Evaluation of Anxiety and Depression Scores in Patients Receiving Radiotherapy During First Wave of COVID-19 Pandemic

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Abstract

Objective: The aim of this study was to assess the anxiety and depression levels of cancer patients who were treated with radiotherapy during the coronavirus disease-2019 pandemic.

Methods: Between April and June 2020, 66 patients were included in the study. The Hospital Anxiety and Depression test was applied in order to determine patients' anxiety and depression levels. Patients filled out the questionnaire before the first day of irradiation.

Results: The rates of anxiety and depression in our study were 53% and 59%, respectively. The mean score of Hospital Anxiety and Depression Scale-Anxiety among women (10.8 ± 3) was above the Turkish population cut-off level of 10. The mean Hospital Anxiety and Depression Scale-Anxiety score among men (7.7 ± 4) was below the Turkish cut-off. Mean Hospital Anxiety and Depression Scale-depression score of women was (8.2 ± 2.9) above the Turkish cut-off level of 7. The mean Hospital Anxiety and Depression Scale-depression scores of men were (6.2 ± 2.7) below the Turkish cut-off level. Females had significantly higher levels of depression and anxiety compared to men ($P = .008$ and $P = .004$; respectively). The highest anxiety and depression levels were observed in breast cancer patients and the lowest levels were in head and neck cancer patients.

Conclusion: Cancer and coronavirus disease-2019 pandemic are serious public health problems. Many patients perceive cancer as the main life-threatening disease. However, the pandemic increases the risk of depression and may affect cancer prognosis. Thus, psychological support for patients with cancer is advised during treatment, especially during the pandemic.

Keywords: COVID 19, HAD test, anxiety, depression, radiotherapy

Introduction

Coronavirus disease-2019 (COVID-19) virus first appeared in China, Wuhan, on December 12, 2019. In Turkey, the first coronavirus case was confirmed on March 11, 2020. As the infection rates augmented, increasing deaths, job losses, and social isolation associated with COVID-19 have been observed and life has become more stressful for most people.[1] Because of high contagion and mortality of COVID-19, anxiety and depression rates increased. Studies have stated that people lose the ability to think clearly because of COVID-19 fear.[2] This affected the quality of life of both patients and healthcare professionals besides the normal population.

It has been shown that historically, previous global disease outbreaks had clear links between pandemic-related anxiety and increased symptoms of stress, contamination concerns, health anxiety, post-traumatic stress, and suicidality.[3] Currently, in the COVID-19 pandemic period, post-traumatic stress disorder has manifested at the rate of 73%, depression at 50.7%, anxiety at 44%, and sleep disturbance at 36% in the Chinese

population.[4] Also, it has been reported that the risk of mortality rate due to COVID-19 infection among cancer patients is 10 times higher than in the non-cancer population.[5] In cancer patients, the frequency of anxiety and depression is already higher at certain rates compared to the general population.[6]

Guidelines about the clinical management of cancer patients during the COVID-19 pandemic have been published to maximize the safety of patients without compromising oncological outcome.[7] Radiotherapy as a vital component of cancer care has been continued throughout the pandemic. However, most of the cancer patients have been concerned about the severe acute respiratory syndrome-coronavirus-2 infection due to the high mortality rate of the virus. Also, fear of delay in cancer treatment or progression of the disease due to the interruption of the treatment schedule may affect the psychology of the cancer patients. Therefore, this study aimed to assess the anxiety and depression scores in cancer patients treated with radiotherapy during the first wave of the COVID-19 pandemic and also evaluated factors associated with the highest levels of depression and anxiety.

Methods

All patients who were older than 18 years and treated with radiotherapy in the radiation oncology department between April and June 2020 were eligible for the study. Patients with organic and symptomatic mental disorders that preclude adequate assessment of questions or patients who did not complete the survey or

the Hospital Anxiety and Depression (HAD) test were excluded from the study.

