ORIGINAL RESEARCH

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# The Impact of the COVID-19 Pandemic on Follow-Up and Management of Cancer Patients

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**ABSTRACT Objective:** This study aimed to evaluate the impact of the coronavirus disease-2019 (COVID-19) pandemic on the follow-up and management of cancer patients. **Material and Methods:** A survey consisting of 15 questions asking whether there was a delay in follow-up or treatment of cancer during the COVID-19 pandemic was applied to the cancer patients who were admitted to our medical oncology outpatient clinic for follow-up or treatment. **Results:** A total of 209 cancer patients were included in this study. In 56 (26.8%) patients, there was a delay in the follow-up or treatment of cancer. The delay in cancer treatment occurred in 37 (66%) patients, and the delay in the follow-up of cancer occurred in 19 (34%) patients. The median delay in the follow-up and treatment of cancer was both 30 days (range 1-120) and (range 2-120), respectively. 12.5% of all patients who encountered delays in cancer follow-up or treatment had subsequent cancer-related complications. Also, the delay was significantly higher in quarantined patients and patients diagnosed with severe acute respiratory syndrome-coronavirus-2. In binary logistic regression analysis, living in rural areas and being quarantined due to the COVID-19 pandemic were determined as independent predictors of the delay. **Conclusion:** The COVID-19 outbreak caused delays in the follow-up and treatment of cancer patients, and acute complications arose due to unavoidable disruptions. To prevent long-term negative consequences of delays in cancer follow-up and treatment, it is necessary to adapt the treatments judiciously without sacrificing patient safety and care.

**Keywords:** Cancer patients; COVID-19; follow-up

The first case of coronavirus disease-2019 (COVID-19) was reported in Wuhan, China, in late December 2019, which then spread more rapidly and extensively to the European region and US.[1] COVID-19 is a contagious disease caused by a severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which can be transmitted by respiratory droplets as well as close contact and can progress from an asymptomatic form to a severe stage, sometimes even leading to death.[2] The number of cases as well as mortality rates in various countries afflicted by COVID-19 varies as they are regulated by several parameters like population, economic status, demographic structure, the efficiency of the health care system, diagnostic criteria, proficiency of local test center capacity along with calibration of testing strategies.[3] In our country, the first confirmed case of COVID-19 was detected on March 11, 2020, whereas the first death due to COVID-19 occurred on March 17, 2020.[4,5]

The COVID-19 pandemic has put enormous pressure on the National Health Service providing basic cancer treatment modalities, from the initial screening, diagnosis process to the resultant surgery followed by other treatment options. The delay in on-

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cological treatment due to the COVID-19 outbreak often relying on the cancer subtypes, patient's age, as well as the stage of cancer, may have disparate undesirable effects on the survival of patients. A study conducted by Maringe et al. evaluated the possible effects of delays in cancer diagnosis on survival outcomes in patients with breast, lung, colorectal, and esophageal cancer and suggested that delays in cancer diagnosis due to the COVID-19 lockdown in the United Kingdom (UK) could be attributable to 3,291-3,621 avoidable deaths as well as 59,204-63,229, the additional years of life lost.[6]

In this study, we aimed to depict whether the COVID-19 pandemic causes a delay in the follow-up and treatment of cancer patients and also determine the factors that may initiate the delay.

## MATERIAL AND METHODS

This study was a single-center survey study. The study was performed according to the Declaration of Helsinki and approved by the Faculty of Medicine, Necmettin Erbakan University, Ethics Committee (Number: 2020/2672, Date: 9/7/2020). The informed consent forms were provided by all the individual participants included in the study.

### PATIENTS

In this study, we recruited 209 cancer patients who were either treated or followed up at the medical oncology department of our cancer center during July 1-July 15, 2020. Subsequently, data on age, gender, comorbidities, histological subtype, and the stage of cancer were recorded.

The patients who continued their cancer treatment were asked whether there was a delay in their treatment during the COVID-19 pandemic, while the patients who were under follow-up without treatment were inquired about a delay in their follow-up during the COVID-19 pandemic and the subsequent duration of delay was recorded in the relevant patients. The questionnaires were conducted face-to-face by a medical oncologist at the medical oncology outpatient clinic, Meram Faculty of Medicine, Necmettin Erbakan University. Moreover, delay-related complications were also duly noted, which might have developed in patients whose cancer follow-up or treatment was hampered due to the COVID-19 pandemic. Table 1 shows the various questions asked in the survey.

