

Research Article

Long-Term Effects of COVID-19 Pandemic on Oncology Patients

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Abstract

Objectives: COVID-19 pandemic affects the health care systems in the whole world. In this study, we try to evaluate the prognostic effect of the chemotherapy delay or cessation of the patients due to hospital fear and social regulations.

Methods: Patients on active cancer treatment were retrospectively analyzed. The age, gender, diagnosis, chemotherapy type, rendezvous, and coming dates were recorded.

Results: Before March 11, 2020, 52 patients experienced four delayed chemotherapy treatments (3.7%), compared to 43 delayed chemotherapy treatments (39.8%) in 107 patients (39.8%) after the first case of COVID-19 was recorded in Turkey and restrictions started to be applied. No reason was given for the delayed treatments of 20 patients who did not show up for their chemotherapy appointments. The overall mortality of those who experienced treatment delays after the announcement of the COVID-19 pandemic was no different from those before.

Conclusion: The non-specific regulations and declarations confused patients and prevented their access to their much-needed treatment. Although the regulations were detrimental to chemotherapy adherence, the overall mortality between groups did not differ.

Keywords: Adherence, cancer, chemotherapy, COVID-19, SARS-COV-2

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After the COVID-19 outbreak, which started in China in the last month of 2019, accumulating evidence supported the highly affected groups were older and immunocompromised patients. The high frequency of fatal respiratory disease was the major problem during the treatment of COVID-19.^[1] Cancer or transplant patients who receive treatment are considered to be at increased risk. This risk was mainly derived from immunosuppressive and immunostimulant drugs.^[2,3] World Health Organization had reported over three hundred million confirmed cases, nearly 5.5 million deaths till February 2022 worldwide.^[4] For both adjuvant and palliative care most of the organizations offered specific propositions for patient care.^[5,6]

After the first case of COVID-19 was reported in Turkey on March 11, 2020, the Ministries of Health and Interior applied some public restrictions, including travel restrictions, traffic restrictions, social distancing homes, and centralized quarantine.^[7] There have been several studies evaluating the effects of the pandemic in oncology practice in Turkey.^[8–11]

Although adherence to both oral and intravenous chemotherapy agents in cancer patients is a highly studied area, there is a lack of data evaluating the prognostic effects of chemotherapy adherence among cancer patients.^[12,13]

The present study evaluates the prognostic effect of the cessation of chemotherapy in patients due to hospital fear and the applied social regulations.

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Methods

Study Participants

The records of patients undergoing active cancer treatment in a Medical Oncology Department were analyzed retrospectively, including the patients' age, gender, diagnosis, chemotherapy type, rendezvous, and coming dates. The dates of last visits, death, and diagnosis, as well as mortality data, were retrieved from the archive files. COVID-19 infection data and the final status of the patients were also recorded. Delays of three consecutive chemotherapy appointments before and after March 11, 2020, were listed. Patients with inadequate records were excluded from the study.

Ethics

The study was approved by both the Turkish Ministry of Health and the ethics committee of Eskişehir Osmangazi University Faculty of Medicine and was conducted following the principles of the Declaration of Helsinki and all applicable regulations (23.09.2021 dated and 03 numbered).

Statistics

IBM SPSS Statistics (Version 22.0. Armonk, NY: IBM Corp.) was used for the statistical analysis. Descriptive data are presented as either mean or median for continuous variables, and frequencies and percentages are reported for categorical variables. A Pearson χ^2 test is used for the assessment of associations among the categorical variables. The rates were compared using Z-test by E-PICOS software.

Results

Enrolled in the study were 108 patients aged 22–83 years (67 female; 41 male), with a median age of 58 years. The most common diagnosis was breast cancer (43.5%), followed by colorectal cancer (24.1%). Of the total, 63 percent of the chemotherapy treatments were adjuvant and 36 percent were palliative (Table 1).

Before the first case of COVID-19 and the application of restrictions in Turkey, four chemotherapy delays (3.7%) were observed among 52 patients, while 107 patients experienced 43 delays in chemotherapy treatments (39.8%) after the first date ($p < 0.001$). After the patients who died during treatment were excluded from the results, there was still a significant difference in the delays in chemotherapy between groups ($p < 0.001$). In terms of adjuvant treatment, the delays or discontinuations differed significantly among the pre- and post-COVID-19 era ($p = 0.002$) (Table 2).

