

Impact of the COVID-19 Pandemic Lockdown on Radiotherapy Patients: A Retrospective Cohort Study

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has led to the imposition of a strict nationwide lockdown, which has affected all aspects of healthcare, including the delivery of standard care to cancer patients. **Objective:** The aim of this study was to report the impact of the COVID-19 pandemic on patient attendance at a radiotherapy department during the lockdown period. **Methods:** This is a retrospective analysis of all patients planned for radiotherapy at the National Institute of Oncology in Rabat. Patient compliance to radiotherapy during the lockdown period was measured and compared with that during the same period in 2019. Data regarding age, sex, tumor site and treatment-related factors were analyzed and compared with those during the same period in 2019. **Results:** We included a total of 650 patients, 348 patients in Group A (control period) and 302 in Group B (lockdown period). Patients were aged between 30 and 70 years in about 85%, with a female predominance in both groups. The most common sites of occurrence of cancer were breast, female reproductive organs and the head and neck. A 13.2% reduction in the number of treated patients and a 16.9% reduction in the number of sessions was observed. There was a significant decrease in the proportion of breast cancers treated ($P = 0.03$). The proportion of patients receiving palliative radiotherapy increased significantly ($P = 0.03$), with a significant increase in the use of single-fraction palliative radiation therapy ($P = 0.006$). There was a significant difference in the compliance to radiotherapy during the lockdown period (92.3% versus 86.4%, $P = 0.01$); delays and interruptions were due to travel restrictions (58.5%) and fear of contamination (29.2%). No patient was tested positive for COVID-19 during radiotherapy during the study period. **Conclusion:** We observed a decrease in

the number of treated patients during the lockdown despite our efforts to maintain the treatment routine. A significant decrease in radiotherapy compliance was noted during the lockdown. The proportion of irradiated breast cancers decreased significantly during the lockdown while patients treated with palliative intent increased significantly, with increased use of single-fraction palliative radiotherapy.

Keywords

Cancer, COVID-19 Pandemic, Lockdown, Radiotherapy, Compliance

1. Introduction

The epidemic of Coronavirus Disease 2019 (COVID-19) evolved into a global pandemic in March 2020, causing more than 118,000 cases and 4291 deaths in 114 countries from Asia to the Middle East, Europe and the United States [1] [2]. The first case of COVID-19 in Morocco was reported on March 2nd, 2020 in Casablanca. The situation worsened daily and the number of cases rose to 1661 by April 11, 2020. The Moroccan Government responded quickly to contain the spread of the virus by implementing a series of restrictive measures. This was followed by a nationwide lockdown from March 20, 2020 to June 20, 2020 [3]. However, these strict restrictions and the unprecedented burden of COVID-19 on our health-care system have disrupted the diagnosis and treatment of other diseases including cancer [4].

Radiation therapy is one of the cornerstones of cancer treatment. Together with surgery and chemotherapy, it plays an important role in the local control of most malignant tumors and the survival of patients. Suboptimal delivery of radiotherapy (including delays, interruptions or omissions) has been demonstrated to compromise both local control and survival [5]. For radiation oncology departments, the COVID-19 pandemic presents a unique challenge for disease protection and prevention for both patients and staff, owing to the weakened immune systems of cancer patients and the need to deliver timely and uninterrupted radiotherapy. Various guidelines have been proposed regarding the practice of radiotherapy to fight the COVID-19 crisis and ensure treatment for those who require it the most [6]. Single-institution studies have reported a sharp decline in the number of treated patients in radiotherapy departments during the lockdown, with a greater decrease in the total number of sessions [7] [8].

In this context, we planned this study with an aim to assess the impact of the COVID-19 pandemic on the attendance of patients receiving radiotherapy as a part of their cancer treatment at a public hospital in Rabat during the lockdown.

2. Materials and Methods

This is a retrospective analysis of all cancer patients planned to receive radiation treatment in the Radiation Oncology department of the National Institute of

Oncology in Rabat, during the national lockdown period from March 20, 2020, to June 20, 2020.

Ibn Sina University Hospital of Rabat is a public general hospital located in the Rabat-Sale-Kenitra region in the northwest of Morocco, covering an area with 4,580,866 inhabitants. It comprises a large complex with 10 hospitals and approximately 2400 beds. The National Institute of Oncology in Rabat is one of them. The Radiation Oncology department has 3 linear accelerators, one VERSA HD and one high dose-rate brachytherapy machine for patient treatment. Approximately 120 patients are treated every day, and there are about 15 first visits every day. In addition, the medical and nursing staff manages 16 hospital beds for inpatients who require special support for concomitant chemoradiation and management of treatment toxicity.

