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ORIGINAL ARTICLE

Radiotherapy in Cancer Treatment During The Covid-19 Pandemic: One Year Results From Northeast Turkey

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OBJECTIVE
The goal of this article was to assess the effects and consequences of strict measures in radiation oncology centers in northeastern Turkey during the coronavirus disease-2019 pandemic and to ensure that the reorganization of programs occurred without interruption to radiotherapy (RT).

METHODS
We retrospectively reviewed the records of 1063 patients (median age 63 years; range 3-93 years) who were treated in RT centers from March 2020 to March 2021. The study cohort was divided into two groups: Group A consisted of patients who received RT in the first 6 months and Group B comprised patients who received RT in the second 6 months.

RESULTS
The age distribution was similar in both groups. The analysis of the intent of treatment showed that 585 (55%) patients were treated with a radical intent in Group A, whereas only 478 (45%) were treated with a radical intent in Group B. Lung, breast, and genitourinary cancers were the most common cancer types in both periods. There was a significant decline in the number of female patients in Group B. Test results of 31 (2.9%) patients, 8 (25.8%) women and 23 (74.2%) men, who had nasopharyngeal swabs, were positive.

CONCLUSION
This study shows that oncology patients in our region are more worried about disease progression than the pandemic and insist on going to RT, especially during the first 6-month period when the pandemic was thought to be temporary. As a result of careful precautions, treatments in the clinics continued without contamination.

Keywords: COVID-19; clinical characteristics; radiotherapy; workflow.

Introduction

Infectious diseases continue to create major health problems for humankind. Throughout history, various pandemics have affected countries sociologically, demographically, and economically, often with dramatic results.

The 2019 coronavirus disease (COVID-19), a severe acute respiratory syndrome caused by the coronavirus 2 (SARS-CoV-2), was first reported on De-

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cember 31, 2019, in Wuhan, China. The World Health Organization (WHO) declared COVID-19 "an urgent public health problem at the international level" in January 2019 and a pandemic in March 2020.[1] Although the WHO and public health officials worldwide desired for limiting the impact of COVID-19, its rapid spread and severe symptoms have prolonged the global fight. On January 10, 2020, the Ministry of Health (MoH) of Turkey established the Coronavirus Scientific Advisory Board consisting of 31 different academicians who followed the disease by reporting its progress, determining treatment protocols, and providing recommendations on measures to be taken.[2]

W<hen someone with COVID-19 on one side of the world sneezes or coughs, people on the other are affected. After the virus manifested in many countries, people were locked in their homes and quarantine processes were initiated. A new and different life began for all people.[3]

The first COVID-19 case in Turkey was announced on March 10, 2020, and took precautions restricting daily life were rapidly implemented by MoH and other relevant institutions. Pandemic committees were established in all provinces and chaired by governors. The first COVID-19 death in Turkey occurred on March 17, 2020.[4] Contact tracing, fieldwork to identify the sources and agents after case reporting, along with identifying, evaluating, and managing individuals who had been exposed to the disease was carried out to interrupt the spread of infectious disease.[5] During this time, the capacity at secondary and tertiary health institutions remained sufficient for carrying out treatment. Data on service provision as of March 2020 showed an increase in the number of single-patient rooms throughout the country as a result of recent policies, thus facilitating the isolation and care processes of patients. Single-patient rooms and intensive care beds, all with state-of-the-art medical devices and materials, along with city hospitals played a major role in providing services during the pandemic, especially in big cities.

Among the various measures implemented, all private and public hospitals were transformed into pandemic hospitals. This allowed the allocation of intensive care and inpatient services in these hospitals to COVID-19 patients and suspended diagnosis, treatment, and surgical procedures, except for emergencies. In addition, hospital staff rotated in these hospitals in the Eastern Black Sea Region as well as throughout the country. Higher cases of severe illness, intensive care admissions, and mortality rates have been reported for COVID-19 patients of advanced age (>65 years of age) or with medical conditions such as hypertension, heart failure, diabetes mellitus, and immunosuppression.[6]

