One Public Health Crisis into Many Others: The impact of COVID-19 on Upstaging of Gastric Cancer

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Abstract

Introduction: We aimed to investigate how COVID-19 affects patients with gastric cancer (GC) and what should be expected to happen in post-CVOID-19 era.

Methods: A case-control study of GC patients referring to our center in two parallel time periods of February 25th to December 25th of 2020 and 2019 was conducted.

Results: Twenty six patients during COVID-19 and 54 patients during pre-COVID-19 time were recruited. Mean age, gender, tumor location and T status distribution were not statistically different between study groups (all p values > 0.05). Regarding N status, distribution of N0, N1, N2 and N3 in pre-COVID group was as follows: 2(3%), 21(39%), 26(48%) and 6 (10%). In COVID-19 group N0 was not reported and N1, N2 and N3 were 7 (27%), 7 (27%) and 13 (46%) (p value < 0.05). Among pre-COVID patients 6 (11%) patients had gross metastasis in staging laparoscopy (SL) and 10 (18.5%) patients had positive malignant cytology. In COVID-19 group positive SL and positive cytology were found in 9(35%) and 11(42%), respectively (all p values < 0.05).

Conclusion: Health care systems should adopt reasonable approaches to cancer management, otherwise the upcoming pandemic is locally advanced and metastatic cancers.

Introduction:

Late months of 2019 was the beginning of the new era, not only in medical history but in the human race existence. This was the time when the World Health Organization (WHO) declared a pandemic of coronavirus disease 2019 (COVID-19)[1]. Although this disease commonly presents with mild to moderate symptoms but the extraordinary potential to spread, relatively high rate of asymptomatic carriers and the fact that the disease course is not completely known caused the health care systems off guard worldwide[2]. In this regard, it was necessary to rearrange staff and capacity toward management of COVID-19. Numerous international and local guidelines were published which endorsed deferment of non-emergent medical and surgical cases[3]. However, this approach will not be without consequences. One of the most important aspects of upcoming changes in caregiving is cancer management [4, 5]. Slowdowns in national screening programs, diagnosis, initiation of treatment, postponed surgery, clinical trials, and research will lead to high cancer mortality over the coming decade with the potential to “turn one public health crisis into many others” said Director of the National Cancer Institute, Norman Sharpless[6, 7].

On the other hand, it was proposed that cancer patients may have higher susceptibility to be affected by COVID-19 and have excess mortality rate from COVID-19 compared to patients without cancer due to higher hospital visits, poor nutritional state, systemic underlining disease and immune-suppression [8, 9]. Thus, for many patients chemotherapy treatments were postponed, elective curative surgeries were delayed or changed into urgent palliative ones, radiotherapy session were abbreviated, and even intravenous therapies changed to oral therapies at home[10, 11].

Gastric cancer is amongst the ten most common malignancies worldwide and it is still one of the leading causes of cancer-related mortality worldwide[12, 13]. The incidence of gastric cancer relies on geographic location, race, and socioeconomic status. Surprisingly, those regions with high incidence of COVID-19 are the same as areas with the highest occurrence of gastric cancer[14]. The most important prognostic factor determining the survival of patients with gastric cancer is early detection of the disease which might be hindered during COVID-19 pandemic[15].

In this study, we shared our experience in management of gastric cancer in the biggest cancer center of Iran in the post-COVID-19 time. We also showed how COVID-19 affected gastric cancer in terms of local invasiveness. To our knowledge this is the first study specifically dedicated to assess the changes occurred in gastric cancer presentation and stage.

Materials And Methods:

This was a retrospective case-control study designed and conducted under the approval of the ethic committee of Tehran University of Medical Sciences. All patients with gastric cancer referring to Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran, during February 25th and December 25th 2020, were enrolled to the study. February 25th was the day Ministry of Health and Medical Education announced COVID-19 as a national disaster and set restrictive rules of social distancing. The control group consisted of the gastric cancer patients whom referred to Cancer Institute during February 25th and December 25th of 2019.