The study included all consecutive patients with cancer who were planned for and who received radiotherapy at our center during the study period. Patients who defaulted after planning radiotherapy were excluded from the analysis. The patients were divided into two groups. Group A comprised patients treated from March to June 2019, which was the control period. Group B comprised patients treated from March to June 2020, which was the lockdown period.

Our primary objective was to assess patients' compliance to radiotherapy during the lockdown period. Our secondary objective was to assess the impact of the pandemic on patients receiving radiotherapy and whether it correlated with the patients' age, gender, sociodemographic factors, site of disease, intent of radiotherapy and treatment-related factors.

The list of all the patients receiving radiotherapy during the study period was extracted from MOSAIQ® software database, and the recorded files were accessed to obtain the required data regarding the patients' age, gender, site of disease and treatment-related information (intent of radiotherapy, use of concurrent chemotherapy, radiation spreading, fractionation and planning techniques).

An analysis of the lockdown period (from March to June 2020) was carried out, and this period was compared with the same period in 2019. Data regarding the overall radiotherapy time and the completion of the planned radiotherapy treatment were evaluated to assess our primary endpoint of compliance to radiotherapy. For our secondary endpoint, additional data regarding the patients' age, gender, sociodemographic factors, site of disease and treatment were analyzed to assess if these factors affected the number of patients receiving radiotherapy during the lockdown.

Data were entered in Microsoft Excel and categorized into Groups A and B. 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.

3. Results

A total of 753 patients were planned to receive radiotherapy during the study period. There were 396 patients in Group A (control period) and 357 in Group B (lockdown period). The number of patients who defaulted from treatment was

48 (12.1%) for Group A and 55 (15.4%) for Group B. Finally, a total of 348 patients were started on radiotherapy in Group A versus 302 in Group B, *i.e.*, a decrease of 13.2%. These 650 patients were further evaluated for the primary and secondary endpoints of the study.

The age group analysis showed that about 85% of the patients were aged between 30 and 70 years in both groups. Forty-three patients were aged over 70 years (12.4%) in Group A and 31 (10.3%) in Group B (Figure 1, Table 1).

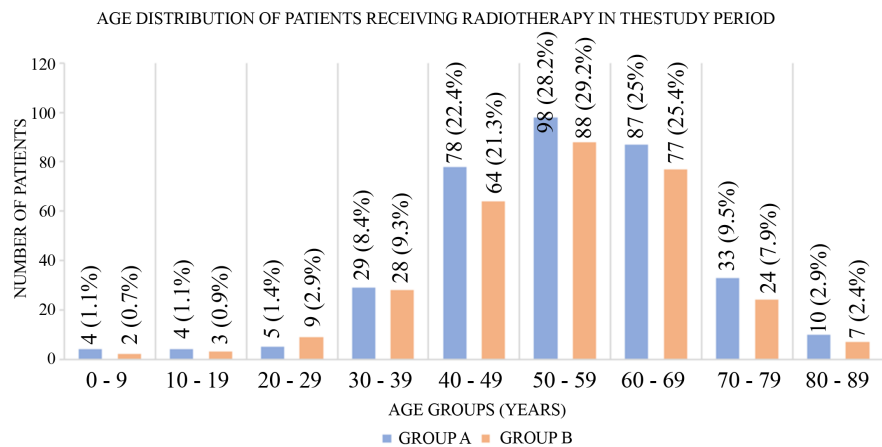


Figure 1. Age distribution of patients who received radiotherapy during the study period. Group A indicates the patients treated during the prelockdown phase and Group B indicates the patients treated during the lockdown phase. The color bars indicate the age in years of the patients.

Table 1. The distribution of age and gender in patients receiving radiotherapy during the study period.