Cancer patients are immunocompromised as a result of the disease and the associated surgery, chemotherapy, and other immunosuppressive drug treatments, making them more prone to infectious diseases. In addition, the fact that cancer patients are generally elderly, often with other diseases in addition to cancer, further increases their risk for COVID-19. Early reports from China and Italy show that cancer patients, in particular, may be more susceptible to COVID-19 and have higher mortality and morbidity compared to non-cancer patients.[7] In a study involving 355 deaths attributable to COVID-19 in Italy, 20% of patients were reported with active cancer.[8] Despite the decision to continue radiotherapy (RT) and chemotherapy services for the treatment of cancer patients, there have been slowdowns and disruptions in oncology services. In our clinics, we sought to safely continue oncologic treatment services while also reducing the transmission, hospitalization, and the number of cases and deaths related to the pandemic.

The overall objective of the study was to investigate the effects of the COVID-19 pandemic on the process of RT centers in northeastern Turkey. This study reports on the precautions that were taken in our oncology centers, the number of patients receiving oncological treatments, the patient groups applying for clinics, and the number of healthcare professionals who got the disease. In addition, the year of study was divided into two 6-month periods in order to to examine the changes and impact of the pandemic on oncology centers over time.

Materials and Methods

Design

This multicenter study involved 1063 patients scheduled for radiation therapy in the following radiation oncology centers in northeastern Turkey between March 2020 and March 2021: Kanuni Research and Education Hospital, Blacksea Technical University, and Recep Tayyip Erdogan University. The Kanuni Research Hospital Department of Radiation Oncology coordinated this study. The patient and treatment information templates were created by the main researcher and delivered to the other centers for completion by the other researchers. The patients' diagnosis, stages, purpose of treatment, treatment field, chemotherapy status, treatment date, and COVID-19 status before and during treatment were recorded. This study

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was reviewed and approved by the Blacksea Technical University Faculty of Medicine Ethical Committee.

Patients

All patients who planned for and received RT at our center during the study period were included in the study. We evaluated the year of study in two periods, the first 6 months and the second 6 months. Data include patient age, sex, location of primary tumor, stages, treatment fields, treatment intent, treating clinician's definition as curative (including preoperative, postoperative, prophylactic) or palliative, RT doses, fractionation schedule, and status of concurrent chemotherapy.

Statistical Analysis

The chi-square test was used to compare the categorical variables between the two groups. A two-sided $p \leq 0.05$ was considered statistically significant.

Results

Demographic and Clinical Characteristics

In the first period during the pandemic, the COVID-19 screening capacity of most countries was scarce, particularly for nucleic acid testing. In most hospitals, including our institute, COVID-19 nucleic acid test screening was not performed for patients without fever and other symptoms associated with COVID-19.[9-11] In the second period, the COVID-19 nucleic acid testing capacity substantially expanded in most countries. From July, we began to conduct COVID-19 nucleic acid testing for all newly admitted patients 1 day before RT. During the weeks of RT, nucleic acid testing was repeated weekly for all patients routinely. For patients with a positive COVID-19 test, RT suspended until two consecutive negative test results were obtained (Fig. 1). There were 610 (57.8%) patients in Group A (first 6 months) and 449 (42.2%) in Group B (second 6 months). A total of 1063 patients matched the inclusion criteria, 614 women (66%) and 449 men (34%). Median age was 63 (interquartile range 3-93). Age distribution of patients was similar in both groups, but there was a significant difference between the gender of patients (p=0.029). A complete list of patient characteristics is available in Table 1. The number of new patients receiving RT was highest during the first lockdown, increasing from March to June 2020 and then gradually decreasing from June to October 2020 (Fig. 2).

