Clinical Outcomes of Patients Treated with Short-course Palliative Radiotherapy in the First Year of the COVID-19 Pandemic: A Single Institution Experience

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ABSTRACT

Objective. This study aimed to describe the clinical profile and treatment outcomes of patients treated with a short course (<10 fractions) of palliative radiotherapy during the first year of the COVID-19 pandemic. Another aim of the study is to compare patients treated with short-course and long-course palliative radiotherapy in terms of the site and volume irradiated.

Methods. An ambispective study comprised 23 patients treated with short-course palliative radiotherapy from March 2020 to February 2021. The retrospective aspect of this study included a review of medical records and radiotherapy plans, while the prospective part involved communication with patients or legally authorized representatives via phone call. Demographic, clinical, and treatment-related information were gathered.

Results. Of 92 patients receiving palliative radiotherapy, 23 were treated with a short course, while 69 were planned for at least ten fractions. Of the 23 patients receiving short-course radiotherapy, most had colorectal (35%) and head and neck (26%) primary malignancies. The most commonly treated sites were the pelvis (24%), vertebral bones (21%), and head and neck masses (21%), and the most common indications were pain (45%) and bleeding (32%). The majority were treated with 20 Gy in 5 fractions (42%) and 25 Gy in 5 fractions (38%). Complete resolution of symptoms was observed in 43% of cases, and more than half reported no side effects (58%). Median survival was 71 days. All patients treated in the lung, stomach, and brain underwent a long course of palliative radiotherapy. Patients with a long course also had higher mean irradiated volumes (1871 cm^3 vs. 2150 cm^3).

Conclusion. In this single institution review, a short course of palliative radiotherapy was proven to provide good symptom control with few side effects. During the COVID-19 pandemic, its use should be strongly considered, especially in patients with poor performance status, transportation difficulties, and limited life expectancy.

Keywords: palliative radiotherapy, COVID-19 pandemic, short course

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INTRODUCTION

Radiotherapy has proven to be a valuable tool in providing palliative relief for a number of symptoms experienced by oncologic patients. Whether these arise from primary tumors or metastatic sites, radiation offers a fast, effective, and affordable means to address symptoms, including pain, bleeding, obstruction, and neurologic symptoms.[1] Palliative radiotherapy commonly utilizes dose regimens of 8 Gy in 1 fraction, 20 Gy in 5 fractions, 24 Gy in 6 fractions, and 30 Gy in 10 fractions. Studies have shown equivalent efficacy rates using shorter fractions compared with longer ones.[2–5] However, the choice of fractionation is still influenced by several factors, including the patient's performance status,

presence of co-morbidities, transportation capabilities, the type of tumor, and potential toxicities.[6]

The coronavirus disease (COVID-19) pandemic has brought a restructuring of cancer care. Different guidelines have advocated prioritization of patients for treatment based on urgency, intent (whether curative or non-curative and radical or adjuvant), type of tumor, and performance status, among others.[7,8] In particular, a recommendation for palliative radiotherapy is to use short regimens to treat different oncologic emergencies. This advocated using five fractions or less, supported by evidence of efficacy and equivalence as with longer fractionation schemes.[9]

In our institution, the most employed fractionation for palliative radiotherapy is 30 Gy in 10 fractions (3 Gy per fraction per day). However, due to the COVID-19 pandemic, our institution has seen a change in how we treat patients with palliative radiotherapy, with the increasing use of shorter fractionation regimens.

This study describes the clinical profile and treatment outcomes of patients treated with a short-course (<10 fractions) of palliative radiotherapy during the COVID-19 pandemic.

METHODS

The University of the Philippines-Manila Research Ethics Board (UPM REB Code 2021-171-01) approved this study.

This is an ambispective study of service patients treated with a short-course (<10 fractions) of palliative radiotherapy in the Division of Radiation Oncology, Philippine General Hospital, since the implementation of enhanced community quarantine in Metro Manila due to COVID-19. This study involved a review of medical records and follow-up of patients via phone call to determine treatment outcomes and assess disease status.

The general objective of this study was to describe the clinical profile and treatment outcomes of patients treated with short-course palliative radiotherapy.

Patients at least 18 years old and treated with a short course of palliative radiotherapy from March 16, 2020, to February 28, 2021, were included in the study. Patients treated with definitive or curative intent were excluded.

