

Research Article

The Radiotherapy Adherence of Patients in Time of COVID-19 Pandemic

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Abstract

Objectives: Radiation therapy is a life-saving treatment that should be given to all cancer patients who have a diagnosis. Treatment capacity can be hampered by a lack of resources, such as space, equipment, and personnel. The present study tried to assess how the fear of hospitals and the pandemic measures affected the radiotherapy course of patients.

Methods: The records of patients receiving active cancer therapy in the department of radiation oncology were retrospectively analyzed. Treatment delays before and after March 11, 2020, were recorded.

Results: None of the 80 patients (0%) failed to complete radiotherapy before March 11, 2020, while 5 of 55 patients (9.1%) had radiotherapy cessation after the first COVID-19 case and the following restrictions in Turkey ($p < 0.01$). There was no difference in treatment type between the groups; no difference between palliative and curative subgroups before and after the pandemic ($p = 0.22$). There was no difference in overall survival between pre- and post-COVID-19 periods ($p = 0.35$).

Conclusion: However, some patients may not receive adequate diagnostic procedures during this period. The regulations to prevent the spread of the COVID-19 may harm specific patient populations such as radiotherapy patients. The non-specific rules and declarations confuse the patients and prevent them from accessing the treatment needed. In the case of pandemic regulations, government decisions may include special considerations for oncological patients.

Keywords: COVID-19, pandemic, cancer, radiotherapy adherence

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The "Corona" spikes formed by the S glycoprotein projecting from the viral capsid give Coronaviruses their name. Angiotensin-converting enzyme 2 is the host receptor, and this protein is responsible for binding to it (ACE2).^[1] The reported most common symptoms are fever, sore throat, and muscle pain or fatigue.^[2] The leading causes of death are acute respiratory distress (ARSD), myocardial damage, and renal failure.^[2, 3] Many tissues, including the cornea, nose, lungs, esophagus, heart, stomach, liver, ileum, colon, gallbladder, kidney, and testicles, contain ACE2 receptors.^[4] When infected with SARS-CoV-2, cancer patients are more

prone to develop severe symptoms as their ACE2 expression rises in the tissues with age.^[5] Because of their severe clinical conditions and continuing therapy, cancer patients are one of the most susceptible individuals.^[6]

The COVID-19 outbreak has presents a significant challenge to healthcare systems across the world. Radiation therapy is a life-saving treatment that should be given to all cancer patients who have a diagnosis. Treatment capacity can be hampered by the lack of resources, such as space, equipment, and personnel.^[6]

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On March 11, 2020, Turkey reported its first COVID-19 case, and the pandemic peaked in early May 2020. Travel restrictions, centralized quarantine, and social separation have all been issued by the Turkish Ministry of Health and Ministry of Interior to the public.^[7] Patients and employees at radiotherapy clinics confronted the unique difficulty of keeping a virus-free environment while completing treatments without interruption. Elective procedures will be postponed, outpatient and inpatient care will be reserved for COVID-19 patients, and all hospital staff will be assigned to these services, according to the Ministry of Health. Despite the fact that the majority of hospitals having radiation facilities had been designated as COVID-19 referral hospitals, it was decided to continue cancer treatments as usual. Personnel working in oncology departments shall not be assigned to COVID-19 units, according to the Ministry of Health's announcement on April 14, 2020. For all radiation oncology workers and radiotherapy patients, the Turkish Society for Radiation Oncology has issued an emergency statement.^[7]

These crucial measures aided in the protection of patients and employees against the spread of COVID-19, as well as the continued provision of radiation services. In the first two months of the epidemic, new patient admissions in 109 departments dropped by up to 50 percent. Only a few independent radiation centers and departments in smaller towns were able to sustain patient admissions at pre-pandemic levels, with comprehensive cancer centers in big cities seems to be the most effected. Patients were unable to attend comprehensive cancer facilities due to inter-provincial travel restrictions and curfews, therefore many chose to begin treatment in home cities.^[8,9]

A recent study based on the estimation of case fatality rate reported that the outbreak in Turkey would be similar to that in European countries, especially France.^[10]

The purpose of this study was to see how patients' fear of hospitals and pandemic precautions influenced their radiation treatment.

Methods

Study Participants

The records of patients receiving active cancer therapy in the department of radiation oncology were retrospectively analyzed. Age, sex, diagnosis, type of radiotherapy, and dates of appointment and admission were recorded. Also, the status of SARS-CoV-2 infection and the last status of the patients were noted. Treatment delays before and after March 11, 2020, were recorded. Patients without adequate records were excluded from the study.

