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Protocol for Dealing with Upper Gastrointestinal Cancers in the COVID-19 Outbreak in Cancer Institute of Tehran University of Medical Sciences

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ABSTRACT

Background: In March 2020, the World Health Organization (WHO) declared the novel COVID-19 infection a pandemic. Among high-risk patients infected by the virus, upper gastrointestinal cancer patients, similar to other immunosuppressed patients, are vulnerable to developing more severe infections. Most of the routine activities of medical centers, especially cancer surgery centers worldwide, are affected by the epidemic. Thus, some modifications are needed to adjust international protocols to deal with upper gastrointestinal cancers worldwide.

Methods: The headings of upper gastrointestinal cancer management protocols have been discussed among the university-affiliated professors in different disciplines involved in upper gastrointestinal cancer management at the first peak of COVID-19 in Iran in March 2020. The discussions were done through an interactive application (WhatsApp and Telegram) in which participants considered the headlines and the latest news about COVID-19. Under each heading, we provide the consensus of all members in the related disciplines.

Recommendations and Conclusion: All members agreed to choose the most effective and the least hazardous recommendations regarding patients and medical staff in each specialty. The members understand that some recommendations may intervene with the standard best practice and reduce the best outcome that the patient can gain with standard management. Therefore, these recommendations are legitimate simply at the peak of the epidemic COVID-19 situation or the surge of any other unknown situations that we may encounter in the future. According to the consensus of cancer surgery professors in several cancer surgery centers, patients with T1 and T2 gastric cancer without lymph node involvement should undergo upfront surgery. Patients with T3 or more and/or lymph node involvement will have total neoadjuvant chemotherapy, and the surgery should be delayed until the end of the COVID-19 peak. Diagnostic laparoscopy should be postponed during the peak of COVID-19 till after the completion of neoadjuvant chemotherapy. Upfront surgery should be performed in patients with esophageal cancer (adenocarcinoma or SCC) with T1 or T2 and without lymph node involvement. In patients with T3 or more and/or lymph node involvement, neoadjuvant chemoradiotherapy (CRT) is recommended. Endoscopic stent placement is preferred for patients who complete neoadjuvant CRT during the peak of COVID 19 and have severe dysphagia. A PET-CT scan will be performed in patients without dysphagia. In the status of high uptake, surgery is reasonable, but in low uptake status without any dysphagia, only conservation is our suggestion.

Keywords: Upper Gastrointestinal Cancers; COVID-19; Outbreak; Cancer Surgery Centers

INTRODUCTION:

In March 2020, the World Health Organization (WHO) announced the novel COVID-19 infection a pandemic [1]. Although all individuals are liable to infection, the mortality rate is significantly higher in patients older than 65, male patients, with immunosuppressed status, and intense comorbidities [2.3]. Most patients with cancer are considered to be immunosuppressed. They are more susceptible to getting COVID-19 infection due to immunosuppression, prolonged hospital stay, and the necessity of multiple visits to the hospital or clinic. At first, according to the literature, it was assumed that cancer patients who get COVID-19 are more prone to severe complications like ICU admission and the need for invasive ventilation and death. However, after two years, some studies are against it. There is not enough evidence to make a conclusive association between cancer and COVID-19, considering if cancer patients are more prone to get the infection, and if they get it are more susceptible to have the severe complications of COVID-19. Thus, the management of patients with cancer in the COVID-19 era is a dilemma [4.5.6].

Following the report of two deaths of COVID-19 in Qom city by the Ministry of Health of Iran on February 20, 2020, and the announcement of the epidemic of COVID19, the decision to perform surgery on cancer patients became challenging. In Iran, the period from March 20 to April 2 is the time for the new year celebration. The coincidence of the New Year holidays with the COVID-19 disease epidemic complicates the situation.

As a result, the Iran Cancer Institute, affiliated with the Tehran University of Medical Sciences, as the oldest institute for cancer diagnosis, research, and treatment in Iran and other cancer surgery centers, decided to change upper gastrointestinal cancer surgeries.