"The patients were divided into 2 groups according to the inclusion of delays in cancer follow-up and treatment; Group 1: patients with delay, Group 2: patients without delay. Factors that could cause a delay due to the COVID-19 pandemic were compared between these 2 groups.

### STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 23.0 (SPSS Inc., Chicago, IL, USA). The distribution of study parameters among the groups was analyzed using the Kolmogorov-Smirnov test. The comparison of parameters showing homogeneous distribution was made by the Mann-Whitney U test, whereas the Independent Samples t-test performed the comparison of non-homogeneous parameters. Categorical variables were compared by Pearson's Chi-square test between all the groups. Variables were defined as mean±standard deviation, median (minimum-maximum), and percentage (%). Logistic regression analysis was applied to determine the factors associated with delayed and non-delayed groups in which stage of cancer, residence, living condition, marital status, quarantine status due to COVID-19 were considered the independent variables. A p value $<0.05$ was required for statistical significance.

## RESULTS

In this study, a total of 209 patients had been enrolled, including 107 females and 102 males, and the 3 major cancer types entailed in the study were colorectal, breast, and lung, respectively. Among 48 cases of colorectal cancer (23%), 38 cases of breast cancer (18.2%), and 24 cases of lung cancer (11.5%), the number of patients with Stage 1, Stage 2, Stage 3, and Stage 4 were 9 (4.3%), 18 (8.6%), 52 (24.9%), and 130 (62.2%), respectively. A total of 155 patients were diagnosed with cancer before March 11, 2020, followed by 54 patients after March 11, 2020.

There were 56 (26.8%) patients in Group 1 and 153 (73.2%) patients in Group 2. Out of all Group 1

**TABLE 1:** Questions in the survey.

| |
|---|
| 1. Where do you live? |
| In the countryside |
| In the city |
| 2. How do you live? |
| Alone |
| With your family |
| 3. What is your marital status? |
| Single |
| Married |
| 4. Do you have any comorbid diseases as hypertension, diabetes, cardiac disorders, chronic obstructive pulmonary disease, immune deficiency, etc.? |
| Yes |
| No |
| 5. Have you been concerned about COVID-19 infection? |
| Yes |
| No |
| 6. Have you been hospitalized with a diagnosis of COVID-19 infection? |
| Yes |
| No |
| 7. Have you been treated with the diagnosis of COVID-19 infection? |
| Yes |
| No |
| 8. Have you been subjected to isolation/quarantine with the suspicion/diagnosis of COVID-19 infection? |
| Yes |
| No |
| 9. Have you had a polymerase chain reaction test for COVID-19 infection? |
| Yes (If so what was the result? Positive or negative) |
| No |
| 10. Has your cancer treatment been delayed due to the COVID-19 pandemic? |
| Yes |
| No |
| 11. If your cancer treatment was delayed due to the COVID-19 pandemic, how many days was it delayed? |
| 12. Do you have any complications related to the delay in your cancer treatment due to the COVID-19 pandemic? |
| Yes |
| No |
| 13. Has your oncological follow-up been delayed due to the COVID-19 pandemic? |
| Yes |
| No |
| 14. If your oncological follow-up was delayed due to the COVID-19 pandemic, how many days was it delayed? |
| 15. Do you have any complications related to the delay in your oncological follow-up due to the COVID-19 pandemic? |
| Yes |
| No |

patients, 37 (66%) had a delay in obtaining cancer treat ment while the rest had a delay in cancer follow-up. The median delay in both cancer follow-up and cancer treatment of Group 1 patients was 30 days in the (range 1-120) and (range 2-120) respectively. In Group 1, 7 out of 56 (12.5%) patients had developed cancer-related complications due to delays. When patients in Group 1 and Group 2 were compared, no significant difference was found in terms of gender, age, comorbidity, concern about COVID-19, and the resultant p values were 0.67, 0.44, 0.11, and 0.24, respectively. Group 1 had a higher rate of single, lonely, and rural patients, which were statistically significant (p values were 0.02, 0.02, and 0.03, respectively). Also, Group 1 contained more patients (44.6%) with early-stage cancer as compared to Group 2 (35.3%), and thus, was statistically significant (p value: 0.006). Moreover, the patients quarantined and diagnosed with SARS-CoV-2 were significantly higher in Group 1 for which resultant p values were (0.002 and 0.001), respectively. Please, refer to Table 2 and Figure 1 for the details.