Statistical Analysis

Statistical analyses of the study were performed using SPSS version 22.0. Descriptive data were presented as either means or medians for continuous variables and frequencies and percentages for categorical variables. The Pearson's χ^2 test was used to assess the associations between categorical variables. Survival was analyzed using the Kaplan-Meier curves.

Results

The study included 135 patients. The patients were aged 33 to 92 years, with a mean of 66 years. There was a male predominance in the study population, and the number of male and female patients was 86 and 49, respectively. Most of the patients had lung cancer (20.7%), followed by breast cancer (16.3%). Two-thirds of the radiotherapies were definitive treatment, while one-third was administered with palliative intent.

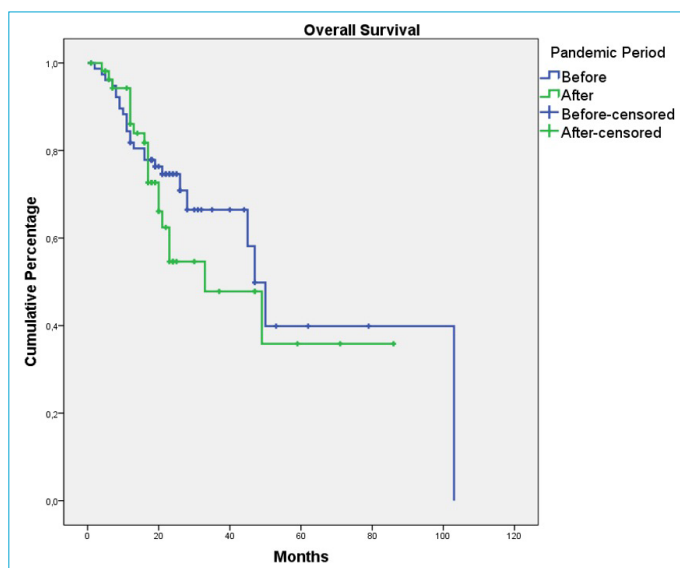
None of the 80 patients (0%) failed to complete radiotherapy before March 11, 2020, while 5 of 55 patients (9.1%) had radiotherapy cessation after the first COVID-19 case and the following restrictions in Turkey ($p < 0.01$). There was no difference in treatment type between the groups; no difference between palliative and curative subgroups before and after the pandemic ($p = 0.22$). Despite the difference in treatment discontinuations between the pre- and post-COVID-19 periods, treatment delays were not statistically different between the groups ($p = 0.18$). The mean duration of treatment delays was 0.4 and 4.8 days in the pre- and post-COVID-19 periods, respectively. None of the treatment discontinuations was due to toxicity. All of the patients discontinued their treatment without excuse or toxicity. The number of patients decreased in the post-COVID-19 period, but the types of diseases treated were almost the same. Breast cancer was the only subtype significantly increased in the post-COVID period ($p = 0.03$) (Table 1). Four patients who completed treatment in the pre-COVID-19 period contracted COVID-19, while five patients who received treatment in the post-COVID-19 period were PCR positive. No statistical difference was identified between the groups ($p = 0.34$). The SARS-CoV-2 infection did not result in treatment discontinuation in any of the patients. In addition, the SARS-CoV-2 infection caused a statistical difference in survival for both groups. The COVID-19 was associated with poorer survival for the patients who received radiotherapy in both pre- and post-COVID-19 periods ($p > 0.001$). There was no difference in OS between pre- and post-COVID-19

Table 1. The characteristics of the study population according to pre- and post-pandemic periods

Characteristics	Pre-COVID-19	Post-COVID-19	p
Sex			
Male/Female	59/21	27/28	0.003
Age			
Median (Mean)	68 (66.8)	66 (64.8)	0.78
Treatment discontinuation (Overall population)			
N: (%)	0/80 (0)	5/55 (9.1)	<0.01
Treatment delay			
Mean days (Median)	0.4 (0)	4.8 (0)	0.10
Treatment Type			
Definitive/Palliative	56/24	33/22	0.22
Diagnosis			
Lung	20	8	0.03
Breast	8*	14*	
Rectum	8	2	
Prostate	14	5	
Gastric	7	3	
Other	23	23	
Number of Fractions			
Median Cycles	25	25	0.96

*: Statistical significance.

periods ($p=0.35$) (Fig. 1). The median survival was 47 and 33 months, respectively. There was also no difference in survival between the groups according to radiotherapy types, and completion of treatment ($p=0.74$; $p=0.79$). Sex was a prognostic factor for survival in the post-COVID-19 period, which resulted in higher mortality in male patients ($p=0.002$). The median OS was not reached in female patients, while male patients had only 21 months of OS.