Upper gastrointestinal cancers have a multimodal treatment strategy ranging from surgery, systemic chemotherapy, and radiation therapy. These patients face a higher likelihood of exposure to the virus due to frequent visits to medical and imaging centers, prolonged hospital stays, and more visits from a family member who desires to support the patients throughout their critical time in the Iranian culture. Moreover, compared to other surgical interventions, patients undergoing Gastrointestinal system (GIS) cancer surgery have a relatively long hospital stay because of several follow-up variables like oral tolerance, movement of bowel loops, leakage of anastomosis, bleeding, and surgical site infection, which may cause high morbidity and mortality. The extended hospital stay is another risk factor that amplifies the risk of infection with COVID-19. Hence, the present study group is highly susceptible to COVID-19 infection [7]. Furthermore, immune suppression associated with most cancer-directed therapies confers a greater risk of severe complications and mortality from infection with COVID-19[7.8]. Developing data didn't confirm any powerful correlation between COVID-19 and cancer, contrary to primary concern about the negative association between these two [9.10]. Data from the USA demonstrated that cancer patients were not at a higher risk of adverse effects of COVID-19. They even declared cytotoxic chemotherapy was not associated with a severe or critical COVID-19 event. Studies from the UK also showed that chemotherapy in the past month had no relation to mortality from COVID-19 [6].

As the pandemic continues, the country's national health system will be increasingly engaged in managing this critical and potentially life-threatening infection. Most staff, sources, and surgical beds will be relocated to manage COVID-19 patients. Further, medical centers hospitalize patients who show more severe presentation of COVID-19. Therefore, the risk of involvement of patients referred for other diseases increases. According to official statistics, Iran is in a dire situation due to the outbreak [11.12.13]. From March 25, 2020, to December 16, 2021, the number of infected patients was 6,162,954, and the deaths were 130,883, based on the reports by the Iranian Ministry of Health [11]. This paper recommends our modifications to the approved upper gastrointestinal cancer guidelines to reduce the frequency of hospital visits for upper gastrointestinal cancer patients as the outbreak continues. We now face the sixth wave of COVID-19 in our country. 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 and limited human sources against COVID-19. A big group of Iranian medical physicians managing cancer patients in large academic centers has contributed to this project through a virtual discussion platform.

Methods:

The headings of upper gastrointestinal cancer management protocols were discussed among university-affiliated professors in different disciplines (multidisciplinary approach) involved in cancer management. The discussions were done through a "WhatsApp" group considering the titles and the latest news about COVID-19. Regarding each topic, we considered the consensus of all members in the related disciplines. The group's admin (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.

Discussion and Recommendations:

A) Infection prevention and control

To diminish the spread of the novel Coronavirus (COVID-19), health care professionals should engage in rigorous handwashing and wear masks 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 might need extra training on personal protective equipment (PPE). Upper gastrointestinal cancer patients who refer to hospitals are advised to protect themselves with personal protective equipment like masks and gloves [12.13]. Their temperature is checked before they enter the hospital.

B) Upper gastrointestinal cancers screening:

To minimize unessential visits to medical facilities, it is suggested that screening procedures, such as esophagogastroduodenoscopy and clinical examinations of high-risk patients for esophageal or gastric cancer, be postponed until the end of the peak of COVID-19 and at least 12 weeks, as these cases were classified as low priority procedures. This measure will help reserve human resources available in hospitals and clinics for COVID-19 patients who need urgent help [12].

C) Neoadjuvant /Adjuvant systemic therapy:

We must choose less toxic systemic therapy for upper gastrointestinal cancer patients because toxicity predisposes them to COVID-19. Oral chemotherapy drugs are preferred instead of their intravenous counterparts. Another important recommendation is promoting "home chemo" for less toxic regimens. In addition, regimens with fewer required visits are preferred, for instance, every 3 weeks as an alternative to every 2 weeks. GCSF for regimens with moderate bone marrow suppression has also been encouraged [14]. Definitive CRT should replace surgery for high-risk and marginally effective surgery [15].

Due to limited human and medical resources, managing the complications will become increasingly challenging. However, according to ASCO recommendation, "withholding critical anti-cancer therapy is not currently recommended" [12.13]. Based on previous studies and ASCO recommendations, we do not postpone adjuvant chemotherapy and begin therapy as soon as possible. We must entirely take after safety precautions, including personal protection, temperature checking, 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 to zero. 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 precisely 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. If there are any of them, radiation therapy will be postponed, and infectious counseling will be requested.