Medical records and radiotherapy plans were reviewed for patients treated with short-course palliative radiotherapy to determine demographic, clinical, and treatment-related information, including treatment outcomes and disease status. Patients or legally authorized representatives were contacted via phone for a short, structured interview after obtaining verbal informed consent to assess the patient's current disease status and treatment outcomes. No audio recording of the interview was taken.

Descriptive statistics (frequency, proportion, mean, median, and standard deviation) were used to summarize patients' demographic, clinical, and treatment outcomes using Microsoft Excel. Survival was defined as the time from the last day of radiotherapy to the date of death from any cause or last known follow-up. Data were analyzed for patterns and trends.

RESULTS

Of 92 patients receiving palliative radiotherapy, 23 were treated with short-course radiotherapy (<10 fractions), while 69 were planned for at least ten fractions of a palliative regimen. Demographic, clinical, and treatment-related data for patients scheduled to receive short-course radiotherapy are in Tables 1 and 2. As demonstrated in Table 2, the mean age at the diagnosis was 49 years old (range: 19-74 years old), and the majority were males (52%). Primary malignancy of the colorectal and head and neck were seen in 35% and 26% of cases, respectively. Pelvic masses (24%) and vertebral bones (21%) were the most commonly treated sites. Indications for palliative radiotherapy included pain (45%), bleeding (32%), and spinal cord compression (13%). The most common dose and fractionation employed were 20 Gy in 5 fractions (42%) and 25 Gy in 5 fractions (38%). Other radiotherapy regimens consisted of 8 Gy in 1 fraction (12%), 16 Gy in 2 fractions (4%), and 21 Gy in 7 fractions (4%). Most patients (56%) were admitted to the hospital while undergoing radiotherapy. Most cases reported complete resolution of symptoms (43%), followed by partial resolution (39%). Most of these patients also reported no side effects (58%). The median survival in this sample of patients was 71 days.

Figure 1 shows the distribution of different short-course regimens according to the body site treated. Pelvic masses and head and neck tumors were most commonly treated with 25 Gy in 5 fractions, while vertebral bones were most commonly treated with 20 Gy in 5 fractions. Head and neck tumors were also treated with a variety of short-course regimens.

Table 3 shows the different body sites treated according to the length of palliative radiotherapy. This indicates that 23 patients were treated at 29 sites with short-course (<10 fractions) palliative radiotherapy, while 69 patients were treated at 95 sites with ten or more fractions. Most patients treated with a longer course received 30 Gy in 10 fractions. Soft tissue masses in the pelvis (24%) and the head and neck (21%) were commonly treated with short-course radiotherapy, whereas vertebral bones and pelvic bones (20%) were commonly treated with longer courses. In particular, long-course radiotherapy was utilized to increase the number of vertebral bone segments. Among those treated in the vertebral bones, spinal cord compression was the indication in 5 and 11 patients treated with short and longer courses, respectively. Moreover, all patients treated in the lung, stomach, brain, and paravertebral regions utilized long course radiotherapy. In terms of the mean PTV volume, those treated with longer fractions also had larger volumes than those treated with short-course radiotherapy (2150 vs. 1871 cm^3).

