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Gastric cancer during COVID-19 pandemic: What changed?

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Ethics Committee Approval
The study was granted approval by the Erzurum Training and Research Hospital ethics committee (ethics committee approval number: 2021/17-261).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: There is no doubt that oncology patients are among the most affected groups by the pandemic. The aim of this study is the evaluation of the effects of COVID-19 pandemic on patients with gastric cancer.
Methods: We carried out a retrospective cohort study in a non-clean hospital from March 1, 2020, when the pandemic became widespread in Turkey, to August 1, 2021. Patients diagnosed with gastric cancer were compared with patients in the pre-pandemic period. The cancer stages, operation types and results of the patients were compared between the groups.
Results: A total of 181 patients were included in the study. While a decrease was observed in stage 1 (P=0.01) and stage 2 (P=0.09) tumors during the pandemic period, an increase was observed in the number of stage 4A (P=0.002) and stage 4B (P=0.001) tumors on admission. Patients who received neoadjuvant chemotherapy during the pandemic were significantly less when compared with the pre-pandemic group (P=0.04).
Conclusions: When the necessary precautions are taken, surgical oncology can be safely performed even in a non-clean hospital. With the spread of similar study results, patients' anxiety-based COVID-19 fear will be overcome.

Keywords: Gastric cancer, COVID-19, Pandemic

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Introduction

Since the beginning of 2020, there has been a global fight against the COVID-19 pandemic. While the pandemic continues, oncological patients and patients with chronic diseases are undoubtedly the most affected. In a study conducted in Italy during the pandemic, there was a reduction of 70% in oncological units on the basis of hospital beds (median: 50%) and a 76% reduction in surgical activities [1]. Centers provide guidelines on what should be the appropriate approach for securing the diagnosis and treatment of other chronic and acute patients, including cancer patients, from these effects. To use the hospital more efficiently, the Centers for Disease Control and Prevention suggested rescheduling elective surgeries [2]. Later, the American College of Surgeons (ACS) and the Society of Surgical Oncology (SSO) published recommendations for elective surgeries [3, 4].

Over 1 million people are diagnosed with gastric cancer each year [5]. As with many malignant diseases, radical surgery and aggressive treatment together constitute the cornerstone of treatment. Delayed treatment results in extensive metastasis, disease recurrence, and reduced survival.

Although the centers have expressed their views on the appropriate timing for the operation during the COVID-19 pandemic, it is not clear how these will affect the results. In the current study, it was aimed to evaluate the effects of the pandemic on the diagnosis and treatment of patients with gastric cancer in a single center.

Materials and methods

Study design and patients

Patients diagnosed with gastric cancer in Erzurum Regional Training and Research Hospital between 01/03/2020 and 01/08/2021, when the pandemic was effective countrywide, were included in the study. The control group consisted of patients who applied to hospital between 1/01/2019 and 01/03/2020, just before the onset of the pandemic and were diagnosed with gastric cancer. This retrospective cohort study, in accordance with Declaration of Helsinki, was granted approval by the Erzurum Training and Research Hospital Ethics Committee (Ethics Committee approval number: 2021/17-261).

After all of the patients participating in the study were evaluated by the tumor council, patients with T1 and T2 tumors, without lymph node metastasis and without bleeding, gastric outlet obstruction, and patients with advanced age who could not tolerate neoadjuvant therapy were operated on. All other patients were operated after receiving neoadjuvant therapy.

Demographic characteristics, comorbidities, complaints on admission, preoperative laboratory parameters and imaging studies, pathological diagnosis, tumor localization, stages defined by American Joint Committee on Cancer (AJCC), neoadjuvant therapy, American Society of Anesthesiologists (ASA) scores, type of operation, total length of stay, Clavien-Dindo classification (CDC) score, postoperative tumor stages, mortality, and 30-day follow-up results after discharge were recorded. Total length of hospital stay was defined as the time between hospitalization and discharge.

Preoperative evaluation during the COVID-19 period

All of the patients who were scheduled to have surgery during the pandemic were hospitalized with their companions and isolated for 5 days. A nasal and pharyngeal swab test (polymerase chain reaction test) was given on admission and in the final 24 hours preoperatively. Patients with negative tests were operated, whereas the surgery was postponed for positive patients. The isolation rules recommended by the guidelines were followed.