E) Upper gastrointestinal cancers surgery:

Due to the crisis of the COVID-19 outbreak, oncologic surgeons have to decide to perform surgery on cancer patients or choose other options. As well as dealing with patients who are reluctant to have surgery due to fear related to this crisis. Since most esophageal and gastric cancers referred to our cancer institute are T2 and higher and N1 or higher, they mostly need neoadjuvant chemotherapy. Therefore, most of our patients are referred to clinical oncologists. According to our institute's consensus of cancer surgery professors, gastric cancer with T1 and T2 without lymph node involvement should have instant surgery. Total neoadjuvant chemotherapy would be done first in patients with T3 or more and with or without lymph node involvement. Surgery should be postponed until the end of the COVID-19 peak or for 12 weeks. In this phase, no diagnostic laparoscopy will be performed. Our recommendation for esophageal cancer is that T1, T2, and N0 should have upfront surgery. Neoadjuvant CRT would be performed for patients with Esophageal cancer with T3, T4, and N1 or more. An endoscopic stent could be located in patients with severe dysphagia. Patients who completed their neoadjuvant CRT during the COVID-19 peak will undergo a PET-CT scan. In the status of high uptake, surgery is performed. Still, in low uptake cases without any dysphagia, only conservation is our suggestion until the outbreak's end or downward trend.

All patients with gastric or esophageal cancer complications like bleeding, obstruction, and perforation, which are not amenable to non-operative management, should undergo surgery. According to Fligor SC et al., increased waiting time for surgery does not decrease the survival rate of patients with gastric cancer. The absence of association between increased time to surgery and gastric cancer survival rate should be cautiously perceived [14]. To postpone invasive procedures, the increased application of neoadjuvant therapy in the updated guidelines might be accountable for the unaffected survival rate of gastric cancer patients after an increased time to surgery, which needs subsequent investigation.

F) Follow-up and supportive care:

According to ASCO's recommendation, "there is no evidence to use prophylactic antiviral therapy for COVID-19 in cancer patients" [9]. We must inform our patients that they should seek medical attention in the event of fever (T>37.3), tachypnea (RR>20), dyspnea, hypoxia (O2 sat<93%), or dry cough, however, ASCO does not recommend COVID-19 testing in all cancer patients [12.16.17.18.19]. It is recommended to restrict follow-up visits and para clinic activities such as blood testing and imaging except for symptoms. To reduce the number of hospital/clinic visits and relieve patients' anxiety, healthcare professionals are encouraged to contact 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 and evaluate the incisions. They should use protective equipment and follow health tips.

Conclusion:

All members agreed to choose minimal intervention in each specialty with the best and least hazardous outcomes. The modifications aim to reduce the workload of the medical centers and provide the least interface for the patients with the medical centers [9.10. 20]. The members declare that some suggestions may interfere with the routine best-practice recommendations and diminish the quality measures in the patient's outcome. Therefore, these proposals are authentic just in the epidemic COVID-19 situation. According to the consensus of cancer surgery professors, gastric cancer with T1 and T2 but N0 should be operated on first. Still, in T3 or N1 or more, the surgery will be recommended after full courses of chemotherapy until the end of the COVID-19 Epidemic. In this phase, no diagnostic laparosco-

py will be performed. In esophageal cancer, T1, T2, and N0 need to be upfront operated on. However, T3, T4, and N1 would undergo neoadjuvant CRT. Endoscopic stent placement will be performed for patients who completed their neoadjuvant CRT and have severe dysphagia. In asymptomatic patients, a PET-CT scan will be performed [9.10.21.22.23]. Surgery might be done in the status of high uptake but in the low uptake cases without any dysphagia; the only conservation is our recommendation. Risk stratification needs to be achieved to maximize the benefit of planned procedures and reduce adverse events, which encompass the risk of infection for the patients and/or medical staff and procedure-related complications, and strategies for healthcare capacity and security optimization, aiming to provide healthcare services to most possible people [6].

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Competing Interests:
The authors declare that they have no competing financial interests or personal relationships which have, or could be perceived to have, influenced the work reported in this article.