Table 1. Summary of patient characteristics and treatment outcomes

No.	Age/ Sex	Diagnosis	Site Treated	Indication	Dose and Fractionation	RT status	Admission Status	Distance from Facility	Efficacy of Radiotherapy	Side Effects	Survival (in days)
1	67/F	Colon adeno-carcinoma with pelvic recurrence and liver metastases	Pelvic mass	Pain and bleeding	25 Gy in 5 fx	Completed	Out-patient	21 km	Complete resolution of bleeding, pelvic pain, and difficulty of voiding	None	196
2	74/M	Rectal adeno-carcinoma with lung, spleen, and retroperitoneal metastases	Pelvic mass	Bleeding	25 Gy in 5 fx	Completed	In-patient	-	Complete resolution of bleeding	Grade 2 dermatitis	334
3	51/F	Rectal adeno-carcinoma with lung and liver metastases	Pelvic mass	Pain	25 Gy in 5 fx	Completed	Out-patient	10 km	Complete resolution of pain	Grade 1 diarrhea	136
4	49/F	Breast cancer with liver, lung, and bone metastases	Breast mass	Bleeding	25 Gy in 5 fx	Completed	In-patient	-	No improve-ment in bleeding	Loss of appetite, insomnia	4
5	58/F	Papillary thyroid cancer (left lobe) and anaplastic thyroid cancer (right lobe) with tumor recurrence	Neck and upper mediastinal mass	Airway obstruction	1st course: 20 Gy in 5 fx 2nd course: 21 Gy in 7 fx	Completed	In-patient	-	Partial relief of dyspnea, with a noted decrease in size of neck mass	None	42
6	36/M	Synovial sarcoma with bone metastases	Cervical and thoracic vertebrae	Spinal cord compression and pain	8 Gy in 1 fx	Completed	In-patient	-	No improve-ment in motor deficits, progression of pain	None	71
7	50/F	Endometrial adenocarcinoma with bone metastases	Pelvis and sacral vertebrae	Pain	20 Gy in 5 fx	Completed	Out-patient	7 km	Partial relief of pain	None	157
8	19/M	Colon adeno-carcinoma with bladder invasion	Pelvic mass	Bleeding	20 Gy in 5 fx	Completed	In-patient	-	Complete resolution of bleeding	None	15
9	21/M	Ewing sarcoma of the right upper extremity with lung and bone metastases	Pelvic bone	Spinal cord compression and pain	20 Gy in 5 fx	Completed	Out-patient	12 km	No improve-ment in motor deficits, no improvement in pain	None	7
10	48/M	Sigmoid colon adenocarcinoma with tumor persistence and lung metastases	Pelvic mass	Pain	25 Gy in 5 fx	Completed	Out-patient	39 km	Complete resolution of pain	None	155
11	69/M	Papillary thyroid cancer with bone metastases	Neck, chest, and thoracic vertebrae	Pain	8 Gy in 1 fx	Completed	In-patient	-	Complete resolution of pain	None	141
12	34/M	Acute myelogenous leukemia	Cervical and thoracic vertebrae	Spinal cord compression	20 Gy in 5 fx	Completed	In-patient	-	Missing data	Missing data	11
13	74/M	Rectal cancer with bone metastases	Rib	Pain	20 Gy in 5 fx	Completed	Out-patient	27 km	Partial relief of pain	None	125

Table 1. Summary of patient characteristics and treatment outcomes *(continued)*

No.	Age/ Sex	Diagnosis	Site Treated	Indication	Dose and Fractionation	RT status	Admission Status	Distance from Facility	Efficacy of Radiotherapy	Side Effects	Survival (in days)
14	32/F	Malignant peripheral nerve sheath of the left leg with tumor recurrence and liver metastases	Left thigh and leg masses	Bleeding and pain	1st site (thigh): 16 Gy in 2 fx 2nd site (lower leg): 20 Gy in 5 fx	Completed	In-patient	-	Partial relief of bleeding and pain	None	41
15	54/M	Medullary thyroid cancer with recurrence	Neck, chest, mediastinum, bilateral axillary masses	Bleeding and local control	25 Gy in 5 fx	Completed	In-patient	-	Complete resolution of bleeding	None	78
16	36/F	Rectal adenocarcinoma with lung metastases	Pelvic mass	Pain	25 Gy in 5 fx	Completed	Out-patient	13 km	Partial relief of pain	Grade 1 dermatitis	332
17	38/F	Breast cancer with bone metastases	Thoracic, lumbar, and sacral vertebrae	Pain	20 Gy in 5 fx	Completed	In-patient	-	Complete resolution of pain	Grade 1 diarrhea, Grade 1 dermatitis	56
18	72/F	Squamous cell carcinoma of the alveolar ridge with lung metastases	Mandibular mass	Bleeding	25 Gy in 5 fx	Completed	In-patient	-	Partial resolution of bleeding	None	13
19	33/F	Breast cancer with tumor recurrence and bone metastases	Breast mass, thoracic vertebrae, and sacrum	Bleeding, pain, and spinal cord compression	20 Gy in 5 fx	Completed	Out-patient	42 km	Complete resolution of bleeding and pain	None	38
20	60/F	Breast cancer with tumor recurrence and liver metastases	Neck and chest wall masses	Bleeding	20 Gy in 5 fx	Completed	In-patient	-	Complete resolution of bleeding	Grade 2 dysphagia	9
21	66/M	Rectal adenocarcinoma with lung metastases	Pelvic mass	Pain and bleeding	25 Gy in 5 fx	Completed	Out-patient	7 km	Partial relief of pain and bleeding	None	437
22	61/M	Papillary thyroid adenocarcinoma with bone metastases	Bilateral shoulders, ribs	Pain	Shoulders: 8 Gy in 1 fx Ribs: 20 Gy in 5 fx	Completed	Out-patient	35 km	Partial relief of pain	Grade 2 dysphagia	263
23	35/M	Oropharyngeal cancer with lung and bone metastases	Neck mass	Bleeding and local control	25 Gy in 5 fx	Completed	In-patient	-	Partial relief of bleeding and pain	None	63