Statistical analysis

SPSS Statistics for Windows 17.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analyses. Numerical variables with normal distribution were shown as the mean (SD), whereas those without normal distribution were shown as the median (minimum-maximum). Categorical variables were presented as numbers and percentages. The Mann-Whitney U and Kruskall-Wallis H tests were used for the intergroup comparisons of the numerical variables without normal distribution. Categorical variables were compared with the $\chi 2$ and Fisher exact $\chi 2$ tests. For the relationships among numerical variables, Pearson and Spearman correlation analyses were used.

Results

The study was conducted with a total of 181 patients, comprising 115 (63.5%) males and 66 (36.5%) females. Of the patients, 92 (50.8%) were evaluated in the pre-pandemic period, and 89 (49.2%) in the pandemic period. The mean age of patients during the pandemic and pre-pandemic period were 65.78 (11.68) and 63.45 (12.32), respectively (P=0.19) (Table 1).

Table 1: Laboratory results, demographic data, and procedure details of the patients

	Pandemic group n: 89	Pre-pandemic group n: 92	*P*-value
Sex (male)	59 (66.3%)	56(60.9%)	0.44
Age (mean (SD))	65.78 (11.68)	63.45 (12.32)	0.19
Hemoglobin (Hgb) (mean (SD))	10.74 (2.48)	12.61 (1.83)	<0.01**
Albumin (mean (SD))	3.88 (0.57)	4.25 (0.34)	0.49
Alarming symptoms (n)	89	92	<0.01**
Positive	80 (44.2%)	47(26%)	
Negative	9 (5%)	45 (24.9%)	
Hospital stay (days) (mean (SD))	13.08 (5.89)	8.53 (2.26)	<0.01**
Tumor localization			
Cardia (n)	42 (47.2%)	58 (63%)	0.03**
Corpus (n)	18 (20.2%)	13 (14.1%)	0.27
Antrum (n)	29 (32.6%)	21 (22.8%)	0.14
Operation type	64 (43.5%)	83 (56.5%)	0.04**
Open procedure	39 (60.9%)	64 (77.1%)	
Minimal invasive surgery (Robotic assisted)	25 (39%)	19 (22.8%)	
Total gastrectomy			
Open	31 (21.1%)	56 (38.1%)	0.02**
Robotic assisted	15 (10.2%)	10 (%6.8)	0.06
Subtotal gastrectomy			
Open	8 (5.4%)	8 (5.4%)	0.58
Robotic assisted	10 (6.8%)	9 (6.1%)	0.39
Tumor histology (n)			
Adenocarcinoma	80	84	0.74
Neuroendocrine tumor	4	2	0.11
MANEC	5	6	0.82
Morbidity (CDC)	12/64 (18.7%)	19/83 (22.8%)	0.52
Grade 1	12	15	
Grade 2	0	1	
Grade 3	0	3	
Grade 4	0	0	
Grade 5	0	0	
Mortality	0	0	

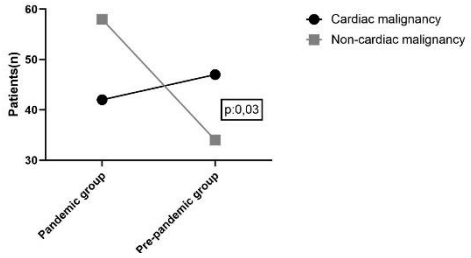
MANEC: mixed adenoneuroendocrine carcinoma, CDC: Clavien-Dindo classification, ** P<0.05 was considered as significant for the statistical analyses.

The mean length of hospital stay was 13.08 (5.89) and 8.53 (2.26) days during the pandemic and pre-pandemic period, respectively (P<0.001).

When the complaints of the patients were classified as alarming symptoms (weight loss, persistent vomiting, dysphagia, anemia) and non-specific symptoms (non-specific epigastric pain, dyspepsia, early satiety), it was observed that the patients presented with alarming symptoms are significantly dominant during the pandemic period when compared with pre-pandemic period (80 (89%) and 47 (51.1%) patients during the pandemic and pre-pandemic period, respectively) (P<0.001). In addition, alarming symptoms were found to be correlated with the clinical stage of the disease (r=0.57, P<0.01).

When the tumor localizations were evaluated during the pandemic period, tumors with antrum and corpus (distal) localization were observed more frequently, while a significant decrease was observed in proximal tumors (P=0.03) (Figure 1).

Figure 1: Gastric tumor location and periodical difference



No significant difference was observed between the groups regarding the tumor histology. The details of the pathological classification according to the tumor stages are shown in Table 2.