Cancer Institute as the pioneer of cancer management in Iran set institutional regulation for hospitalization of cancer patients during COVID-19 pandemic with the primary goal of delivering the best available treatment as timely as possible. In order to achieve this, each patient regardless of cancer type must had proceeded these steps before elective hospitalization and during preoperative, operation and postoperative days:

1. Prior to hospitalization, patients were referred to infectious disease clinic, where they were visited by attending infectious disease specialists who had fellowship in infectious disease of immunocompromised and transplanted patients. Every patient monitored for COVID-19 sign and symptoms and those with high susceptibility were examined utilizing spiral chest computed tomography scan (SCCT) and polymerase chain reaction (PCR) for SARS-CoV-2. If a patient had positive result of either SCCT or PCR, he/she was managed either in outpatient or inpatient setting for COVID-19 treatment based on national protocol and subsequent cancer management was postponed. If it was confirmed that patient is eligible for hospitalization and entering operation room, he/she was admitted to surgical oncology ward.
2. During pre-operative days, all patients were hospitalized in single or double bed room, family members were not allowed to accompany except for under legal aged patient and those who need special attention because of the low performance status. All patients were educated about COVID-19 transmission routs and preventive measures and asked to respect social distancing, wear facial

mask and wash hands using alcohol-based antiseptic formulas given. Each patient underwent daily monitoring for sign and symptoms of COVID-19, heart rate, blood pressure, temperature and oxygen saturation by commercially available pulse oximetry devices. In case of developing signs and symptoms related to COVID-19 or unexplained temperature > 38 , oxygen saturation $< 93\%$ or > 5 unit drop in oxygen saturation from the baseline, infectious disease consultation was ordered.

3. During operation time, the minimum number of personnel needed to activate a safe operation environment whom were fully equipped with personal preventive clothing including surgical cap, gown, facial mask and shield were present at the theater. The operation theater was well ventilated.
4. During post-operative days, for both intensive care unit and ward patient, daily monitoring of signs and symptoms related to COVID-19 besides unexplained temperature > 38 , oxygen saturation $< 93\%$ or > 5 unit drop in oxygen saturation from the baseline, C-Reactive Protein Level > 40 persistent for 3 days activated infectious disease consultation.

Patients were enrolled to the study as if they gave written consent of participation, had confirmed gastric cancer using esophago-gastro-deudenoscopy and pathologically proven biopsy and spiral thoraco-abdomino-pelvic computed tomography scan prior to surgery. All patients became candidates to undergo staging laparoscopy (SL) in order to investigate local and peritoneal invasion of the tumor based on National Comprehensive Cancer Network guideline for gastric cancer 2020. Patients with following criteria were excluded from the study; radiological evidence of metastatic disease, current or previous history of chemotherapy.

All patients underwent SL by the same two attending oncosurgeon, using the same technique and the same laparoscopic device. Under general anesthesia and in supine position SL was performed. A 10 mm optic laparoscopic port was inserted via the midline incision below the umbilicus using Hasson technique. All four quadrants of the abdomen as well as pelvis were inspected during laparoscopy and biopsy was taken from any suspicious lesion through insertion of 5mm port. All specimens underwent cytological evaluation by two independent pathologists. The presence of any malignant cells, regardless of the number, confirmed the positive cytology. In the event of discordant reports between two pathologists, specimens were sent for the third review by a pathologist who was blinded to the previous results. Laparoscopic evaluation was considered positive as if adjacent organ involvement, omental involvement or peritoneal seeding were seen.

Data were collected on the following variables: age, gender, tumor location, gastric lesion pathology and clinical stage based on the 8th edition of the American Joint Committee on Cancer tumor-node metastasis staging system for gastric cancer[16].

Categorical variables are shown as number and relative frequency. Also, continuous variables are shown as mean $\pm$ SD. Collected data for categorical variables were compared using the chi-squared test. An independent student t-test was used to compare means between the two groups. All analyses were performed by the two-sided method using Statistical Package of Social Science software (SPSS version 22; SPSS, Inc., Chicago, IL), and the p-value of < 0.05 was set as statistically significant.