There were no hospitalizations that resulted in treatment discontinuations or delays. The three main reasons for

Table 1. The features of the study population

Features		
Gender	Male	Female
N: (%)	41 (38%)	67 (62%)
Age	Mean	Median
Years	58.02	58
Diagnosis	Numbers	Percentage
Breast	47	43.5
Colorectal	26	22.2
Lung	14	14
Other	23	21.3
Stage	Numbers	Percentage
I	3	2.8
II	25	23.1
III	41	38
IV	39	36.1
Treatment type	Adjuvant	Palliative
Adjuvant	69	63.9
Palliative	39	36.1
N: (%)	69 (63.9)	39 (36.1)

delay or cessation were hematologic toxicity, no reason, and other (imaging, COVID-19 investigation, infection, or death). In the pre-pandemic period, two patients developed hematologic toxicity, one had imaging for symptoms while one patient had the non-COVID infection for treatment delay. In the pandemic period, nine patients developed hematologic toxicity resulting in a treatment delay. Two patients died, reasons which are related to cancer. Eleven patients had other reasons not showing up for chemotherapy including death. Twenty-three patients did not show up for their chemotherapy appointments. The delays in treatment without reason were significantly different in the pre- and post-COVID-19 pandemic study periods ($p = 0.04$). The hematologic toxicity rates were similar in the pre- and post-COVID-19 periods ($p = 0.18$) (Table 3). There were no COVID-19 infections and or COVID-19-related deaths in the study.

A total of 33 patients died during follow-up. There was no difference in the overall survival of those whose treatments were or were not delayed ($p = 0.16$) (Fig. 1), with median survival times of 36 and 62 months, respectively. There was also no difference when the study population was stratified according to gender, stage, and chemotherapy type ($p = 0.96$; $p = 0.19$; $p = 0.20$, respectively). There was a significant survival difference in the breast cancer subgroup, with the median survival time not being reached in the chemotherapy adherent group ($p < 0.001$) (Fig. 2).

Table 2. The delay or discontinuation treatment among groups

Features			
Treatment delay (All population)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	4/52 (3.7)	43/107 (39.8)	<0.001
Treatment delay (Adjuvant treatment)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	3/31 (9.7)	28/69 (40.6)	0.002
Treatment delay (Palliative treatment)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	1/21 (4.8)	15/38 (39.4)	0.004
Treatment delay (Breast Cancer)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	1/24 (4)	13/47 (27.6)	0.01
Treatment delay (Lung Cancer)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	0/8 (0)	6/13 (46.3)	0.02
Treatment delay (Colon Cancer)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	1/13 (7.6)	12/24 (50)	0.01
Treatment delay (Other Cancers)	Pre-COVID-19	Post-COVID-19	p value
N: (%)	2/7 (28)	12/23 (52)	0.36

Table 3. Comparison of reasons for treatment delays

Group	Pre-COVID-19	Post-COVID-19	p
Hematologic toxicity n (%)	2/4 (50%)	9/43 (20.9%)*	0.18
No reasons	0/4 (0%)	23/43 (53.8%)	0.04
Other (imaging, infections, COVID-19 investigation, death)	2/4 (50%)*	11/43 (25.5%)	0.29

*: One patient had two treatment delays.

Discussion

It was found in the present study that the COVID-19 pandemic and the resulting social regulations led to a decline in intravenous chemotherapy adherence in patients. Although chemotherapy adherence was disturbed by the regulations and coronaphobia, the OS did not change significantly between the groups.

The study population was heterogenous in terms of the different cancer types. In terms of breast cancer; although different considerations were offered by organizations for treatment types such as chemotherapies and bone modifying agents.^[14] When considering chemotherapy adherence only in breast cancer patients, a significant disruption was noted in treatments, which resulted in decreased survival levels in this patient subgroup (p<0.001). Although the

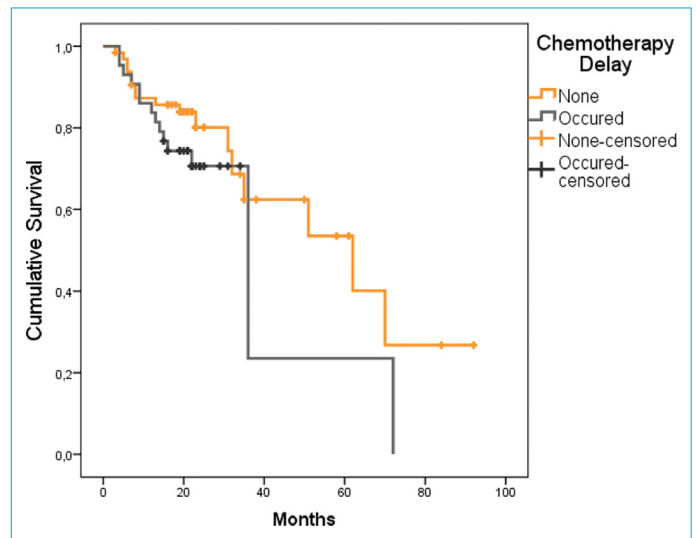


Figure 1. The Kaplan-Meier curves of the study population according to chemotherapy delay.