The survey study consisted of 2 parts. One part included a questionnaire that contained 30 items related to sociodemographic characteristics. Age, gender, and education level were acquired as demographic data. Education level was classified as low (primary school level or lack of education), intermediate (high school level), or high (university level). Type of cancer, stage of the disease, type of radiotherapy (radical, postoperative, and palliative), and administration of concomitant chemotherapy were assessed as clinical information from the patients' file.

The other part included HAD test. The Hospital Anxiety and Depression Scale was created to measure the anxiety and depression levels of the patient in hospital settings. HAD test was translated into Turkish and validated for our population by Aydemir et al[8]. For the Turkish population, the values of receiver operating characteristics for Hospital Anxiety and Depression Scale-Anxiety (HADS-A) was 10 and Hospital Anxiety and Depression Scale-Depression (HADS-D) was 7. In this study, the Turkish version of HAD was used to evaluate the anxiety and depression levels of our patients. It is a self-assessment scale. The HAD consists of 14 questions; anxiety is evaluated with 7 questions (HADS-A) and depression is evaluated with 7 questions (HADS-D). Each item has a 4-point (0-3) response category so the total score ranges from 0 to 21 for anxiety and 0 to 21 for depression. Scores between 0 and 7 points are assessed as "normal," whereas 8-10 points are assessed as "borderline," and scores ≥11 are considered to be an indication of psychological morbidity.[9-11] Eligible patients filled the HAD questionnaire prior to the first day of radiotherapy.

Intensity modulated radiation theraphy (IMRT) and 3-dimensional conformal radiotherapy plans were generated for each patient using the Eclipse version 8.6 treatment planning system. Radiotherapy was applied to all patients with Rapid arc (Varian Medical Systems, Palo Alto, Calif, USA), and 13 patients received concomitant chemotherapy with radiotherapy. All patients were followed up once a week during radiotherapy and side effects of treatment were reported.

For the analysis of the research findings, Kruskal–Wallis analyses were used for numerical values, percentage distributions, mean, standard deviation, correlation, variance, and non-parametric data. The computer software Statistical Package for the Social Sciences version 21 for Windows (IBM Corp., Armonk, NY, USA) was used for all statistical analyses and $P < .05$ was considered for statistical significance. The ethics review committee of İstanbul University-Cerrahpaşa, Cerrahpaşa School of Medicine approved the research protocol. All participants gave informed consent.

Results

A total of 66 patients were included in the study. The mean age was 52.2 years (range: 20-79). Out of 66 patients, only 7 patients were above 65 years; 35 patients were female and 31 patients were male. All patients had functional capacity evaluation scores (Karnofsky) above 90%. The distribution of patients between cancer groups was as follows: 12 patients had breast cancer, 9 patients had head and neck cancer, 7 patients had gastrointestinal cancer, 3 patients had gynecologic cancer, 2 patients had brain cancer, 2 patients had lung cancer, 1 patient had hematologic cancer, and 1 patient had sarcoma; 33 patients had postoperative, 22 patients definitive, and 11 patients palliative radiotherapy. All patients completed the radiotherapy. None of the patients had an interruption of radiotherapy due to COVID-19, but only 1 patient had treatment interruption because of myocardial infarction. Acute grade 1-2 side

effects were detected in 10% of the patients. No acute grades 3-4 were reported. The patients' characteristics are given in Table 1.

The rates of anxiety and depression in our study were 53% and 59%, respectively. The mean HADS-A score was 9.4 (0-17), and the mean HADS-D score was 7.3 (1-17). The cut-off scores of HADS-A and HADS-D for the Turkish population were 10 and 7, respectively.[8] In the present study, 31 patients had anxiety score below the Turkish cut-off and 27 patients had depression score below the Turkish cut-off. On the other hand, 26 patients had both scores above the cut-off level. The highest HADS-A level was seen in patients with breast cancer (mean: 11.5) and the lowest HADS-A level was observed in patients with head and neck cancer (mean: 6.3).