Results:

Data on 26 patients during COVID-19 and 54 patients during pre-COVID-19 were analyzed. Mean age $\pm$ SD of COVID and pre-COVID-19 groups were 59.7 ± 11.9 (minimum and maximum: 30–76) and 67 ± 1.2 (minimum and maximum: 44–86) years, respectively. In both groups male gender were higher in numbers and male to female ratio was 18:8 and 36:18 in COVID and pre-COVID-19 group, respectively. The distribution of tumor location in pre-COVID-19 group was cardia, fundus, body, and antrum in 31 (57%), 3 (6%), 13 (24%), and 7 (13%) of cases, respectively. In COVID-19 group, the tumor was located in the cardia, fundus, body, and antrum in 9 (35%), 5 (19%), 10 (38%), and 2 (8%) of cases, respectively. Regarding T status, distribution of T3 and T4 in pre-COVID group were as follows: 32(59%) and 22(41%). T3 and T4 in COVID-19 group were 16 (61.5%) and 10 (38.5%), respectively. Regarding N status, distribution of N0, N1, N2 and N3 in pre-COVID group were as follows: 2(3%), 21(39%), 26(48%) and 6 (10%). In COVID-19 group N0 was not reported and N1, N2 and N3 were found in 7 (27%), 7 (27%) and 13 (46%) cases. Pathology report of gastric lesion in pre-COVID group was as follows: 8(15%) well-differentiated adenocarcinoma, 20 (37%) moderately differentiated adenocarcinoma, 17 (31.5%) poorly differentiated adenocarcinoma and 9 (16.5%) signet ring cell carcinoma. COVID-19 group had 5(19%) well-differentiated adenocarcinoma, 8 (31%) moderately-differentiated adenocarcinoma, 7 (27%) poorly-differentiated adenocarcinoma and 6 (23%) signet ring cell carcinoma. Among pre-COVID patients 6 (11%) patients had gross metastasis in SL in form of peritoneal seeding or omentum involvement and 10 (18.5%) patients had positive cytology report of peritoneal lavage specimen. In COVID-19 group positive SL and positive cytology were found in 9(35%) and 11(42%) cases, respectively.

The statistical analysis regarding the difference observed between age, gender, tumor location, T status and gastric lesion pathology failed to show significant difference (all p values > 0.05). However, the difference between pre-Covid-19 and COVID-19 group in terms of N status, peritoneal involvement by tumor and positive peritoneal lavage for malignancy was statistically significant (all p values < 0.05). Table 1 demonstrate study variables among two groups.

Table 1
Study groups characteristics. * Statistically significant result.

		COVID-19 group	Pre-COVID-19 group	P value
Age, mean $\pm$ SD		59.7 $\pm$ 11.9	67 $\pm$ 1.2	0.84
Gender, n (%)	Male	18 (69%)	36 (66.5%)	0.90
	Female	8 (31%)	18 (33.5%)	
Tumor location	Cardia	9 (35%)	31 (57%)	0.08
	Fundus	5 (19%)	3 (6%)	
	Body	10 (38%)	13 (24%)	
	Antrum	2 (8%)	7 (13%)	
T status	T3	16 (61.5%)	32(59%)	0.82
	T4	10 (38.5%)	22(41%)	
N status	N0	0(0%)	2(3%)	0.004*
	N1	7 (27%),	21(39%)	
	N2	7 (27%)	26(48%)	
	N3	13 (46%)	(10%)	
Gastric lesion Pathology	Well-differentiated Adenocarcinoma	5(19%)	8(15%)	0.61
	Moderately-differentiated Adenocarcinoma	8 (31%)	20 (37%)	
	Poorly-differentiated Adenocarcinoma	7 (27%)	17 (31.5%)	
	Signet Ring Cell Carcinoma	6 (23%)	(16.5%)	
Gross peritoneal Metastasis		9(35%)	6 (11%)	0.02*
Positive peritoneal lavage for malignancy		11(42%)	10 (18.5%)	0.001*

Discussion:

In this study, we showed that although the age and gender distribution of gastric cancer have not changed during COVID-19 pandemic but there is a shift toward more locally advanced tumors; as N stage is getting higher and more cases are presented with disseminated peritoneal cancer at the time of SL.

