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The Incidence of Clinical Covid-19 Infection in Patients Undergoing Radiotherapy During the Two First Waves in a University Hospital in Iran

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ABSTRACT

Background and Objective: During the COVID-19 epidemic, concerns about cancer patients undergoing radiotherapy have increased because of the numerous hospital visits, which may increase the risk of contracting COVID-19. We aimed to investigate the incidence of COVID-19 among patients visiting our radiation oncology department during the first and second peaks of the epidemic.

Methods: In this cross-sectional study, we included all patients who underwent radiotherapy from November 2019 to September 2020. We contacted the patients and asked if they had COVID-19 during this time and how they were diagnosed. Clinical signs and a positive PCR test were acceptable as COVID-19 diagnostic criteria. We also gathered cancer and treatment status data from the patients' records in the ward medical library. This study was approved by the institutional review board and ethics committee (code: IR.TUMS.VCR.REC.1399.104).

Results: During the study period, 687 patients were admitted to our radiation oncology ward. The patients' median age was 55 (IQR: 44-65), of whom 424 (61.7%) were females. Twenty-three (3.3%) patients developed COVID-19, 15 (65.2%) of whom were diagnosed with clinical symptoms and 8 (34.8%) with PCR. Twelve and 11 patients contracted COVID-19 in the first and second epidemic peaks, respectively. Even though no patients with skin cancer or sarcomas of the bone or soft tissue contracted COVID-19, the highest frequency of COVID-19 was seen among patients with intrathoracic or lung cancer with 38 times the odds of patients with head and neck cancer to develop COVID-19. Highly susceptible patients were those with hematologic and upper gastrointestinal (GI) and gynecologic cancers, respectively. We found a significant association between intrathoracic (mainly lung) cancers and infection with COVID-19 (P-value = 0.02).

Conclusion: Patients undergoing intrathoracic cancer radiotherapy are at a higher risk of developing COVID-19. We believe these patients should be prioritized in cancer patients' screening, case-finding, or vaccination programs.

Keywords: COVID-19, Neoplasms, Radiotherapy, Lung Neoplasms, Screening, Vaccination

INTRODUCTION:

Coronavirus disease 2019 (COVID-19) is a contagious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) characterized by fever, fatigue, cough, and respiratory problems [1].

The COVID-19 pandemic has raised concerns over cancer patients because preliminary reports indicated a higher mortality rate and severity among patients with underlying diseases [2]. There are many reasons why cancer patients are more prone to infections than others, including a weakened immune system due to the disease itself and its treatments and a higher rate of exposure due to frequent visits to cancer centers. There are three cornerstone treatments for cancer, including surgery, radiation therapy, and systemic therapy.

Cancer patients have to go to the radiotherapy clinic for several weeks during their radiotherapy treatment. For example, in patients with palliative treatment, 10 fractions (2 weeks) and in patients with prostate cancer, 35 to 37 fractions (7 weeks) are required. Moreover, the patients should be present for fixation, simulation, CT scan, and treatment planning before starting treatment. They may also go to other services for their routine post-treatment checkups. Frequent and long-term visits to health care centers increase the risk of developing COVID-19.

Radiotherapy staff may also work in COVID-related departments due to limited staffing and may be asymptomatic carriers of COVID at the time of their exposure to cancer patients.

Also, radiotherapy wards are usually located on the lower floors or underground, and the air conditioning may not be well.

Another downside for cancer patients is the Iranian culture, which requires relatives to visit them when someone has an unfortunate event or grave crisis such as a cancer diagnosis. This would reduce social distancing and result in a higher risk of COVID-19 infection.

For these reasons, at our service and department of radiation oncology, we have considered protocols for treating patients that are fully mentioned elsewhere [3]. These protocols follow the global guidelines and facilities of our hospital, but due to the high burden of patients and the inadequate equipment of the ward, we face many limitations.

Despite all these protocols, in this study, we aimed to investigate the incidence of COVID-19 among individuals visiting our service during the first (from February 2020 to May 2020) and second (from May 2020 to September 2020) waves of the epidemic.