The mean HADS-A score of women (10.8 ± 3) was above the Turkish population cut-off level of 10. The mean HADS-A score of men (7.7 ± 4) was below the Turkish cut-off level. The mean HADS-D score of women was (8.2 ± 2.9) above Turkish cut-off

Table 1. Sociodemographic and Clinical Variables		
	n	**%**
Gender		
Male	31	47
Female	35	53
Education		
Primary school	37	56
High school	16	24
University	13	20
Cancer type		
Head and neck	13	20
Gastrointestinal	8	12
Breast	13	20
Gynecologic	5	7.5
Brain	7	10
Lung	4	6
Fractionation		
Hypofractionation	13	32
Simultaneous integrated boost (SIB)	12	30
Conventional radiotherapy	15	37
Concomitant chemotherapy treatment	15	37
Postoperative	33	50
Palliative	11	16
Definitive	22	33
Treatment modality		
IMRT/VMAT	48	8.5
3-DCRT	8	12
3-DCRT, 3-dimensional conformal radiotherapy.		

level of 7. The mean HADS-D score of men was (6.2 ± 2.7) below Turkish cut-off. The mean HADS-A score of primary school graduates was 10.2, high school graduates was 8.5, and university graduates was 9.6. The mean HADS-D scores of the same subgroups were 7.7, 6.8, and 7.3, respectively.

In univariate analysis, females had significantly higher levels of depression and anxiety compared to men (*P* = .008 and *P* = .004, respectively). There was no statistically significant correlation in HADS-A and HADS-D scores with comorbidity, education status, age group, and treatment intent. The median age of our patients was 52, and only 7 patients were older than 65 years. Depression and anxiety levels were similar in patients younger than 52 years (53%) and in elderly patients (52%). The highest anxiety level was observed in breast cancer patients (mean: 11.5), while the lowest level was observed in head and neck cancer patients (mean: 6.3) (Table 2).

Discussion

There are limited data regarding anxiety and depression related to the COVID-19 pandemic among cancer patients. Oncology patients are more vulnerable and more susceptible to depression than the general population. It has been shown that the risk of mortality rate due to COVID-19 infection among cancer patients is 10 times higher than in the non-cancer population.[5] However, patients are concerned about the potential to develop progressive disease due to disruption of the treatment schedules. So, receiving radiotherapy during COVID-19 pandemic conditions is challenging. In our study, we analyzed the anxiety and depression levels of our patients who were irradiated during the first wave of COVID-19 pandemic era.

The first COVID-19 case was diagnosed in March 2020 and serious restrictions were introduced due to epidemic in Turkey. After the initial peak of COVID-19 cases, radiation oncology operations slowly and cautiously returned to a new normal and most of the people got accustomed to this situation in Turkey. Our study was

carried out between March and June 2020 since we would like to observe the impact of the first peak of COVID-19 on cancer patient's depression and anxiety levels during lockdown. Also, we decided to apply the questionnaire before the start of radiotherapy in order to obtain the highest anxiety and depression levels of the patients. Dunn et al[12] showed that patients' anxiety levels have been decreased in the following week of radiotherapy compared to the beginning of radiotherapy. Also, as the pandemic evolved, habituation to the current circumstances has been observed in patients.

Different scales and questionnaires can be used to analyze anxiety and depression levels. We preferred to use the HAD test since it is more specific in terms of diagnosis compared to other tests, and it was validated and translated into Turkish by Aydemir et al. In terms of HADS cut-off points, 23.6% of the population scored above the depression cut-off point, whereas 45.1% scored above the cut-off point for anxiety in the Turkish population during the pandemic.[13] For clinical interpretation of certain HAD cut-offs, Annunziata et al[14] suggested that scores of anxiety and depression above HADS cut-offs of 9 and 7, respectively, may be useful in diagnosing anxious and depressive status in cancer patients. In our study, we observed similar results (mean HADS-A: 9.4 and mean HADS-D: 7.3). Also, the rates of anxiety and depression were 53% and 59%, respectively. Thus, both cancer diagnosis and pandemic increased anxiety and depression levels in our patients.