	Group A Prelockdown period (n = 348), n (%)	Group B Lockdown period (n = 302), n (%)	Absolute difference (%)	P
Age				
0 - 9	4 (1.1)	2 (0.7)		
10 - 19	4 (1.1)	3 (0.9)		
20 - 29	5 (1.4)	9 (2.9)		
30 - 39	29 (8.4)	28 (9.3)		
40 - 49	78 (22.4)	64 (21.3)		
50 - 59	98 (28.2)	88 (29.2)		
60 - 69	87 (25)	77 (25.4)		
70 - 79	33 (9.5)	24 (7.9)		
80 - 89	10 (2.9)	7 (2.4)		
Gender				
Male	106 (30.4)	98 (32.4)	2	
Female	242 (69.6)	204 (67.6)	1.94	0.58

A gender-wise analysis showed that there were 242 (69.5%) female patients in Group A; this number decreased to 204 (67.6%) in Group B. Similarly, the number of male patients decreased from 106 in Group A to 98 in Group B, but their proportion increased from 30.4% to 32.4%. The difference was not statistically significant ($P = 0.58$) (Table 1).

Most of the patients came from disadvantaged socio-economic backgrounds and lived far from Rabat. In both groups, the most common sites of occurrence of cancer were breast, female reproductive organs and the head and neck. The number of patients with breast, gynecology and head, and neck cancers were 138 (39.7%), 57 (16.4%), and 34 (9.8%), respectively, in Group A and 87 (28.8%), 74 (24.5%), and 37 (12.3%), respectively, in Group B. There was a significant decrease in the proportion of breast cancers treated from period A to B ($P = 0.03$) (Table 2).

The analysis of the intent of treatment showed that 316 patients (90.9%) were treated with a curative intent in Group A versus 258 patients (85.5%) in Group B. Conversely, the proportion of patients treated with a palliative intent increased from 32 (9.1%) in Group A to 44 (14.5%) in Group B and the difference was statistically significant ($P = 0.03$). As to the planning technique, about 82% of the patients received three-dimensional conformal radiation therapy in both groups, whereas 18% were treated with volumetric modulated arc therapy (VMAT).

Similar radiation fractionation was used for patients treated with curative intent in both groups. However, there was a significant increase in the use of single-fraction radiation protocol in patients treated with a palliative intent during period B ($P = 0.006$). Only 15.6% of the patients in Group A received single fraction of radiation therapy as compared to 45.5% in Group B. There was a significant decrease in the use of more prolonged radiation protocols such as 30 Gy/10#, and 20 Gy/5# for the patients treated with palliative intent during the lockdown (Table 3).

Table 2. Site-wise distribution of patients receiving radiotherapy during the study period.

	Group A Prelockdown period (n = 348), n (%)	Group B Lockdown period (n = 302), n (%)	Absolute difference (%)	P
Breast	138 (39.7)	87 (28.8)	10.9	0.03
Gynecological	57 (16.4)	74 (24.5)	8.1	
Head and neck	34 (9.8)	37 (12.3)	2.5	
Gastrointestinal	21 (6.0)	23 (7.6)	1.6	
Genitourinary	14 (4.0)	8 (2.6)	1.4	
Lung	21 (6.0)	6 (2.0)	4.0	
Brain	11 (3.2)	10 (3.3)	0.1	
Bone and Soft tissue	10 (2.9)	5 (1.7)	0.8	
Others	42 (12.0)	52 (17.2)	5.2	

*Others: Pediatric, skin, lymphomas and hematologic, secondary tumors.

Table 3. Intent of treatment, use of concurrent chemotherapy, details of radiation technique and the fractionation used for treating patients with a palliative intent during the study period.

	Group A Prelockdown period (n = 348), n (%)	Group B Lockdown period (n = 302), n (%)	Absolute difference (%)	P
Intent of treatment				
Curative	316 (90.9)	258 (85.5)	5.4	0.03
Palliative	32 (9.1)	44 (14.5)	5.4	
Concurrent chemotherapy				
	166 (47.7)	131 (43.4)	4.3	0.26
Radiotherapy technique				
3D CRT	286 (82.1)	248 (82.1)	0	
VMAT	62 (17.9)	54 (17.9)	0	
Radiotherapy fractionation				
8 Gy/1#	5 (15.6)	20 (45.5)		0.006
13 Gy/2#	2 (6.3)	6 (13.6)		
20 Gy/5#	13 (40.6)	10 (22.7)		
30 Gy/10#	12 (37.5)	8 (18.2)		

3D CRT: Three-dimensional conformal radiation therapy, 30 Gy/10#: 30 Gray in 10 fractions delivered at 3 Gray per fraction, 20 Gy/5#: 20 Gray in 5 fractions delivered at 4 Gray per fraction, 13 Gy/2#: 13 Gray delivered in two fractions delivered at 6.5 Gray per fraction, 8 Gy/1#: 8 Gray delivered in a single fraction.