In binary logistic regression analysis, the place of residence [Beta: 0.773, odds ratios (OR): 2.16, 95% confidence intervals (CI): 1.095-4.284, p: 0.03] and being quarantined due to COVID-19 (Beta: 1.73, OR: 5.66, 95% CI: 2.05-15.61, p: 0.001) were determined as independent predictors of the delay.

**TABLE 2:** Demographic and disease characteristics of patients according to the groups.

| Parameters | Group 1 (n=56) | Group 2 (n=153) | p value |
|---|---|---|---|
| Age (mean) | 60±11.4 | 58±12 | 0.44 |
| Sex | | | 0.67 |
| Male | 26 (46.4%) | 76 (49.7%) | |
| Female | 30 (53.6%) | 77 (50.3%) | |
| Stage | | | 0.006 |
| 1 | 3 (5.4%) | 6 (3.9%) | |
| 2 | 11 (19.6%) | 7 (4.6%) | |
| 3 | 11 (19.6%) | 41 (26.8%) | |
| 4 | 31 (55.4%) | 99 (64.7%) | |
| Inhabitant | | | 0.03 |
| Urban | 24 (42.9%) | 91 (52.5%) | |
| Rural | 32 (57.1%) | 62 (47.5%) | |
| Living condition | | | 0.02 |
| Alone | 7 (12.5%) | 6 (3.9%) | |
| With family | 49 (87.5%) | 147 (96.1%) | |
| Marital status | | | 0.02 |
| Single | 16 (28.6%) | 22 (14.4%) | |
| Married | 40 (71.4%) | 131 (85.6%) | |
| Anxiety about COVID-19 | | | 0.24 |
| Yes | 30 (53.6%) | 68 (44.4%) | |
| No | 26 (46.4%) | 85 (56.6%) | |
| Diagnosis with SARS-CoV-2 disease | | | 0.001 |
| Yes | 11 (19.6%) | 8 (5.2%) | |
| No | 45 (90.4%) | 145 (94.8%) | |
| Quarantine of SARS-CoV-2 | | | 0.002 |
| Yes | 12 (21.4%) | 10 (6.5%) | |
| No | 44 (78.6%) | 143 (93.5%) | |
| Comorbidity | | | 0.11 |
| Yes | 30 (53.6%) | 63 (41.2%) | |
| No | 26 (46.4%) | 90 (58.8%) | |

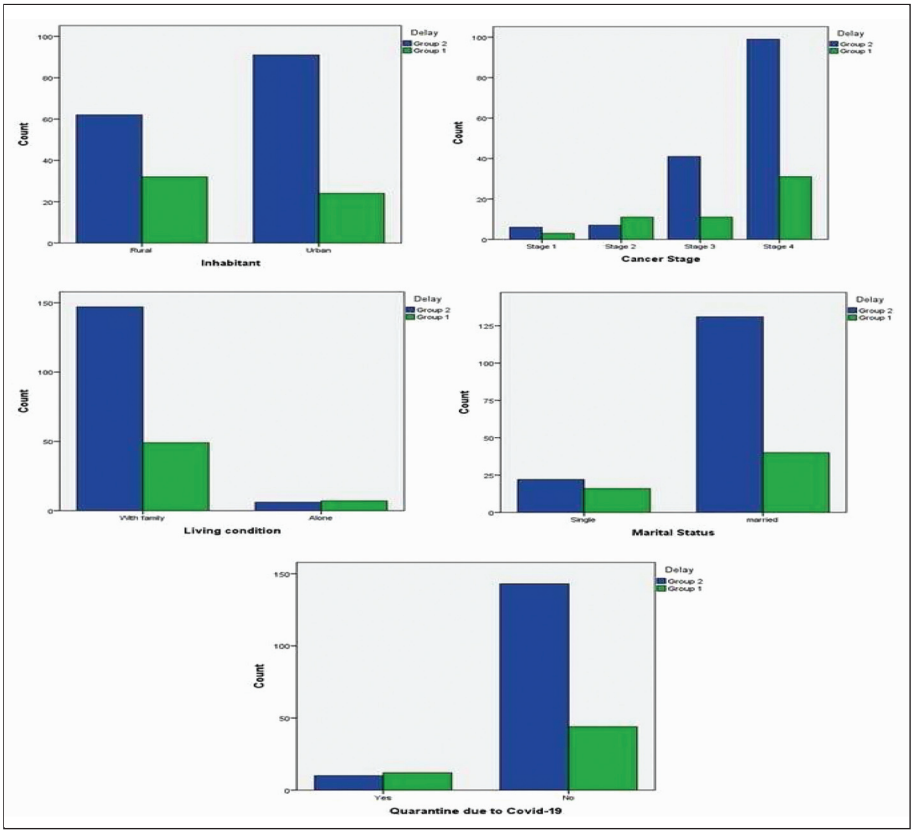


**FIGURE 1:** Comparison of the (inhabitant, cancer stage, living condition, marital status, and quarantine due to COVID-19) between Group 1 and Group 2.