REFERENCES

1. Branswell H, Joseph A. WHO declares the coronavirus outbreak a pandemic 2020
   Reporting from the frontiers of health and medicine. March 11, 2020. . https://www.statnews.com/2020/03/11/whodeclares-the-coronavirus-outbreak-a-pandemic
2. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020;21(3):335-7.
3. Wang H, Zhang L. Risk of COVID-19 for patients with cancer. Lancet Oncol. 2020.volume 21,issue 4,E181,April 01.2020https://doi.org/10.1016/ S1470-2045(20)30149-2
4. Xia Y, Jin R, Zhao J, Li W, Shen H. Risk of COVID-19 for patients with cancer. Lancet Oncol. 2020 Apr;21(4):e180. doi: 10.1016/S1470-2045(20)30150-9. Epub 2020 Mar 3. PMID: 32142622; PMCID: PMC7130057.
5. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. Volume 395, Issue 10229, P 1054-1062, March 28 2020. https://doi.org/10.1016/S0140-6736(20)30566-3
6. Fernando, S. Veli, M. Mohammadi, B. et al. COVID-19 and Its Impact on Upper Gastrointestinal (GI) Cancer Management. Cancers 2021, 13, 397. https://doi.org/10.3390/cancers 13030397
7. Kamboj M, Sepkowitz KA. Nosocomial infections in patients with cancer. Lancet Oncol. 2009;10(6):589-97.
8. Lindesy H. Preventing infection in immunocompromised cancer patients: Latest recommendations. Oncology Times. 2008;30(18): 25-6.
9. Doran S.L.F., Patel P.H., Chaudry A., et al. COVID-19 infection in patients following hepato-pancreatico-biliary intervention: an early experience. Eur J Surg Oncol. 2020 Apr 28 doi: 10.1016/j.ejso.2020.04.045. pii: S0748-7983(20)30443-1. [Epub ahead of print] [CrossRef] [Google Scholar]
10. Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020;323(13):1239–1242. doi:10.1001/jama.2020.2648
11. Iranian Ministry of Health and Medical Education medical guidelines, Infographic / Existing Statistics of COVID-19 Patients - March 20 2020 to March 21 2020.https://www.isna.ir/news/99010602727
12. ASCO Survey on COVID-19 in Oncology (ASCO). Care of Individuals with Cancer During COVID19. March 2020, https://www.asco.org /asco-coronavirus-information/care-individualscancer-during-covid-19
13. General Information about COVID-19 & Cancer. March 2020.https://www.asco.org /asco-corona-

virus-information/care-individualscancer-during-covid-19
14. Fligor SC, Wang S, Allar BG, et al. Gastrointestinal malignancies and the COVID-19 pandemic: evidence-based triage to surgery. J Gastrointest Surg. 2020;24: 2357–73. https://doi.org/10.1007/s11605-020-04712-5.
15. Wojciech Piotr Polkowsk ,Katarzyna Sędłak ,Karol Rawicz-Pruszyński. Treatment of Gastric Cancer Patients DuringCOVID-19 Pandemic: The West is More Vulnerable. Cancer Management and Research 2020:12 6467–6476
16. National Center for Immunization and Respiratory Diseases (NCIRD) DoVD. About Coronavirus Disease 2019 (COVID-19), March 2020. https://www.cdc.gov/coronavirus/2019ncov/about/index.html
17. National Center for Immunization and Respiratory Diseases (NCIRD) DoVD. Coronavirus Disease 2019 (COVID-19), Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19). March 2020.https://www.cdc.gov/coronavirus /2019ncov/prepare/prevention.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov-%2Fcoronavirus%2F2019-ncov%2Fabout%2Fprevention. Html
18. WHO Regional Office for the Eastern Mediterranean, Daily report on COVID-19 in the Eastern Mediterranean Region, March 26 2020. http://www.emro.who.int/index.html
19. Onder G., Rezza G., Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. J Am Med Assoc. 2020 Mar 23 doi: 10.1001/jama.2020.4683. [Epub ahead of print] [CrossRef] [Google Scholar]
20. Liang W., Guan W., Chen R., et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020 Mar;21(3):335–337. doi: 10.1016/S1470-2045(20)30096-6. Epub 2020 February 14. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
21. Zeng MH, Boni L, Fingerhut A .Minimally Invasive Surgery and the Novel Coronavirus Outbreak: Lessons Learned in China and Italy. Ann Surg2020 Jul;272(1):e5-e6. doi: 10.1097/SLA.0000000000003924
22. Caricato, M., Baiocchi, G.L., Crafa, F. et al. Colorectal surgery in Italy during the Covid19 outbreak: a survey from the iCral study group. Updates Surg 72, 249–257 (2020). https://doi.org/10.1007/s13304-020-00760-3
23. Mao R, Liang J, Shen J, et al. Implication of COVID-19 for patients with pre-existing digestive disease. Lancet Gastroenterol Hepatol. 2020;5:426–428. doi: 10.1016/S2468-1253(20)30076-5. [PMC free article] [PubMed] [CrossRef] [Google Scholar]