**Figure 1.** Comparison of OS pre and post pandemic period.

Discussion

The present study found that the COVID-19 pandemic and the social regulations harmed radiotherapy adherence of the patients. Although oncological treatment adherence is a highly investigated topic, there is a lack of literature for adherence to radiation therapy during the pandemic.

Several centers across Europe have been affected by the pandemic and trying to cope with the regulations and the fear of COVID-19. The treatment modalities changed, resulting in telemedicine, short-course radiotherapies, and delays in low-risk patient groups.^[6] The main driver of treatment plans was the sensitive patient population of radiation oncology. Another significant factor was the lack of protective equipment in radiotherapy centers.^[6]

Supportive data were reported in medically treated breast cancer patients, showing that patients were classified according to the urgency of therapy.^[11] The present study established a significant difference in the subtype of breast cancer among the patients, which was increased in number after the first COVID-19 case and the following regulations. The rate of breast cancer patients was significantly increased after the pandemic. This phenomenon might be related to pre-planned radiotherapy of the adjuvant patients who had undergone surgery before the pandemic. No difference was identified in the type of radiotherapy in palliative or definitive settings.

Telemedicine or other methods of long-distance communication between patients and physicians are not highly available in Turkey. Failure to radiotherapy adherence might also be related to these circumstances.

The delay of curative treatment for lung cancer, such as surgery or adjuvant chemotherapy, has not been recommended during the COVID-19 pandemic. Furthermore, delays in palliative treatments for metastatic settings may reduce performance status, causing loss of the chance for treatment. The postponement of palliation may also increase hospital admissions, leading to a loss of valuable hospital capacity for the treatment of COVID-19 patients.^[12] Despite the decreased number of lung cancer patients after the pandemic started, there was no statistical difference. Low patient numbers might be involved in this finding. Another reason might be the low rate of definitive radiation in the overall lung cancer population. The adherence of lung cancer patients to other oncological treatments was affected by the pandemic.^[13]

The Turkish authorities for oncology announced that every chemotherapy-receiving patient should be independently evaluated for possible risks and benefits but did not recommend delaying treatment at any cost.^[14] In a recent study, Guven et al. reported a significant reduction in outpatient admission after the first COVID-19 patients in a single oncology center. The authors identified a considerable difference in the number of outpatients, while there was a significant increase in patient admission for chemotherapy. The patients' adherence to radiotherapy was not reported.^[15]

The sex difference in OS between the groups might be related to the cancer subtype, which is in favoring breast cancer in females. The OS was numerically poorer in the post-COVID-19 period but not statistically significant ($p=0.35$). The results may be attributed to the heterogeneous and small patient population.

We believe that poor radiotherapy adherence resulted from both social regulations and the fear of hospitals. Besides, some patients may delay their treatments due to the COVID-19 testing. There is increased awareness among oncological patients in Turkey, which may result in treatment delays, but also this phenomenon occurred in decreased COVID-19 infection and related death. This hypothesis is also supported by the decreased number of patients presenting for medical advice.^[15]

However, some patients may not receive adequate diagnostic procedures during this period. The regulations to prevent the spread of the COVID-19 may harm specific patient populations such as radiotherapy patients. The non-specific rules and declarations confuse the patients and prevent them from accessing the treatment needed. In the

case of pandemic regulations, government decisions may include special considerations for oncological patients.

Limitations

The study had a retrospective design, causing low-quality data. Although the complications or other hospital interventions were recorded, some social factors were unknown, which might cause delays in radiotherapy appointments, but such factors were considered equal for both pre- and post-COVID-19 periods. The reasons for delays were also not evaluated; both may be related to restrictions, fear of hospitals, or other factors.

Conclusion

Social regulations and fear of hospitals resulted in significant treatment delays. Special attention must be paid to specific patient populations before making decisions on social regulations. Further studies are needed to prove the impact of the COVID-19 pandemic on the oncological patient population.

Disclosures

Ethics Committee Approval: Eskisehir Osman Gazi University Non-invasive Clinical Research Presidency of Ethic Committee (E-25403353-050.99,2610-2021).

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