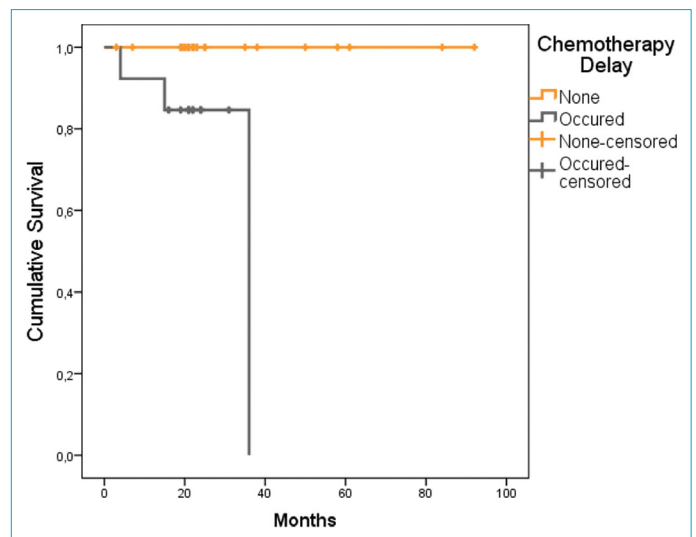


Figure 2. The Kaplan-Meier curves of breast cancer subgroup according to chemotherapy delay.

number of patients was low in our study, there is an indication that breast cancer patients may be more susceptible to treatment delays or cessation.

The European Society of Medical Oncology recommends that stage 2 colorectal cancer patients undergo MSI testing for treatment decisions. To meet this recommendation, treatments should be as short and ambulatory as possible. Patients must be evaluated following the IDEA study, and a three-month treatment period must be decided if necessary. The American Society of Clinical Oncology makes essentially identical recommendations, other than stating that non-curative treatments should be decided upon on a case-by-case basis according to the risk/benefit ratio.^[15] Overall survival rates were not different in colorectal cancer patients (p=0.52).

In the era of the COVID-19 pandemic, curative lung cancer treatments such as surgery or adjuvant chemotherapies should not be postponed, and it should be kept in mind that delaying palliative therapies for metastatic conditions may result in a decline in performance status, leading to a loss of treatment options. Delaying palliation may also result in an increase in hospitalization and a loss of valuable hospital capacity for COVID-19 patients.^[16] Despite the effects of lung cancer treatment delays noted in our study, the COVID-19 pandemic led to a considerable decline in IV chemotherapy adherence. In contrast to the decline in adherence, there was no difference in survival in those undergoing palliative and adjuvant chemotherapies ($p=0.20$). The Turkish oncologic authorities state that they would review each chemotherapy patient on an individual basis with a risk-benefit analysis, but would not offer to postpone treatment at any cost.^[17] Guven et al.^[10] observed a significant decrease in out-patient hospitalizations among the first COVID-19 patients treated in a unique oncology facility in a recent trial. Although a significant difference was noted in out-patient care, they also noted a significant rise in patients admitted to the hospital for chemotherapy. Patient adherence to chemotherapy, however, was not reported.

Disruptions to chemotherapy adherence have been attributed to both social regulations and hospital fear, although some chemotherapy programs were postponed while COVID-19 infections were investigated. None of the study population developed a COVID-19 infection or died. In Turkey, there is a higher level of awareness among oncologic patients that may lead to delays in treatment, but it has also resulted in a reduction in COVID-19 infections and death. This is further supported by the decline in patients seeking medical advice in other disciplines.^[10]

The pattern of treatment delays before and after the first instances of COVID-19 in Turkey revealed that a large proportion of patients abruptly ceased their therapies for no apparent reason. Despite our analysis of the decreased adherence to chemotherapy among patients in the present study, it is still debatable whether or not non-adherence to treatment results in a reduction in survival. Aside from the breast cancer subgroup, the majority of the study participants were unaffected. In the COVID-19 pandemic, cancer-related survival can be expected to be reduced, as patients may not undergo adequate diagnostic procedures, or have access to certain treatment options or supportive care. Specific patient populations, such as chemotherapy patients, may be harmed by the laws designed to prevent the spread of COVID-19 and may be confused by non-specific rules and statements that hinder their access to the necessary treatments. In the development of pandemic regula-

tions, oncologic patients should be given special considerations in government decisions, and special measures must be determined for susceptible patient groups, such as oncology patients.

Limitations

The data quality in the present study is low due to the retrospective study design. Although complications and other hospital interventions were recorded, social factors that may have led to delays in chemotherapy treatments were unknown but could be considered to be equal for both the pre- and post-COVID-19 periods. Furthermore, the reasons for delays were not evaluated but could have been linked to restrictions, hospital fear, or other causes. The difference in treatment counts between the pre and post-COVID-19 period is related to the new establishment of the cancer center. The small study population and the short follow-up period may cover the decreased survival in non-adherent patients.

Conclusion

Treatments have been severely delayed as a result of social regulations and institutional concerns. Before putting social regulations in place, special consideration must be paid to specific patient populations. More research is needed to investigate the decreased survival associated with collateral damage in oncologic patients.

Disclosures

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