Overall, a decrease in the number of radiotherapy sessions was observed between the two periods: from 9820 sessions in group A to 8155 sessions in group B, which represented a 16.9% reduction.

The number of patients receiving concurrent chemotherapy decreased from 166 (47.7%) in Group A to 131 (43.4%) in Group B, but this difference of 4.3% was not statistically significant ($P = 0.26$) (Table 3). Oral administration was encouraged as much as possible, and weekly chemotherapy protocols were replaced by triweekly regimens in period B.

There was a significant difference in the compliance to radiotherapy between the two groups. The proportion of patients who completed radiotherapy was 92.3% in Group A as compared to 86.4% in Group B ($P = 0.01$). Suboptimal delivery of radiotherapy was observed in 41 patients in Group B, including delays in 14 patients (4.6%) and interruptions in 27 patients (8.9%) (Table 4). Most common reasons for discontinuing or interrupting treatment during the lockdown were lack of transportation and travel restrictions in 24 patients (58.5%) and fear of contamination in 12 patients (29.3%). Disease progression led 5 patients (12.2%) to interrupt treatment.

Table 4. Radiotherapy completion in the cohort of patients receiving radiotherapy during the study period.

	Group A Prelockdown period (n = 348), n (%)	Group B Lockdown period (n = 302), n (%)	Absolute difference (%)	P
Radiotherapy compliance	321 (92.3)	261 (86.4)	5.9	0.01
Interruptions	8 (2.3)	14 (4.6)	2.3	
Delays	19 (5.4)	27 (8.9)	3.5	

Every patient was checked for Covid-19 symptoms before starting the radiation treatment at our department. Patients who were asymptomatic were not tested prior to starting radiotherapy. No patient was tested positive for COVID-19 during radiation therapy during the study period in our department.

4. Discussion

The coronavirus pandemic has led to many changes in health policies worldwide, directing all efforts toward COVID-19 treatment. The routine management of all other noncommunicable diseases, including cancer, was disrupted [4].

Cancer patients have been recognized as a highly vulnerable group in the current pandemic due to their immunocompromised status caused by the malignancy and its treatments as well as the limited availability of cancer treatment facilities [9] [10].

With about 50% of cancer patients receiving radiation therapy as part of their management, radiotherapy management is particularly complicated in this situation. The cost-effectiveness balance must be evaluated not only regarding cancer treatment but also regarding the risk of infection by patients who need to come every day to the radiotherapy facility for treatment. Radiotherapy remains a valuable treatment option for cancer during this pandemic for several reasons. Radiotherapy protocols are only moderately immunosuppressive when compared to chemotherapy. The availability of hypofractionated regimens for several cancer types has drastically reduced the number of visits for patients, thus limiting the risks of exposure, while maintaining timely treatment schedules. Another important role of radiotherapy is its potential to safely replace surgery in certain settings, including cancers of the head and neck, esophagus, pancreas, prostate or bladder, and non-small-cell lung cancer (NSCLC). Radiotherapy can be delivered safely to the patients with the use of proper personal protective equipment, both by the patient and the health-care personnel. In addition, radiotherapy is delivered in a setup that does not routinely require the use of critical hospital resources such as the intensive care unit and ventilators [5].

Therefore, the main policy of our department was to continue the treatment of cancer patients.

However, specific modifications according to available scientific evidence were permitted to preserve the patient's outcomes while simultaneously mini-

mizing the risk of COVID-19 contagion in these patients. Safety measures were established to protect patients and staff, and specific recommendations and policies were adopted so as not to impact patient care.

This study was conducted at the largest public cancer hospital in Rabat region. To the best of our knowledge, this is the first Moroccan study comparing the number and distribution of patients coming for radiotherapy before and during the lockdown period among the COVID-19 pandemic.

We observed a decrease in the number of treated patients, as expected, of around 13%, with a higher decrease in the number of radiotherapy sessions (16.9%). However, this decline was not specific to our department, and has been reported by many institutions in the literature. The European Society for Radiation and Oncology (ESTRO) surveyed a large number of European radiation oncology centers to evaluate the impact of COVID-19 on their practice. A decline in patient volume was noticed in 60% of the departments. A comparison of the European data with data from North-America, shows many similarities. In the ASTRO report, 84% of centers reported a decrease in patient volumes to 80% or less compared to normal [4] [11].