Primary tumor regions were as follows: 28.1% (299) lung, 23.9% (254) breast, 4.9% (52) head and neck,

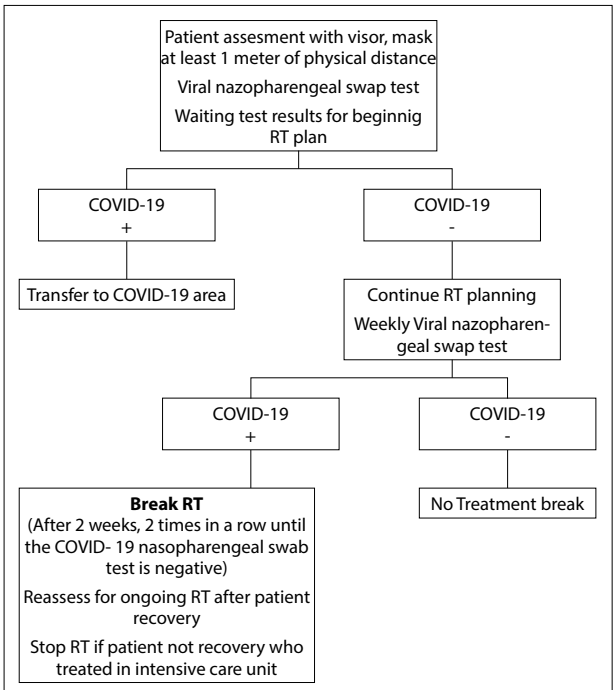

Fig. 1. Flow-chart of the management procedures for all newly admitted patients during the 1 year of pandemich.
RT: Radiotherapy.

15.2% (162) genitourinary, 8.9% (94) gastrointestinal, 5.6% (60) gynecological, 2.9% (31) soft tissue sarcoma, and 71% (6.7) other. Metastatic disease was reported for 478 (45%) patients. In both groups, the three most common sites of occurrence of cancer were lung, breast, and male reproductive organs. The number of patients in Group A with lung, breast, and genitourinary cancers were 167 (27.4%), 132 (29.2%), and 78 (22.4%), respectively, and in Group B 132 (29.2%), 95 (21%), and 74 (18.5%). Although there was an increase in the proportion of patients with lung cancer and a decrease in the proportion of patients with genitourinary and breast cancers from the first to second period, the difference was not statistically significant. The analysis of the intent of treatment showed that 354 (58%) patients were treated with a radical intent in Group A, whereas 231 (51%) were treated with a radical intent in Group B. Conversely, the proportion of patients treated with a palliative intent also decreased from 256 (42%) in Group A to 222 (49%) in Group B. The number of patients treated with palliative intent increased by 11.96% from the first to second period, and the difference was statistically significant ($p<0.001$) (Fig. 3). A complete list of tumor characteristics is available in Table 1.

Table 1 Patient characteristics

Characteristics	Group a first 6 months (%)	Group b second 6 months (%)	Total (%)	p
The number of patients	610 (57.4)	453 (42.6)	1063 (100)	
Age (year)				0.452
Median (range)	62 (3-93)	63 (8-89)	63 (3-93)	
<40	49 (8)	35 (7.7)	84 (7.9)	
40-59	205 (33.6)	153 (33.8)	358 (33.7)	
60-79	328 (53.8)	234 (51.7)	562 (52.9)	
80≤	28 (4.6)	31 (6.8)	59 (5.5)	
Gender				0.029
Male	335 (54.9)	279 (61.6)	614 (57.8)	
Female	275 (45.1)	174 (38.4)	449 (42.2)	
Location of primary tumor				0.062
Lung	167 (27.4)	132 (29.2)	299 (28.1)	
Breast	159 (26.1)	95 (21)	254 (23.9)	
Central nervous system	22 (3.6)	18 (4)	40 (3.8)	
Head and neck	36 (5.9)	16 (3.5)	52 (4.9)	
Gastrointestinal	60 (9.8)	34 (7.5)	94 (8.9)	
Genitourinary	78 (12.8)	84 (18.5)	162 (15.2)	
Gynecological	35 (5.7)	25 (5.5)	60 (5.6)	
Soft tissue	17 (2.8)	14 (3.1)	31 (2.9)	
Others*	36 (5.9)	35 (7.7)	71 (6.7)	
Stage				0.023
I-III	354 (58)	231 (51)	585 (55)	
IV	256 (42)	222 (49)	478 (45)	
Radiotherapy setting				0.005
Preoperative	36 (5.9)	13 (%2.9)	49 (4.6)	
Postoperative	185 (30.3)	104 (%23)	289 (27.2)	
Definitive	133 (21.8)	114 (%25.1)	247 (23.2)	
Metastatic	256 (42)	222 (%49)	478 (45)	
Treatment intent				0.023
Curative	354 (58)	231 (51)	585 (55)	
Palliative	256 (42)	222 (49)	478 (45)	
Raditherapy fractionation-curative				0.164
Conventional	318 (89.8)	216 (93.5)	534 (91.3)	
Hypofraction	36 (10.2)	15 (6.5)	51 (8.7)	
Raditherapy fractionation-palliative				0.004
20 Gy/40#	6 (2.3)	11 (5)	17 (3.6)	
30 Gy/10#	139 (54.3)	156 (70.3)	295 (61.7)	
25 Gy/5#	1 (0.4)	-	1 (0.2)	
20 Gy/5#	109(42.6)	46 (20.7)	155 (32.4)	
40 Gy/16#	1 (0.4)	9 (4)	10 (2.1)	
Concurrent chemotherapy				0.701
No	211 (59.6)	134 (58)	345 (59)	
Yes	143 (40.4)	97 (42)	240 (41)	