Table 2: Distribution of the tumor histology and stage among the groups

	Pandemic group (n)	Pre-pandemic group (n)	*P*-value
Adenocarcinoma	80 (100%)	84 (100%)	0.74
Stage 1	4 (5%)	16 (19%)	0.005**
Stage 2A	0	0	
Stage 2B	6 (7.5%)	17 (20.2%)	0.01**
Stage 3	33 (41.3%)	40 (47.6%)	0.41
Stage 4A	16 (20%)	3 (3.6%)	0.001**
Stage 4B	21 (26.3%)	8 (9.5%)	0.005
Neuroendocrine tumor	4 (100%)	2 (100%)	0.11
Stage 1	1	0	
Stage 2	0	0	
Stage 3	1	2	
Stage 4	2	0	
Mixed adenoneuroendocrine carcinoma	5 (100%)	6 (100%)	0.82
Stage 1	1 (20%)	2 (33.3%)	0.63
Stage 2A-2B	0	0	
Stage 3	0	2 (33.3%)	
Stage 4A	0	1 (16.7%)	
Stage 4B	4 (80%)	1 (16.7%)	0.03**

** P<0.05 was considered as significant for the statistical analyses.

In the clinical staging of the disease, a decrease was observed in stage 1 (P=0.01) and 2B (P=0.009) tumors during the pandemic period, while an increase in the number of stage 4A (P=0.002) and 4B (P=0.01) tumors was observed (Figure 2). In the postoperative pathological staging, significant difference was not observed between the groups (P=0.22), except the significant increase in stage 3B during the pandemic period (P=0.04) (Table 3).

Figure 2: Differences in the tumor stages between periods

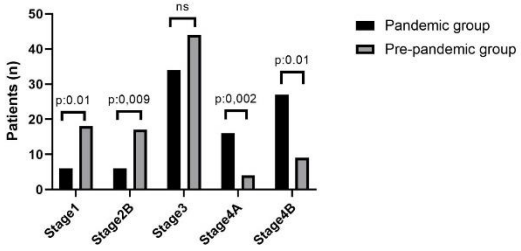
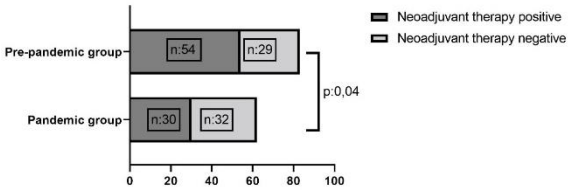


Table 3: Clinical and pathological stages of the patients

	Pandemic group (n: 89)	Pre-pandemic group (n: 92)	*P*-value
Clinical stage			
Stage 1	6 (3.3%)	18 (10%)	0.01*
Stage 2A	0	0	
Stage 2B	6 (2.8%)	17 (9.4%)	0.009*
Stage 3	34 (18.9%)	44 (24.4%)	0.21
Stage 4A	16 (8.8%)	4 (2.2%)	0.002*
Stage 4B	27 (14.9%)	9 (5%)	0.001*
Postoperative stage			
Neoadjuvant group	30/62 (48.3%)	54/83 (65%)	0.04*
Complete response	0	2 (1.4%)	0.21
Stage 1	8 (5.4%)	9 (6.1%)	0.75
Stage 2	6 (4.1%)	15 (10.2%)	0.22
Stage 3	16 (11%)	28 (19%)	0.46
Non-neoadjuvant group			
Stage 1A	2 (1.4%)	3 (2.0%)	0.87
Stage 1B	1 (0.7%)	2 (1.4%)	0.21
Stage 2A	4 (2.7%)	7 (4.8%)	0.61
Stage 2B	6 (4.1%)	2 (1.4%)	0.06
Stage 3A	10 (6.8%)	11 (7.5%)	0.68
Stage 3B	8 (5.4%)	3 (2%)	0.04*
Stage 3C	1 (0.7%)	1 (0.7%)	0.85

Patients receiving neoadjuvant therapy were found to be significantly less common during the pandemic period than the pre-pandemic period (30 (48.3%) patients vs. 54 (65%); P=0.04) (Figure 3). Minimally invasive surgery was performed on 25 (39.06%) patients during the pandemic period and 19 (22.89%) patients during the pre-pandemic period. Details of the surgical procedures applied are given in Table 1.

Figure 2: Differences between the groups in terms of neoadjuvant therapy



Mortality in postoperative first month was not observed in either groups. There was no difference between the groups regarding the postoperative morbidities (12 and 19 patients in pandemic and pre-pandemic period, respectively, P=0.52) (Table 1).