Factors such as gender, age, educational status, and the presence of COVID-19 may affect the depression and anxiety status of the patients. In the survey of European study of the European Network of Gynaecological Cancer Advocacy Groups (ENGAGe), the psychological effects of the COVID-19 pandemic on European gynecological cancer patients from 16 countries were evaluated using HAD scale. In multivariate analysis, they observed age, type of treatment or cancer, comorbidities, being afraid more of COVID-19 than fear of cancer progression if the treatment was canceled did not have any significant effect on patients' anxiety levels. For depression levels, only the presence of comorbidities was identified as an independent prognostic factor.[15] For possible prognostic factors, we evaluated gender, change of fractionation regimens, treatment interruption, age, and educational status.

We observed that female cancer patients were more anxious and depressed to be irradiated during the COVID-19 pandemic compared to males. Similarly, Sigorski et al[16] showed that anxiety level was higher in female individuals. In the present study, the highest anxiety level was seen in breast cancer patients and the lowest anxiety level was observed in head and neck cancer patients. It should be noted that all of the patients with breast cancer were female and most of the patients with head and neck cancer were male. However, in a meta-analysis on the prevalence of depression and anxiety in COVID-19 patients, Deng et al[17] did not observe a significant difference between gender subgroups

Karacin et al[18] reported that anxiety and fear of being infected with COVID-19 were the most common causes of delayed treatment. None of our patients had an interruption of radiotherapy due to COVID-19. Even though none of them had COVID-19 infection, fear of cancer treatment delay might still be increasing their anxiety levels. Holland et al[19] noted that patients having treatment for cancer get emotional challenges and anxiety, especially at the start of treatment, due to worry about the side effects and fear of recurrence after.

The main limitation of our study is the small sample size. This is a single-center study performed on 66 patients in a limited

Table 2. Values of Mean HADS-A and HADS-D Scores in this Study

	HADS-A	*P*	HADS-D	*P*
Gender				
Female	10.8	.004	8.2	.008
Male	8.2		6.2	
Education status				
Primary school	10.0	.22	7.54	.44
High school and university	7.5		6.97	
Comorbidity				
Presence	9.2	.7	7.18	.75
Absence	9.63		7.41	
Age				
<55	9.61	.71	7.67	.31
>55	9.21		6.91	

HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HADS-D, Hospital Anxiety and Depression Scale-Depression.

period. However, we would like to analyze the anxiety and depression levels of our patients who were irradiated during the first wave of the COVID-19 pandemic era. Yet, in the study of the ENGAGe (on the perspectives of cancer patients during the pandemic, only 133 Turkish patients were included country-wide.[15] Most of our patients had only primary school graduation; therefore, as another limitation, this might decrease the quality of the questionnaire. Education level might be an important factor for comprehending the questions.[20] Treatment schema of our patients differed. Therefore, we did not have homogeneous group data. Many other factors like time from diagnosis, total treatment duration and living conditions of patients, socioeconomic status, and television watching and following news and social media can adhere to the level of anxiety. In addition, we did not know whether these patients had anxiety and depression due to cancer or pandemic. Another limitation is the absence of a control group. Since our study analyzed the anxiety and depression levels of patients who are about to have radiation treatment, it was not possible to simulate the same treatment stress in a healthy control group.

In conclusion, we assumed that COVID-19-related anxiety is significantly lower than cancer-associated anxiety. Many patients still see cancer as the main threat to their lives and do not see COVID-19 as a real life-threatening condition. However, depression scores were higher than the cut-off. Apparently, COVID-19 by itself is a more evident depression source. Female patients and patients with breast cancer had the highest anxiety and depression levels. Cancer and COVID-19 pandemic are serious public health problems. The pandemic also increases the risk of depression and may affect the prognosis in cancer patients. For this reason, psychological support for cancer patients is advised during the treatment.

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