*Others: Pediatric, skin, lymphomas and hematologic, bone tumors

Management of COVID-19 Patients

Test results of 31 (2.9%) patients, 8 (25.8%) women and 23 (74.2%) men, who had nasopharyngeal swabs were positive. Median age was 68 (range 19-89), and reported symptoms were fever 21 (67.7%), sore throat 17 (54.8%), pneumonia 15 (48.4%), muscle pain 24 (77.4%), cough 23 (74.2%), dyspnea 14 (45.2%), and anosmia and ageusia 11 (35.5%). A complete list of symptoms is available in Table 2. Within the cohort, 11 (35.5%) patients died. The median age was 67 years

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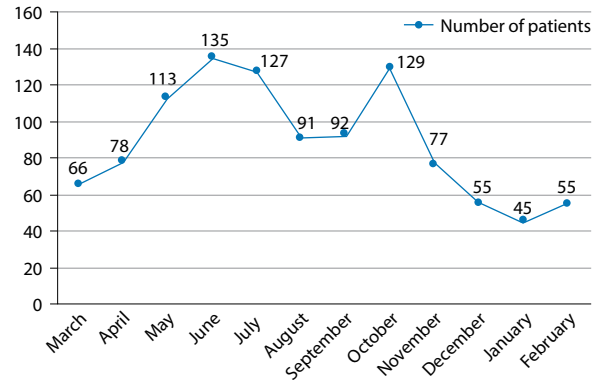

Fig. 2. Trend in the number of new patients undergoing radiotherapy by months of study.

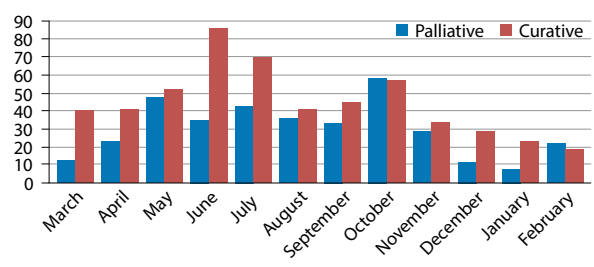

Fig. 3. The distribution of the intent of treatment in patients who received radiotherapy during the study period.

(range 32-81). These patients were infected through close contact with a COVID-19 patient outside of the clinic and were hospitalized in an intensive care unit due to complications with SARS-CoV-2. All patients who died were symptomatic and had severe symptoms. One had not started RT; the remaining patients stopped RT during treatment.

Workflow Modifications

Our report demonstrates how RT departments in Eastern Turkey coped with the COVID-19 disturbance. Significant reorganization and modifications in RT practice were quickly implemented in response to COVID-19. Our priority was to achieve a delicate balance between patient care and confidence while protecting the healthcare professionals, particularly in the initial stages of the pandemic. Approximately 50 new accesses every week enrolled in all divisions for RT treatments. We performed a nasopharyngeal swab screening for all patients before scheduled RT. In each session, patients were queried for suspicious symptoms (fever >37.5°C, cough, dyspnea, flu syndrome, conjunctivitis, and diarrhea). In the likelihood of COVID-19, patients were restricted access to the division and isolated in dedicated zones, pending nasopharyngeal swab, and assessed for potential transfer to a COVID-19 hospital in the region. Additionally, patients and their relatives from abroad were not admitted to the department within a 14-day quarantine period. In order to prevent the transmission of COVID-19, a reorganization of the operation was also carried out in oncology centers in our region in accordance with MoH guidelines and recommendations from the Turkish Society for Radiation Oncology (TROD). An appropriate working model was constructed to ensure the social distancing of employees throughout the workplace.