RT = radiotherapy; fx = fractions

DISCUSSION

This study described the demographic, clinical, and treatment-related profile of cancer patients treated with a short course of palliative radiotherapy. Due to COVID-19, the use of shorter radiotherapy regimens for treating different oncologic diseases has been advocated.[7–9] This is to minimize the exposure of patients and radiotherapy personnel to COVID-19, travel restrictions, and transportation difficulties. This recommendation is not without rationale, however, as several published data have established comparable symptom relief with shorter radiotherapy schedules as with longer ones.[2–5] Despite this, our results revealed that a significantly larger proportion of patients were treated with ten fractions or more of radiotherapy. Choice of radiotherapy schedule is influenced by several elements, including patient factors such as performance status, co-morbidities, transportation capabilities; tumor factors, such as number, location, and behavior of tumor; and treatment factors such as toxicities, history of irradiation on the same anatomical site, and potential toxicities from other modalities of treatment.[6]

Our results revealed that masses in the pelvic region were among the most commonly treated with short-course palliative radiotherapy. As seen in Table 1, 7 out of 13 patients

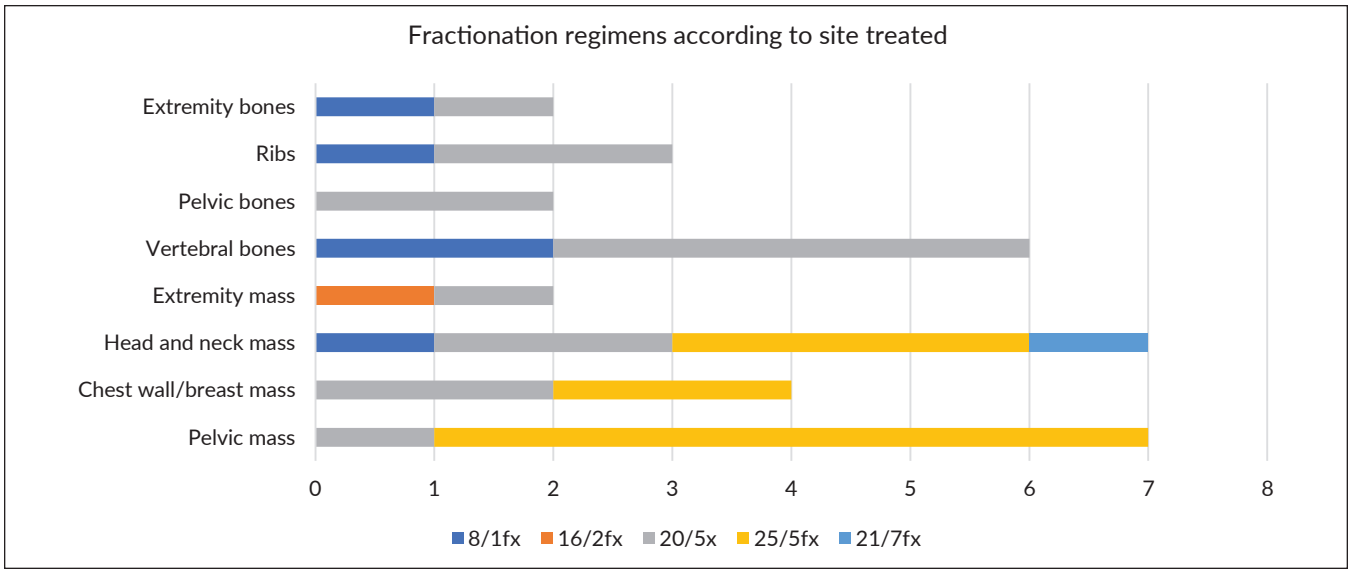

Figure 1. Distribution of different fractionation regimens according to site/region treated. A single patient may have been treated at multiple sites with the same or different fractionation regimens.

treated with a 25 Gy in 5 fraction regimen had metastatic bulky colorectal malignancies referred for palliation of pain, bleeding, or both. In such cases, the ease of adopting shorter regimens is likely attributed to the fact that 25 Gy in 5 fractions is also considered a standard neoadjuvant radiotherapy approach for rectal malignancies.[10] Hence, it may be reasonable to extrapolate said practice to other pelvic malignancies. It should be noted that aside from rectal cancer, other diseases treated with 25 Gy in 5 fractions in our sample included colon cancer, anal cancer, and head and neck malignancies,