This decrease was partly due to reduced referrals to radiotherapy. In order to increase the availability of sub-intensive and intensive care units (ICU), the number of surgical procedures in our hospital decreased drastically and only non-deferrable surgeries were maintained. Likewise, to decrease potential exposure of patients during the pandemic outbreak, decisions to skip or postpone scheduled chemotherapy were made for both curative and palliative treatments [6] [12].

Radiotherapy prioritization and protection procedures allowed balancing between cancer patient care and safety while safeguarding the healthcare staff. Based on international guidelines, old principles were adopted as new behaviors to radiation oncologists: Safety, Avoidance, Rescheduling and Shortening. Avoidance means omission of radiation therapy when the risk of severe complication from COVID-19 (for elderly patients and/or with serious underlying health conditions) outweighs the benefit of radiation therapy. Rescheduling means deferring/delaying radiotherapy when there is no or little expected adverse effect on outcome from the delay [11].

Thus, the number of patients scheduled for radiotherapy was reduced as a part of our departmental policy during the lockdown. This was done with the intent of decreasing the patient load on the machines and the waiting area, so that proper sanitization and social distancing could be maintained for the safety of patients and the hospital staff. There was also the possibility of omission or delays/deferrals in irradiation for certain disease sites.

Besides, about 15% of the patients planned for radiotherapy during the lockdown defaulted from their treatment. It could be due to the fact that a certain number of patients refused treatment initially, as many patients who required adjuvant radiotherapy and were not symptomatic decided to defer their treatment. A major problem with our patients is their financial status. Most of them depend on government funds and schemes for financial assistance for their can-

cer treatment, the sanction of which got delayed due to sudden closure of all offices, another reason for patients not taking their planned treatment.

Radiotherapy usually requires weeks of continuous treatment that can extend from 1 to 7 weeks, depending on the intent of treatment and the fractionation used. Once the treatment was started, there was a significant decline in the number of patients who completed the planned radiation protocol in the lockdown period. The most important cause for interruptions or delays was the restriction on the public transport. As most of our patients belong to the low socioeconomic stratum and come from the distant rural areas for their treatment, they are entirely dependent on the public transport system for their travel. The travel restrictions and the difficulties due to the quarantine laws implemented in the city had a great impact. Although travel for medical emergencies and treatment was allowed during the lockdown, a lack of clarity on advisories issued by the government, particularly among the illiterate patients. Moreover, the unavailability of accommodation near the cancer center, due to the closure of hotels and guest houses was another important reason for patients not completing their radiation treatment [13].

More than lockdown measures, it is the fear of getting infected with the coronavirus that slowed down access to treatment. Vanni *et al.* reported that COVID-19-related anxiety and fear of contagion could affect patients' decision-making process, leading to higher rates of treatment refusal [14].

Our analysis of the behavior of numbers according to diagnosis revealed a larger negative impact on breast cancer treatment. This could be related to the decline in breast cancer patients diagnosed during the pandemic. All non-urgent services, as breast cancer screening, were temporarily suspended during lockdown, reserving examinations for patients with symptoms (auto palpation of a mass, for example) [15] [16]. More worryingly, although travel for care was authorized, general practitioners and specialists have observed a significant drop in their consultations. According to Gosset *et al.*, attendance at doctors' offices has dropped by nearly 30% even when counting teleconsultations, compared to the same period in 2019 [17].

This may also indicate that other treatment options were offered to breast cancer patients. Following the directives of international guidelines, in order to limit the risks of contamination for patients and increase the reception capacities of intensive care units, the usual protocols have been changed significantly [18] [19] [20]. Breast cancer surgery was deferred in several situations. Surgery for in situ carcinomas could be postponed for up to six weeks or even longer for low-grade tumors. Hormone therapy was possible in the event of co-morbidities and tumor expressing hormone receptors, in order to delay surgery or radiotherapy [6] [17].

Besides, patients with breast cancer requiring adjuvant radiation are usually asymptomatic, and hence, they preferred to defer the treatment as they feared COVID-19 more than cancer progression.

The decrease in the number of female patients treated for breast cancer during

the lockdown could also be explained by the fact that female patients, especially from the low socioeconomic background, are dependent on the male members of their families to travel long distances. The sudden lockdown and imposed travel restrictions might have forced the earning male members to stay back at their place of work, and thus they could not bring their female relatives to the hospital. Besides, in our society, most of the household responsibilities are taken care of by the female members; therefore, many of them might have intentionally delayed their treatments with the intention of taking care of their families during the lockdown.