This finding may be due to the interruption in national cancer screening programs, the use of diagnostic modalities, closure of medical facilities related to oncological evaluation because of resource modification, delay in multidisciplinary sessions for treatment planning of the cancer patients, patients' fear to come to hospitals and overcrowded hospitals with COVID-19 patients[17–19].

New York Society for Gastrointestinal Endoscopy [20, 21] and the European Society of Gastrointestinal Endoscopy (ESGE)[22] emphasized to minimize endoscopy utilization during the pandemic because its aerosol-generating potential may cause COVID-19 infection. Zhu et al[23]., adopted these guidelines and demonstrated that there was an expeditious decrease in elective endoscopic procedures compared to pre-COVID-19 time (911 vs 5746). Their study was suggestive of an increase in the detection rate of upper gastrointestinal malignancies during the pandemic (7.2% Vs 2.2%) but, we assume this finding is because of reduction in total number of endoscopic procedures performed. In our study, we did not found a significant increase in total number of gastric cancer diagnosed.

COVID-19 pandemic subtracted resources away from all other disease; thus even in developed countries and properly funded facilities there are short comes in the budget [24, 25]. This may be a reason to cancel elective surgeries including gastrectomy. Torzilli et al[26]., reported a vast reduction in surgical beds dedicated to cancer patients, a decrease in number of oncologic surgeries performed per week and increased interval time between multidisciplinary team decisions for surgery and performing it in Italy after the pandemic. In our center, we experienced the same situation as described above besides a tragedy happened in our operation room. Before the beginning of the first wave of national lockdown during June 21th and June 28th nearly all the staff of the operation room became infected with the COVID-19. As a result, the operation room was shut down for one week. This disaster ringed a bell to reconsider all the protocols of patient admission, personal protective equipment quality and availability and daily number of staff attending to work.

The Society of Surgical Oncology (SSO) [27]and the European Society for Diseases of the Esophagus (ESDE) [28]proposed guidelines for the surgical management of esophageal or gastric cancer cases during the pandemic which are quite the same in principle rules and adoption of more conservative approaches toward early stages of cancer and leaving the surgery for hemorrhage or gastric outlet obstruction which are refractory to endoscopic/interventional radiological management. The other group of gastric patients who needed to be operated are those who had already completed their neoadjuvant chemotherapy and had undergone a post-chemotherapy assessment of resectability/treatment response. A quite remarkable study was done by Fligor et al[29]., in form of a systematic review aiming at investigating the impact of time to surgery on oncologic outcomes of gastric cancer. Although the studies investigated in this systematic review had heterogeneous populations in terms of gastric cancer stage, neoadjuvant chemotherapy, number of participants and time interval to surgery but finally the authors concluded that the interval to surgery did not impact overall survival or disease-free survival, but the time to surgery over 6 weeks improved pathologic complete response. This statement is in contrast with what was found in Sud et al[30]., study. They designed a per-day hazard ratios of cancer progression from observational studies and applied these to age-specific, stage-specific cancer survival for England 2013–

2017. As a result, it revealed that the greatest rates of deaths arised following even modest delays to surgery in aggressive cancers, with >30% reduction in survival at 6 months and >17% reduction in survival at 3 months for patients with stage 2 or 3 cancers of the bladder, lung, esophagus, ovary, liver, pancreas and stomach. This finding is shocking that each day delay may have devastating results. Turaga et al[31]., used the National Cancer Database and developed models to examine the effect of each one week delay in definitive surgery from diagnosis. The earliest interval when the effect estimate was worse than the previous interval, and statistically different from the baseline was defined as the inflection point. Time to inflection point beyond median current wait time was considered the safe postponement period. For patients with gastric cancer whom underwent surgery prior to chemotherapy; 6, 12, 12 and 12 weeks can be safely deferred from the time of diagnosis without significant impact on 1-year, 3-year, 5-year mortality rates and possibility of complete tumor resection, respectively. Also, for those patients underwent neoadjuvant chemotherapy 12, 12, 9 and 12 weeks are safe intervals without jeopardizing survival benefits after 1-year, 3-year, 5-year and feasibility to completely resect the tumor, respectively. Based on the current guidelines for management of gastric cancer like NCCN 2020 and UpToDate®, SL is needed to accurately investigate the stage of local invasion of the tumor. Nevertheless, the performance of this modality can be challenging as the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) and the European Association for Endoscopic Surgeons (EAES) advised to defer elective laparoscopic surgeries. As we showed, this delay might result in an increase in N stage of the tumor and change treatment plan. Besides in patients who received neoadjuvant chemotherapy, presumptive peritoneal seeding might be cleared with treatment but as the time interval between chemotherapy cession and surgery gets longer, the possibility to reach R0 resection gets lower.