Another site commonly treated was the vertebral bones. Radiotherapy regimens included 20 Gy in 5 fractions (4/6) and 8 Gy in 1 fraction (2/6) (Table 1). In 2014, the American Society of Radiation Oncology (ASTRO) released guidelines through its Choosing Wisely Campaign advocating the use of no more than ten fractions of radiotherapy, stating that 30 Gy in 10 fractions, 20 Gy in 5 fractions, and a single 8 Gy fraction have equivalent rates of pain relief.[11] Additionally, a strong recommendation was made for a single 8 Gy fraction for patients with a limited prognosis or transportation difficulties. Despite this, most patients with vertebral metastases receiving short-course radiotherapy were treated with five fractions during the pandemic.

Moreover, as seen in Table 3, most patients planned for radiotherapy of 10 fractions were treated to the vertebral bones. However, some osseous metastases of the appendicular skeleton (i.e., shoulders, humeri, and femora) were treated with a single fraction. In our institution, concerns about using a single fraction regimen include higher retreatment rates and the potential for toxicities.[2] Concerns for acute hematologic toxicity may arise when treating large volumes of the spine, especially since the patients we receive have advanced metastatic disease at multiple sites. The vertebrae comprise 42.3% of the total red bone marrow (3.4% for cervical, 14.1% for thoracic, 10.9% for lumbar, and 13.9% for sacrum).[12] It can be assumed that the larger the irradiated volume, the greater the marrow toxicity. However, in the evidence-based guideline released by ASTRO in 2017, single fraction radiotherapy was regarded as appropriate for treating bone metastases involving the spine and other critical structures.[13] There is currently a lack of data correlating the radiotherapy dose and irradiated volume of the spine to the extent of hematologic toxicity.

Nonetheless, when looking at the subset analysis of the landmark trial, Radiation Therapy Oncology Group 97-14, comparing 8 Gy in 1 fraction and 30 Gy in 10 fractions of palliative radiotherapy to the spine, more acute grade 2-4 toxicities were seen in the latter (10% vs. 20%, p=0.01). Of note, only two patients experienced grade 4 neutropenia in the study, and both were treated with 30 Gy in 10 fractions.[2] A possible explanation may be that a shorter radiotherapy duration allows for faster bone marrow recovery, primarily when delivered to smaller volumes.[14] Consequently, treatment of the spine ultimately depends on an interplay of patient factors, including performance status and logistics, pre-treatment hematologic parameters, the irradiated volume, and physician comfort level.

All patients treated with whole brain radiotherapy (WBRT) for brain metastases were treated with 30 Gy in 10 fractions (Table 3). None of the patients were treated with a shorter regimen. ASTRO also published an evidence-based guideline on the radiotherapeutic and surgical management of newly diagnosed brain metastases. The recommended fractionation schemes include 30 Gy in 10 fractions and 20 Gy in 5 fractions.[15] The regimens of 30 Gy in 10 fractions and 20 Gy in 5 fractions have been compared in treating brain

Table 2. Demographic, clinical, and treatment-related information of patients

	Number of cases, n=23 n (% of total responses)
***Age** (mean ± SD)*	49 ± 16.89
Sex	
Male	12 (52.2)
Female	11 (47.8)
Primary Malignancy	
Head and Neck	6 (26.1)
Breast	4 (17.4)
Colorectal	8 (34.8)
Gynecologic	1 (4.3)
Hematologic	1 (4.3)
Sarcoma	3 (13)
Target Site/Organ	
Pelvic mass	7 (24.1)
Chest wall/breast mass	4 (13.8)
Head and neck mass	6 (20.7)
Extremity mass	1 (3.4)
Vertebral bones	6 (20.7)
Pelvic bones	2 (6.9)
Ribs	2 (6.9)
Extremity bones	1 (3.4)
Palliative Indications	
Pain	14 (45.2)
Bleeding	10 (32.3)
Spinal cord compression	4 (12.9)
Airway obstruction	1 (3.2)
Local control	2 (6.5)
Dose and Fractionation	
8 Gy in 1 fraction	3 (11.5)
16 Gy in 2 fractions	1 (3.8)
20 Gy in 5 fractions	11 (42.3)
25 Gy in 5 fractions	10 (38.5)
21 Gy in 7 fractions	1 (3.8)
Admission Status	
Outpatient	
<20 km from the facility	5 (21.7)
≥20 km from the facility	6 (26.1)
Inpatient	12 (52.2)
Efficacy of Radiotherapy	
Complete resolution	10 (43.5)
Partial resolution	9 (39.1)
No improvement	3 (13)
Undocumented	1 (4.3)
Side Effects	
None	14 (58.3)
Dermatitis	3 (12.5)
Diarrhea	2 (8.3)
Dysphagia	2 (8.3)
Insomnia	1 (4.2)
Anorexia	1 (4.2)
Undocumented	1 (4.2)
***Median survival** (days)*	71 ± 121.39