## DISCUSSION

The COVID-19 pandemic caused a delay in oncological follow-up or treatment in 26.8% of our patients. Besides, it caused cancer-related complications in 12.5% of the delayed patients. Delays were observed more in Group 1 due to critical factors like quarantine and COVID-19 disease.

Factors that increase the risk of mortality from COVID-19 include advanced age, male gender predilection, diabetes, hypertension, cardiovascular disease, chronic obstructive pulmonary disease, and cancer.[7] The first study analyzing the risk of COVID-19 in patients with cancer reported by Liang et al. in China stated that 18 out of 1,590 patients with COVID-19 were afflicted with cancer in which the most frequent category was lung cancer (5 of 18 patients), four cancer patients affected with COVID-19 had received chemotherapy or surgery within the past month, the other 12 patients were cancer survivors in routine follow-up after primary resection and 2 patients had unknown treatment status.[8] In another study, Tian et al., after a comparison between COVID-19 patients with and without cancer, reported that COVID-19 patients diagnosed with cancer developed more severe infections than patients without cancer, thus, revealing that the advanced tumor stage is a critical risk factor for developing COVID-19 complications.[9] Robilotti et al. conducted a study on 423 cancer patients with COVID-19 and reported that since 56% of patients had metastatic diseases whereas 59% had developed comorbidities, it was suggested that these patients had increased rates of both severe respiratory infections (20%) and mortality rates (12%) due to COVID-19.[10] Lee et al., in a prospective cohort study, evaluated 800 cancer patients with COVID-19 and showed that 28% of patients died from COVID-19. Moreover, it was also reported that most of these deceased patients were older males, having more comorbidities, and had received chemotherapy in the previous month. However, in the multivariate analysis, they found no significant rela-

tionship between survival and age, gender, comorbidity, and any other therapies such as chemotherapy, immunotherapy, hormonotherapy, and targeted therapy acquired in the last month.[11] Similarly, Barlesi et al. revealed that 58% of 137 cancer patients with COVID-19 were in the metastatic stage, and the resultant mortality rate was 14.6%. Further, there was no evidence that COVID-19 was more lethal or aggressive in these patients than in the general population.[12] Although the long-term results are not fully investigated yet, our study results anticipate that the delays in the clinical diagnosis and treatment of patients will negatively affect the results of the patients due to the aforementioned reasons. Therefore, it is recommended that patients undergoing curative cancer treatment continue anti-cancer therapy throughout the COVID-19 pandemic.[13-17]

The Turkish government implemented a series of nationwide measures on March 11, 2020, to combat the COVID-19 outbreak in which people over the age of 65 were banned from going out, and several domestic travel restrictions, as well as containment measures, were imposed; and subsequently, a decrease was observed in the number of hospital admissions for cancer patients. In addition, the innate fear of contracting SARS-CoV-2 infection was another implicating reason for the decline in hospital admissions of cancer patients. However, various national and local measures have been taken to manage cancer patients as the entire follow-up and treatment process has been remodeled on the local prevalence and impact of COVID-19. Many oncology centers have reduced non-emergency outpatient services to reduce the risk of cancer patients' exposure to SARS-CoV-2 infection, several non-curative treatments have been postponed, or treatment schemes have been re-arranged to bring patients to the hospital with a minor frequency whereas the routine follow-up visits of patients who are not receiving active anti-cancer treatment have been postponed. A study conducted by Guven et al. compared the outpatient and inpatient data of the initial 30 days after March 11, 2020, when the first COVID-19 case was reported with the data of the same period in the previous 3 years and reported that all newly diagnosed cancer patient admissions to the outpatient clinic decreased significantly, except for the lung cancer, head and neck cancer, and palliative care clinic admissions. On the other hand, they stated that although there was no significant decrease in the number of inpatients, the median length of stay in hospitals decreased significantly.[18] Our study found that all these measures mentioned above caused a delay in cancer follow-up and treatment in 26.8% of our patients during the COVID-19 pandemic. Moreover, we revealed that when patients who experienced a delay due to the COVID-19 pandemic were compared with the others, there was no significant difference between the groups regarding age, gender, comorbidity, and concern about COVID-19. However, the delay due to the COVID-19 pandemic was significantly higher in single, lonely, rural patients and patients with early-stage cancer. In a study by Akagunduz et al., while evaluating the effect of coronaphobia on cancer patients' adherence to treatment and follow-up, a considerable coronaphobia was found to be significantly associated with non-compliance with follow-up and treatment of such cases.[19] Also, our study results displayed that the latency was 2.1 times more significant in rural patients and 5.6 times more substantial in the patients quarantined due to COVID-19. In contrast, Erdem et al. surveyed a total of 300 cancer patients where most of the patients (73.6%) had an advanced-stage disease and (60%) of those patients were receiving active treatment. It was observed that there was no delay in 98% of these patients in terms of cancer treatments or follow-up appointments.[20] However, it is essential to note that Erdem et al. had performed this study on patients treated or followed up in private hospitals, whereas the patients examined in our study received health services from a university hospital.[20] The difference in the results between the above-mentioned studies is that in private hospitals and polyclinics, application services may differ from state hospitals and university hospitals.