Table 2 Patient reported symptoms

Symptoms	n (%) (total n=31)
Muscle pain	24 (77.4)
Cough	23 (74.2)
Fever	21 (67.7)
Sore throat	17 (54.8)
Pneumonia	15 (48.4)
Dyspnea	14 (45.2)
Anosmi/ageusia	11(35.5)

Patient admissions were reduced in outpatient clinics in the 1 month of the pandemic. Admission to the hospital was restricted only to patients and a single accompanying individual at their established time out of clinical necessity. Waiting rooms for patients were arranged with seats located at a safe distance between each other. All patients, visitors, and staff had to wear two surgical masks, one over the other, during the pandemic. Before patients and caregivers entered the hospital and clinics, their temperatures were checked in the physical distancing patient corridor.

One critical group of cancer patients is those over the age of 65. The restrictions resulting from the pandemic caused disruptions in access to health services for this age group. Patients with cancer diagnosis treatment were able to access oncology centers with permission letters from health institutions. However, those with cancer symptoms who had yet to be diagnosed faced problems in reaching oncology centers for diagnosis and treatment.

As a result of intercity travel restrictions in response to the pandemic, the flow of patients from small cities to well-equipped centers in large metropolitan areas almost completely stopped. Patients either started treatment in oncology centers in the city they were in or waited until the transportation ban to metropolitan areas was lifted.

In the Eastern Black Sea Region, the number of patients in radiation oncology centers began to increase, especially 1 month after the onset of the pandemic.

In the following months, appointment restrictions were extended. Due to pandemic precautions and lack of personnel, there were limitations in external RT applications. Chemotherapy and hormonotherapy options were prioritized in order to reduce hospital capacity according to the region and type of cancer.

In order to reduce the number of people in our RT centers while at the same time prevent employees from being infected, isolated teams consisting of radiation oncologists, health physicists, nurses, and RT technicians were established in most centers, and these teams worked in different shifts ranging from a few days to a week.

MoH guidelines in RT centers, TROD, and international professional organizations (such as the American Society for Radiation Oncology, European Society for Radiation Oncology) have been shown to be effective and increasingly popular hypofractionated treatment schemes have been frequently applied.

Although there was no change in concurrent chemotherapy regimens used for patients treated for curative purposes in both groups, palliative treatments were altered by selecting programs with less fractions.

Staff Training

Employees received occupational health and safety online trainings on handwashing, distance rules, and proper use of personal protective equipment, such as masks, goggles, gloves, and gowns. Recommendations regarding family and social life were also included in the trainings. Treatment machine staff was required to wear protective visors while laying patients on the treatment table due to close contact.

Personal Equipment

In clinics where there was direct contact with people with suspected infection or a risk of contamination, employees were provided with fully closed eye or face protection/visors, protective clothing, respiratory protection (FFP2 or FFP3) ventless masks, and gloves.

Business trips, conferences, congresses, and other events organized abroad were postponed when possible. Online congresses and meetings were held in the autumn months when the pandemic was still under control. In cases where it was necessary to do so, audio and visual communication facilities were used. In cases where travel was necessary due to work, the recommendations of the MoH were followed.

Discussion

The COVID-19 pandemic caused by SARS-CoV-2, caused high morbidity and mortality worldwide. Since the start of the outbreak, research teams worked to develop COVID-19 vaccines (in excess of 198 vaccines were in preclinical or clinical development at the time of writing).[12] CoronaVac, also known as Sinovac, is one of several vaccine candidates to fight COVID-19 that has shown good immunogenicity in preclinic tests with vaccine-induced neutralizing antibodies for SARS-CoV-2, which could counteract ten delegate strains of SARS-CoV-2.[13] After statements from Health Minister Dr. Fahrettin Koca during a Coronavirus Scientific Committee Meeting, the first coronavirus vaccine was given emergency-use approval by MoH.