The current study suffers from few limitations should be kept in mind while interpreting the results. We used retrospective design with limited numbers of patients in each group. Also, the diagnostic evaluations were not completely unified as some patients had their CT scan or ultrasound upper endoscopy in facilities other than our center which might have impact on the reported T and N.

Conclusion:

In conclusion the medical world after COVID-19 is not the same as before and it needs justification to meet its old responsibilities. Regardless of how, this pandemic will over, and the world after that might face high numbers of cancer patients at their late stages. Thus, today is our chance to get repared for upcoming cancer waves of tomorrow among those affected by the COVID-19 pandemic and those not.

Declarations

Data availability statement: Data will be available upon direct request to the corresponding author.

Funding statement: This study was conducted using no special grant or funding.

Conflict of interest disclosure: All authors declare that there is no conflict of interest to disclose.

Ethics approval statement: Ethic committee of Tehran University of Medical Sciences approved the study protocol and it is registered under the ID of [IR.TUMS.IKHC.REC.1399.414](https://ethics.research.ac.ir) at <https://ethics.research.ac.ir> .

Patient consent statement: Written informed consent was obtained from all the patient before including in the study. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Permission to reproduce material from other sources. There is no material used from other sources to perform this study.

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Authors' contributions:

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Ramesh Omranipour. M. D.: Critical review

Amirhossein Poopak. M. D.: Writing the paper, Critical review, Data collection and/or processing

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References

1. Salari A, Jalaeefer A, Shirkhoda M. *What is the best treatment option for head and neck cancers in COVID-19 pandemic? A rapid review*. American Journal of Otolaryngology, 2020: p. 102738.
2. Di Fiore F, et al. COVID-19 epidemic: Proposed alternatives in the management of digestive cancers: A French intergroup clinical point of view (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, SFR). Digestive and Liver Disease; 2020.
3. Johnson BA, et al. A systematic review and meta-analysis of surgery delays and survival in breast, lung and colon cancers: Implication for surgical triage during the COVID-19 pandemic. The American Journal of Surgery; 2020.
4. Wu JT-Y, et al. Changes in Cancer Management due to COVID-19 Illness in Patients with Cancer in Northern California. JCO Oncology Practice; 2020. p. OP–20.
5. Zaniboni A, et al. A review of clinical practice guidelines and treatment recommendations for cancer care in the COVID-19 pandemic. Cancers. 2020;12(9):2452.
6. Sharpless NE. COVID-19 and cancer. American Association for the Advancement of Science; 2020.