Materials and Methods

WIn this cross-sectional study, 687 patients were studied. Patients who underwent radiotherapy (with or without other treatment modalities) at our center from November 2019 (i.e., 3 months before the first wave of the epidemic in Iran) to September 2020 (end of the second wave) were included. We contacted the patients and asked if they had COVID-19 during this period, and if so, how it was diagnosed; what the probable source of the infection was; if their COVID-19 directed therapies were done in either outpatient or inpatient setting; if COVID-19 disrupted their cancer treatment; how their cancer treatment continued following recovery from COVID-19; etc. Clinical signs or a positive PCR test were acceptable as COVID-19 diagnostic criteria. Patients who died before our phone call were excluded from the study. We also collected cancer data and treatment status data from the patients' records in the ward medical library. This study was approved by the institutional review board and ethics committee (code: IR.TUMS.VCR.REC.1399.104).

Results

During the study, 687 patients were admitted to our radiation oncology ward. The median age was 55 (IQR: 44-65), and 424 (61.7%) were females. Twenty-three (3.3%) patients developed COVID-19, 15 (65.2%) of whom were diagnosed with clinical symptoms and 8 (34.8%) with PCR. Twelve and 11 patients contracted COVID-19 in the first and second epidemic peaks, respectively. Among those who had COVID-19, 4 (17.4%) died due to the disease, 6 (26.1%) were treated in an outpatient setting, 7 (30.4%) were admitted in non-ICU wards, and 6 (26.1%)

were asymptomatic.

There were interruptions in the treatment process of otherwise healthy patients due to the COVID-19 pandemic. Four (0.6%) patients discontinued their planned treatment, 9 (1.4%) faced a transient pause in the middle of treatment, 11 (1.7%) started their treatment with a delay, and 14 (2.1%) did not attend for follow up visits after the beginning of the pandemic. Nevertheless, the remaining 626 (91.1%) patients continued their treatment based on the protocol settled in the ward without any considerable changes.

All patients infected by COVID-19 were treated with external radiotherapy, and no one who underwent brachytherapy contracted COVID-19. No significant association was found between smoking and opium use, type of radiotherapy (external or brachytherapy), number of fractions, and gender with the risk of COVID-19 infection. Although the rate of COVID-19 was higher among those patients with two or more underlying diseases compared with one or none, the association was not statistically significant.

The distribution of various cancer subsites has been depicted in Figure 1. We could not find the primary diagnosis for 13 patients. Even though no patients with skin cancer or sarcomas of the bone or soft tissue contracted COVID-19, the highest frequency of COVID-19 was seen among patients with intrathoracic or lung cancer with 38 times the odds of patients with head and neck cancer to catch COVID-19 (table 1). The highly susceptible patients were those with hematologic and upper GI and gynecologic cancers, respectively. We found a significant association between intrathoracic cancers (mainly lung cancer) and COVID-19 infection (P-value = 0.02).

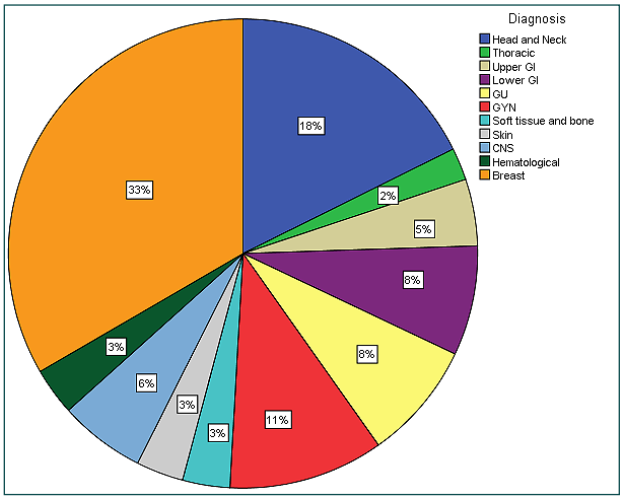

Figure.1. Distribution of known cancer subsites among patients admitted to radiation oncology ward during the study period