Indefinite suspension of all non-emergency and elective procedures to provide more opportunities for the treatment of COVID-19 patients has also caused unavoidable delays in the diagnosis of new cancer patients. Any latency in resultant cancer treatment can result in worsening of disease symptoms, subsequent

disease progression, and impaired patients' performance. Besides, delay in cancer diagnosis may also result in the disease being diagnosed at a more advanced stage, which may negatively affect the survival rates. Sud et al. investigated the outcomes of latency in cancer surgery in Stage 2 and Stage 3 of aggressive cancers such as bladder, lung, esophagus, ovarian, liver, pancreatic, and stomach cancer and suggested that a 3-month and 6-month delay in cancer surgery could result in >17% and >30% reduction in survival, respectively.[21] Sud et al. also evaluated the effect of delays in the two-week wait rule in a UK cancer institution during the COVID-19 pandemic and suggested that the annual number of cancer cases diagnosed in Stage 1-3 via the two-2-week-wait pathway involved assimilation of 2-week-wait age-specific and stage-specific effects. Based on 2013-2016 data, 6,281 patients with Stage 1-3 cancer were diagnosed via the 2-week wait pathway per month, whereas 27% of these patients were predicted about the likelihood of death within 10 years from cancer. Moreover, the researchers showed that the delays in the presentation via the 2-week-wait pathway over a 3-month lockdown period could result in 181 other lives and 3,316 life-years lost due to a backlog of referrals of 25%, 361 other lives, and 6,632 life-years lost for a 50% backlog of referrals, and 542 other lives and 9,948 life-years lost for a 75% backlog in referrals. It was concluded that a 2-month delay in 2-week-wait researcher referrals resulted in a loss of between 0.0 and 0.7 life-years per referred patient due to the tumor type and age.[22]

However, Alimoglu et al. noted that the cancer patients could be operated safely via the cumulative protective measures taken during the pandemic. In this study, the researchers operated on 39 patients, 21 with colorectal cancer and 18 with breast cancer, between March 10, 2020, and April 16, 2020, by taking all possible COVID-19 precautions (transferring patients to the operating room with a surgical mask, all surgical team members wore protective glasses, waterproof sterile surgical gowns, N95 masks with a single surgical mask and standard sterile surgical gloves during the operation), and reported that no COVID-19 symptoms were detected in any of these patients in the postoperative follow-up period.[23] In the current practice, it is recommended not to postpone any curative cancer surgery during the COVID-19 pandemic, as delaying the cancer surgery can lead to adverse long-term consequences.[16,24-26]

## CONCLUSION

In conclusion, the COVID-19 pandemic has become a major global crisis which has, increased the complexities of cancer treatment. The findings in our study revealed that cancer patients have experienced delays in their follow-up and treatment due to the COVID-19 outbreak, but currently, there is no evidence to support delaying or terminating the treatment in cancer patients during the pandemic. Ensuring continuity of care for cancer patients is extremely vital, so healthcare professionals must adapt active cancer surveillance and treatment strategies without compromising patient safety and care. The clinical decision to terminate or continue the treatment and follow-up in cancer patients during the COVID-19 pandemic should be made judiciously in accordance with the scientific evidence-based conversations between the patients and the physician.

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***Conflict of Interest***

*No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.*

***Authorship Contributions***

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