The 2.5% increase in the number of patients with head and neck cancer seen during the lockdown period could have resulted from the deferral of surgery and referral for nonsurgical treatments [21].

Low cancer awareness, the lack of screening and the difficulty to access health-care lead to diagnosis in an advanced stage in a large number of our cancer patients [22]. Our study reported a significant increase in the number of patients coming for palliative-intent radiotherapy. A similar observation has been reported by Ghosh *et al.* and Chauhan *et al.* [8] [23]. The fact that treatment for patients in emergency situations is always prioritized may justify this finding. Besides, patients receiving palliative treatment worried more about disease progression than acquiring COVID-19. This is likely because they were aware of their poor prognosis and were concerned about further deterioration of their condition. Another reason could be the unbearable pain and other symptoms that these patients suffer, for which they seek relief through palliative radiotherapy.

During the COVID-19 crisis, a worldwide series of treatment policies and recommendations regarding radiation treatment were published and summarized in a review by Vordermark [24]. Many of these suggestions recommend more extensive use of hypofractionated schedules when appropriate to reduce hospital visits, *i.e.*, a reduced number of fractions with a higher dose/fraction that produce the same biological effect as conventional fractionation. In our department, there was no change in the radiotherapy fractionation protocol of patients treated with a curative intent, as we currently use various hypofractionated radiation protocols that already allow a lower number of visits to the hospital, especially for breast, prostate and head and neck cancers treatment.

However, we treated a significantly higher number of patients with single-fraction radiotherapy in the palliative setting during the lockdown period. Single fraction radiotherapy is a valid option for patients requiring palliative radiotherapy, especially for those with symptomatic uncomplicated bone metastases [25]. With the use of single-fraction radiotherapy with 3D conformational radiotherapy, the patients could both complete the treatment and return home on the same day. In addition to solving the issue of accommodation for the patient and their caregivers, this protocol also decreased the patient load on the radiotherapy machine.

Our study showed no significant change in the use of concurrent chemothe-

rapy during the lockdown period. A study by Patil *et al.* that compared the pattern of care among patients with head and neck cancer before and during the pandemic also showed that there was no change in the pattern of selection of patients for concurrent chemotherapy during the pandemic period. However, oral administration and triweekly protocols were preferred to reduce patient exposure to the risk of COVID-19 contamination. Similarly, Patil *et al.* also preferred the use of oral metronomic chemotherapy over intravenous chemotherapy as it did not require hospital admission and was less toxic with good outcomes [26].

Being retrospective and observational in design, our study had several limitations. The cause for defaulting from the treatment could not be assessed. As we enrolled all consecutive patients whose radiotherapy was started during the study period, the database comprised a diverse group of patients with cancers arising in various sub-sites and different staging systems. Thus, a generalized stage-wise distribution of patients coming for the treatment in the prelockdown and lockdown periods could not be assessed. Moreover, no follow-up data have been included, which could have provided insights into the patient-related outcomes.

5. Conclusions

The COVID-19 pandemic has created an unprecedented challenge for health care systems and has presented numerous impacts on social life and human behavior worldwide. The evaluation of oncology practices in the wake of the COVID 19 pandemic is essential to understand its real impact, and prepare for possible future crises. Many hospitals have deprogrammed patients because cancer is an additional risk factor for COVID-19. The coronavirus frightened patients who were dissuaded from consulting and getting diagnosed. Cancer patients have suffered postponements of surgeries as well as delays in chemotherapy treatments, leading to reduced referrals to radiotherapy. We observed a decline in the number of patients receiving radiotherapy and the number of sessions delivered in our department during the lockdown, despite our efforts to maintain the continuity of care. The proportion of irradiated breast cancers decreased significantly during the lockdown. The number of patients being treated with palliative intent radiation increased significantly with the increased use of single-fraction radiation treatment. A significant decrease in radiotherapy compliance was noted during the lockdown. Interruptions and delays were due to travel restrictions, unavailability of accommodation, and fear of contagion. No patient was tested positive for COVID-19 during treatment in the first few months of the pandemic in Rabat, Morocco.

We hope that observational studies like ours will expand our experience of using radiotherapy in patients with cancer during the pandemic.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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