Vaccinations were launched across Turkey in January 2021, with priority given to health workers, who received two doses within 28 days. In the first phase of the vaccination program, more than one million healthcare workers had received their first dose of vaccine. Vaccination continued by age group, starting with people aged over 80 and some high-risk groups with underlying conditions.

This study is one of the first from our region comparing the number and distribution of patients seeking RT during the COVID-19 pandemic. The present study was conducted at the largest radiation oncology center in the Northeast Turkey. RT remains a valuable treatment option for cancer during this pandemic for various reasons.

In northern Turkey, radiation oncology clinical procedures went uninterrupted during the 1 year of study at our RT centers despite COVID-19. A screening workflow was performed before all patient admission. Patients were notified regarding the requirements for entering RT areas. Modifications were implemented to fit special COVID-19 protection requirements.

Slotman et al.[14] introduced a global view of RT patient management during the pandemic, revealing how the radiation oncology community rapidly coordinated to ensure the best treatment options and, simultaneously, protected patients and healthcare professionals. As demonstrated by a recent survey supported by AIRO,[15] the vast majority of RT departments reported between a 10% and 30% reduction of clinical activity. During the first phase of the pandemic in our region, the number of patients coming for RT was higher in the first 6 months than in the second. The patients and their relatives stated that fear of getting infected could not alter living with cancer. As a

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result, the number of patients were higher in the first period. However, the continuation of the pandemic in the second period and the increase in deaths may have caused a decrease in patients in the field of oncology and less hospital admissions.

The COVID-19 protection and prevention measures effectively allowed for a safe and seamless clinical operation in our RT centers and prevented transmission of COVID-19 infections. It was determined that the transmission paths of our employees who got sick were from their spouses at home. Thanks to the measures in our clinic, there was no transmission from these personnel to other healthcare professionals.

During the COVID-19 pandemic, implementation of hypofractionated RT schedules may have reduced the commute of patients to the hospital. There are several other explanations and suggestions for conducting RT as well. Through these recommendations, radiation oncologists may be able to more adequately provide patients with the needed RT during the pandemic. It should be taken into account that most recommendations have been made in a comparatively short time in response to the pandemic, and futher discussion and evidence for some recommendations are needed. In addition, many have recommended deferring or excluding RT in nonurgent cases. In situations where higher daily doses were applied and fractions reduced, the number of patients going to the oncology centers was much less. However, in our region, such solutions were not possible during the pandemic period, especially for curative treatments, due to lack of experience and the low amount of insurance reimbursement. The concern about the possibility of transmission of COVID-19 in the early stages of the pandemic caused financial anxiety for many people over time. Although healthcare professionals were rewarded with extra wages in the first 3 months of the pandemic in Turkey, their earnings have started to decline over time due to the country's complex processes.

Our study reported a significant increase in the number of patients coming for curative RT, especially in Group A, though a decrease was shown for Group B. This is likely because patients in Group B were aware of deaths of COVID-19 and were no longer willing to go to hospitals. On the other hand, there was a slight decrease in palliative RT compared to curative treatments. A study by Glosh et al.,[16] reported that patients receiving palliative treatment more worried about cancer progression than becoming sick with COVID-19.

Despite the pandemic in Northeastern Turkey and the high number of daily patients in our division, the limited number of positive cases in our unit suggested that disinfection procedures were clearly delineated and implemented. In summary, we had a successful year in such a way as to set an example for all healthcare organizations in all pandemics, measures taken such as mask-related measures, care for personal hygiene and isolated living, and close symptom monitoring in the clinic, which are among the leading measures taken in struggling the COVID-19 pandemic.

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Conflict of Interest: All authors declared no conflict of interest.

Ethics Committee Approval: The study was approved by The Karadeniz Technical University Faculty of Medicine Ethics Committee (No: 2021/55, Date: 05/05/2021).

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