7. Chan JW, Lee VHF. Will the COVID Pandemic Lead to Uncounted Cancer Deaths in the Future? *Int J Radiat Oncol Biol Phys.* 2020;108(2):351.
8. Chan JW, Lee VH. Will the COVID Pandemic Lead to Uncounted Cancer Deaths in the Future? *Int J Radiat Oncol Biol Phys.* 2020;108(2):351.
9. Vanni G, et al. Delay in Breast Cancer Treatments During the First COVID-19 Lockdown. A Multicentric Analysis of 432 Patients. *Anticancer research.* 2020;40(12):7119–25.
10. Gundavda MK, Gundavda KK, *Cancer or COVID-19? A Review of Guidelines for Safe Cancer Care in the Wake of the Pandemic.* *SN comprehensive clinical medicine,* 2020: p. 1–11.
11. Arpino G, et al. Optimising triage procedures for patients with cancer needing active anticancer treatment in the COVID-19 era. *ESMO open.* 2020;5(5):e000885.
12. Thrift AP, El-Serag HB. Burden of gastric cancer. *Clin Gastroenterol Hepatol.* 2020;18(3):534–42.
13. Orman S, Cayci HM. Gastric cancer: factors affecting survival. *Acta Chir Belg.* 2019;119(1):24–30.
14. Sarmadi M, Marufi N, Moghaddam VK. Association of COVID-19 global distribution and environmental and demographic factors: an updated three-month study. *Environ Res.* 2020;188:109748.
15. Polkowski WP, Sędlak K, Rawicz-Pruszyński K. Treatment of Gastric Cancer Patients During COVID-19 Pandemic: The West is More Vulnerable. *Cancer Management Research.* 2020;12:6467.
16. Wang H, et al., *Superiority of the 8th edition of the TNM staging system for predicting overall survival in gastric cancer: Comparative analysis of the 7th and 8th editions in a monoinstitutional cohort.* *Molecular and Clinical Oncology,* 2018. **9**(4): p. 423–431.
17. Rebecchi F, et al. Impact of COVID-19 outbreak on esophageal cancer surgery in Northern Italy: lessons learned from a multicentric snapshot. *Diseases of the Esophagus;* 2020.
18. Wahed S, et al. Delivering esophago-gastric cancer care during the COVID-19 pandemic in the United Kingdom: a surgical perspective. *Dis Esophagus.* 2020;33(9):doaa091.
19. Ke J, et al. Strategies and recommendations for the management of gastrointestinal surgery during the COVID-19 pandemic: experience shared by Chinese surgeons. *Gastroenterology report.* 2020;8(3):167–74.
20. Philip M, et al. Joint Guidance from SGEI, ISG and INASL for Gastroenterologists and Gastrointestinal Endoscopists on the Prevention, Care and Management of patients with COVID-19. *Journal of Clinical and Experimental Hepatology;* 2020.
21. Sethi A, et al. Donning a new approach to the practice of gastroenterology: perspectives from the COVID-19 pandemic epicenter. *Clinical Gastroenterology and Hepatology;* 2020.
22. Gralnek IM, et al. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic. *Endoscopy.* 2020;52(6):483.
23. Zhu L, et al. *Analysis of selective endoscopy results during the epidemic of coronavirus disease 2019 (COVID-19).* *Zhonghua wei Chang wai ke za zhi = Chinese. J Gastrointest Surg.* 2020;23(4):327–31.

24. Moletta L, et al., *International guidelines and recommendations for surgery during covid-19 pandemic: a systematic review*. International Journal of Surgery, 2020.
25. Akula SM, et al., *Cancer therapy and treatments during COVID-19 era*. Advances in biological regulation, 2020: p. 100739.
26. Torzilli G, et al. A snapshot of elective oncological surgery in Italy during COVID-19 emergency: pearls, pitfalls, and perspectives. Annals of surgery. 2020;272(2):e112.
27. Bartlett DL, et al. Management of cancer surgery cases during the COVID-19 pandemic: Considerations. Annals of Surgical Oncology; 2020. pp. 1–4.
28. Barbieri L, et al. Esophageal oncologic surgery in SARS-CoV-2 (COVID-19) emergency. Dis Esophagus. 2020;33(5):doaa028.
29. Fligor SC, et al., *Gastrointestinal malignancies and the COVID-19 pandemic: evidence-based triage to surgery*. Journal of Gastrointestinal Surgery, 2020: p. 1–17.
30. Sud A, et al. Collateral damage: the impact on outcomes from cancer surgery of the COVID-19 pandemic. Annals of Oncology; 2020.
31. Turaga KK, Girotra S. Are we harming cancer patients by delaying their cancer surgery during the COVID-19 pandemic? Annals of Surgery; 2020.

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