Discussion

The pandemic continues to affect life worldwide. Oncological patients are among the most affected people. In this study, it was aimed to evaluate how patients diagnosed with gastric cancer were affected by the pandemic period and to evaluate the surgical results. As a result, it was observed that patients were adversely affected during the pandemic period and usually presented with more advanced tumors.

First of all, the presence of anemia and alarming symptoms on admission was remarkable in the pandemic group. The presence of alarming symptoms and anemia in gastric cancer, which compels the patient to apply to the hospital during the diagnosis process, is quite specific for the diagnosis, but indicates a poor prognosis. In previous studies, it was found that the presence of at least 1 alarming symptom decreased the 5-year survival rate by 26% on average [6–8] and was associated with a 3-fold increase in the risk of death [6]. One of the most important reasons for the low 5-year survival rate in gastric cancer in Eastern studies (8%–26% in Eastern series, 50%–60% in Western series) is thought to be the widespread screening programs in Western regions without considering alarming symptoms [9–14].

The effect of delayed surgery on survival in gastric cancers is not clear. In a systemic review evaluating the oncological results of the time to surgery for colorectal, pancreatic, and gastric cancers between 2005 and 2020, Fligor et al. [15] stated that in case of serious resource limitations, a delay of surgery up to three months in early-stage gastric cancers and up to six weeks in advanced gastric cancers can be considered. On the other hand, Brenkmann et al. [16] analyzed the long-term survival of 2077 gastric cancer patients who were not treated with neoadjuvant therapy, and found no significant difference between patients operated in less than five weeks and those operated after eight weeks. There is not any randomized study showing the effect of the waiting time on survival in gastric cancer. Undoubtedly, it was not foreseen that the COVID-19 pandemic, which broke out in early 2020, would still continue. In this study, it was observed that patients mostly applied with advanced stage tumors during this 17-month period of the pandemic.

The current recommendations for neoadjuvant chemotherapy (FLOT) or chemo-radiotherapy are to delay extended total gastrectomy as much as possible [4, 17]. If the treatment ends during the pandemic, it is controversial how to continue the treatment. However, considering the non-negligible risk of immunosuppression, surgery can be recommended to patients with a low risk [18]. In line with these recommendations, an increase was predicted in patients receiving neoadjuvant therapy, but it was observed that the rate of patients who received neoadjuvant therapy during the pandemic period decreased as the disease progressed to an advanced stage and they could not tolerate neoadjuvant therapy. The lack of sufficient data on this subject today will become clear with the studies carried out.

Interestingly, the number of proximal gastric tumors was significantly reduced in patients who applied during the pandemic period, and gastric tumors were more distally located. Proximal gastric tumors show less clinical signs [19] and this result might be from patients not applying to the hospital without their complaints being obvious. As a matter of fact, the significantly higher number of patients with alarming symptoms in this period compared to those with non-specific symptoms supported the inference herein. Considering the histopathological features, it was also observed that patients with a diagnosis of MANEC applied more frequently with advanced tumors in this period. This may show that MANEC is a more aggressive tumor than both adenocarcinoma and isolated neuroendocrine tumors.

Although, due to the lack of data, the centers apply different protocols on the evaluation of patients for COVID-19 before the operation, isolation undoubtedly seems to be the key point to implement [20]. Thorax CT one day preoperatively is no longer recommended in the updated protocols for the detection of asymptomatic patients [21]. Patients were routinely hospitalized for 5 days, except for emergencies, and PCR test was performed at the time of admission and 1 day before the operation. There was no COVID-19 related morbidity or mortality during this period.

In addition to the fact that the results of this study were single-centered, the most important limitation of our study is the short follow-up period and the lack of long-term survival results, but still, a similar study on gastric cancer patients has not yet been published and the results are brand new in the pandemic period.

Conclusion

As a result, in this study, in which the patients who applied to our hospital due to gastric cancer within the 17-month period of the pandemic and pre-pandemic period were compared, it was found that the patients during the pandemic presented with more advanced cancer. In addition, when the necessary precautions were taken during the pandemic process, it was seen that the treatment of diseases such as cancer, for which, surgery is the basis of curative treatment, can be safely performed even in a pandemic hospital. We believe that as a result of reserving the formerly prepared departments for oncological patients and increasing similar studies, anxiety-based COVID-19 fear will be overcome and the patients will safely admit to the hospital.

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