DISCUSSION

Unlike most studies on cancer patients and COVID-19 [8-11], the proportion of women in our study was higher than men (3.8% vs. 2.7%); perhaps because our study was limited to the outpatients of the radiotherapy ward in which the majority of patients (33%) were women with breast cancer. In contrast, other studies have selected patients from all radiotherapy and non-radiotherapy wards, including outpatients and inpatients. In most of these studies, lung cancer, more common in men than women, was the most common cancer among patients. The adjusted prevalence of COVID-19 until August 20, 2020, was estimated as 14.2% [12]. However, the prevalence of COVID-19 in cancerous patients in our study was 3.3%, which is lower than the general population. There may be two hypothetical reasons for this: (a) Cancer patients pay more attention to recommended precautions; and (b) few studies show that angiotensin-converting enzyme 2 (ACE2)-lowering antineoplastic compounds, including mTOR/PI3K inhibitors and antimetabolites, may have a protective effect against COVID-19 [13-15]. Our study found the highest number of COVID-19 infections among patients with intrathoracic or hematological cancers. Although we did not have data on the severity of COVID-19 in our patients, consistent with several other studies, our study showed that the prevalence of COVID-19 in patients with lung and hematologic cancers was higher than other cancers [16]. There are some hypotheses justifying this association. The overlapping pulmonary signs and symptoms due to lung cancer can mimic COVID-19 infection regarding clinical and radiographic manifestations. These similarities can pose a major challenge to clinicians in distinguishing lung cancer evolution from severe viral pneumonia based on radiological and clinical evidence [17, 18]. Second, consid-

	Not infected with COVID-19	Infected with COVID 19	P-value
Age	55 (44-65)	56 (44-63)	0.810
Gender			
Male	256 (97.3%)	7 (2.7%)	0.517
Female	408 (96.2%)	16 (3.8%)	
Smoking			
Yes	77 (98.7%)	1(1.3%)	0.28
No	587 (96.4%)	22 (3.6%)	
Opium			
Yes	48 (98%)	1 (2%)	0.59
No	616 (96.6%)	22 (3.4%)	
Underlying disease			
None or one	645 (93.8)	20 (3.1)	0.16
Two or more	42 (6.2)	3 (7.1)	
Subsite			
Head & Neck	117 (98.3%)	2 (1.7%)	Ref.
Breast	219 (97.3%)	6 (2.7%)	0.191
Gynecological	68 (94.4%)	4 (5.6%)	0.096
Lower GI	50 (98%)	1(2.0%)	0.512
GU	54 (98.2%)	1 (1.8%)	0.998
CNS	38 (95%)	2 (5%)	0.155
Upper GI	29 (93.5%)	2 (6.5%)	0.105
Skin	22 (100%)	0	0.998
Soft Tissue & Bone	22 (100%)	0	0.999
Hematological	20 (90.9%)	2 (9.1%)	0.061
Intrathoracic	12 (80%)	3 (20%)	0.020
Stage			
I – III	594 (97.1)	18 (2.9)	0.095
IV	70 (93.3)	5 (6.7)	
RT type			
External Beam	644 (96.7%)	23 (3.3%)	0.5
Brachytherapy	20 (100%)	0 (0)	
RT intent			
Curative	599 (96.9)	19 (3.1)	0.276
Palliative	65 (94.2)	4 (5.8)	
No of Fractions	25 (20-30)	25 (18-30)	0.601

Table 1. The rate of COVID-19 contraction based on the studied variables

ering the coexistence of chronic obstructive pulmonary disease and lung cancer in smokers, chronic use of corticosteroids may place patients at increased risk of contracting and severity of COVID-19 [16]. Changes in the anatomy of airway and pulmonary tissues (mechanical tumor obstruction or previous lung surgery) may predispose patients to established COVID-19 infection [19-21]. Because most patients with hematologic malignancy are immunodeficient, it makes sense to become infected with a lower virus load.

Based on the pieces of evidence regarding lung and hematological cancer patients presented in this study and the fact that these patients pose a higher mortality risk with COVID-19 [22], for these patients, we recommend:

1.An accurate COVID-19 screening model using PCR tests other than serology testing [23] for early detection of COVID-19 in lung cancer patients can potentially reduce the risk of severe complications and mortality considering that lung cancer patients show similar clinical symptoms, including cough, fever, and dyspnea with SARS-CoV-2.

2.Try to minimize hospital visits without removing active treatments to decrease nosocomial transmission.

3.Implant strict protocols for such patients during radiation oncology consultation, treatment simulation, delivery, and post-treatment follow-up visits.

4.These patients should be given priority in receiving the booster dose of the COVID-19 vaccine and regular checkups for antibody level and vaccination efficacy.

About the mortality of COVID-19, the rate observed in our cohort is slightly lower than our previous reports of cancer patients with inpatient settings [24]. However, this rate is not significantly different based on the 95% confidence interval between 17 and 43%.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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