients to do the same. Social distancing should be reinforced for patients and their families until the pandemic subsides. Information regarding these preventative measures must be distributed among patients through social media or other online outlets and during every medical encounter. Maximum protective care for health care professionals and hospital employees who are in contact with cancer patients is crucial. Clinic staff may need additional training on the use of personal protective equipment (PPE). Lower gastrointestinal cancer patients who refer to hospitals are advised to protect themselves with personal protective equipment like masks and gloves (10,11).

B) Lower gastrointestinal cancers screening

To minimize unessential visits to medical facilities, it is suggested to postpone screening procedures, such as colonoscopy and clinical examinations. This measure will help to reserve human resources available in hospitals and clinics for COVID-19 patients in need of urgent help.

C) Neoadjuvant/Adjuvant systemic therapy

All our wards must provide services to COVID-19 patients. We must choose less toxic systemic therapy for lower gastrointestinal cancer patients, given that toxicity predisposes them to COVID-19 infection, and controlling the complications will become increasingly difficult due to limited human and medical resources. However, according to ASCO's recommendation, “withholding

critical anti-cancer therapy is not currently recommended" (12). Based on previous studies and ASCO recommendations, we do not postpone adjuvant chemotherapy and begin therapy as soon as possible. It is clear that we must strictly follow safety precautions, including personal protection, checking fever and other symptoms like cough and dyspnea for both patients and their families before each cycle of chemotherapy. We need better time management to shorten waiting times before chemotherapy and minimize the number of allowed visitors for each patient. After chemotherapy, the room will be thoroughly cleaned with disinfectants, and the distance between beds of patients in need of chemotherapy has increased.

D) Radiation therapy

All patients requiring radiotherapy will be treated exactly as prescribed protocols. However, after the patient leaves the room, the entire room will be cleaned with disinfectants. Only patients with protective equipment such as a mask, gloves, and gowns will be allowed to enter the ward. In addition, all signs and symptoms of COVID-19 disease will be checked before radiotherapy, and if there are any of them, radiation therapy will be postponed, and infectious counseling will be requested.

E) Lower gastrointestinal cancers surgery

Due to the COVID-19 outbreak, cancer surgeons have to decide whether to have surgery for cancer patients and are reluctant to perform surgery due to the risks related to this crisis. Since most rectal cancers need neoadjuvant chemoradiotherapy, most patients are referred to clinical oncologists. According to the multidisciplinary decision of cancer surgery professors in our institute, all rectal cancers 8-12 weeks after the neoadjuvant chemoradiotherapy are referred for surgery. Therefore, if a patient is a new case of rectal cancer, he/she is referred for performing neoadjuvant chemoradiotherapy. But if the patient comes eight to twelve weeks after receiving chemoradiotherapy in accordance with the COVID-19 epidemic phase, it may be possible to delay surgery, according to the consensus of cancer surgery professors of the Iranian Cancer Institute. According to Donglin Du et study, performing surgery after a waiting interval of >8 weeks after the end of preoperative nCRT (neoadjuvant chemoradiotherapy) is safe and efficacious for patients with locally advanced rectal cancer, significantly improving pCR (pathologic compete for response) without increasing operative time or incidence of postoperative complications, compared to a waiting interval of <8 weeks (13). According to the É. J. Ryan *et al.*, study, A minimum 8-week interval from the end of nCRT to TME (total mesorectal excision) increase pCR and downstaging rates and improves recurrence-free survival without compromising surgical morbidity (14). According to Min Jung Kim *et al.*, delaying surgery by 9 to 11 weeks may increase TN downstaging, but delaying for over 11 weeks may not increase additional tumor downstaging from long-course CRT (15). A stent can be implanted in a patient with rectal cancer who presents with obstructive symptoms during the COVID-19 epidemic phase. Hence, surgery can be postponed until resolving the crisis of the COVID-19 epidemic or its downward trend.

For colon cancer, we will request a thoracic spiral CT scan for both metastases to work up and rule out COVID-19 patchy infiltration. If there was no evidence of pulmonary involvement with coronavirus, the patient is a candidate for surgery. Therefore, the patient will undergo an open surgery considering health and protection tips.

All surgeries will be performed openly in the coronavirus outbreak. Because laparoscopy is an aerosol-generating procedure and it will be possible to contaminate the operating room. However, those who were presented with complete bowel obstruction or peritonitis due to tumor necrosis or perforation, or other emergent conditions underwent a laparotomy and an end colostomy with or without tumor resection according to the patient conditions.

F) Follow-up and supportive care

According to the ASCO recommendation, "there is no evidence to use prophylactic antiviral therapy for COVID-19 in cancer patients" (16). We must inform our patients that they should seek medical attention in the event of fever (T>37.3), tachypnea (RR>20), dyspnea, hypoxia (O_2 sat <93%), or dry cough, however, ASCO does not recommend COVID-19 testing in all cancer patients (16-18). It is recommended to restrict follow-up visits and para clinic activities such as blood testing and imaging except in the presence of symptoms. To reduce the number of hospital/clinic visits and relieve patients' anxiety, healthcare professionals are encouraged to be in touch with them via telephone or web-mediated consulting to support patients remotely and meet their needs. It is possible to learn about symptoms and solve many of our patients' problems without necessarily meeting them in person. Only patients who have undergone surgery during this crisis should refer to the clinics seven days after surgery to remove sutures, provided that they use protective equipment and follow

health tips.

In conclusion, in each specialty, all members agreed to choose as minimal intervention as possible. The modifications aim to reduce the workload of the medical centers and provide the least interface of patients with the medical centers. The members know that some recommendations may interfere with the routine best-practice recommendations and decrease the quality measures in the patient's outcome. Therefore, these recommendations are valid just in the epidemic COVID-19 situation in the country. According to the consensus of colorectal and cancer surgery experts, if a patient is a new case of rectal cancer, he or she should be referred to undergo neoadjuvant chemoradiotherapy. However, if the patient comes eight to twelve weeks after receiving chemoradiotherapy in accordance with the COVID-19 epidemic phase, it may be possible to delay surgery. A stent can be placed in a patient with rectal cancer who presents with obstructive symptoms, and surgery can be postponed until resolving the crisis of the COVID-19 epidemic or its downward trend. For colon cancer, we will request a thoracic spiral CT scan. If there was no evidence of pulmonary involvement with COVID-19, the patient would undergo open surgery considering the patient's health and protection tips.

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