**A single patient may have been treated on multiple sites, with multiple palliative indications, and with multiple fractionation regimens*

Table 3. Comparison of short course and long course palliative radiotherapy according to site/organ treated

Site/Organ	Palliative Radiotherapy	
	<10 fractions n=29	≥10 fractions n=95
Soft tissue		
Pelvis	7 (24.1)	3 (3.2)
Chest wall/breast	4 (13.8)	7 (7.4)
Head and Neck	6 (20.7)	3 (3.2)
Extremities	1 (3.4)	2 (2.1)
Lung		2 (2.1)
Gastric		2 (2.1)
Brain		23 (24.2)
Paravertebral		1 (1.1)
Bones		
Vertebral bones		
1-5 segments	2 (6.9)	7 (7.4)
6-10 segments	3 (10.3)	13 (13.7)
>10 segments	1 (3.4)	12 (12.6)
Pelvic bones	2 (6.9)	19 (20)
Rib	2 (6.9)	(0)
Extremities	1 (3.4)	1 (1.1)
Mean PTV volume ± SD	1871.3 ± 1361.45	2150.4 ± 1256.4

**23 patients treated at 29 sites*
***69 patients treated at 95 sites*
PTV = planning target volume

metastases. Results revealed that the WBRT schedule had no impact on the survival of patients, and the rates of acute toxicity were <5% in both treatment groups. This concluded that short-course WBRT with 20 Gy in 5 fractions is preferable for most patients as it is less time-consuming and associated with similar outcomes as with longer schedules.[16] As noted in this study, all patients treated with WBRT were managed with 30 Gy in 10 fractions, and none were treated with 20 Gy in 5 fractions. The choice of the palliative regimen likely depended on the prognosis of patients, with those having a more favorable prognosis receiving longer treatment schedules. Another factor may be physician comfort level, as giving a higher dose per fraction may theoretically induce more soft tissue edema.

Additionally, gastric and lung malignancies were preferentially treated with 30 Gy in 10 fractions. Radiotherapy is efficacious in the hemostasis of gastric bleeding. In a retrospective cohort study, the hemostasis rate was 73% after a median interval of two days after initiation of radiotherapy. Moreover, 80% of patients in this study received 30 Gy in 10 fractions.[17] Another retrospective study compared longer radiotherapy regimens (>5 fractions) with shorter ones (<5 fractions) and revealed that both demonstrated similar hemostatic effects. Furthermore, longer regimens were not associated with a reduced incidence of re-bleeding but instead accompanied by increased treatment interruptions and hospital days.[18] For lung malignancies, palliative radiotherapy, may benefit symptomatic patients, those with

metastatic disease, and those with locally advanced patients unfit to receive definitive treatment.[19] Higher doses and longer fractionation regimens (30 Gy in 10 fractions or greater) are recommended by ASTRO for patients with good performance status as this is associated with modest improvement in survival and symptoms. However, shorter fractionation schedules may also offer good symptomatic control with lesser side effects for patients with poor performance status.[20] As with WBRT, patients treated with palliative radiotherapy to the lung and stomach were treated with long schedules, which may likewise be explained by the prognosis and performance status of the patients at the time of referral.

With the COVID-19 pandemic, we've seen increasing practice of utilizing shorter fractionation regimens for palliative radiotherapy, although its proportion compared with longer fractions remains smaller. This shows that the COVID-19 situation is only one of many considerations when deciding on a patient's treatment. This study also showed that short-course radiotherapy provided high complete and partial symptomatic relief rates. Patients included in the analysis also had poor prognoses with a median survival of 71 days. This figure is somehow anticipated as patients treated with short-course palliative radiotherapy often have an expected survival of less than three months. As these patients often have limited life expectancy, using shorter fractionation regimens would benefit palliate symptoms and maximize quality near the end of life.

This study is limited by its study design. The retrospective aspect of the study consisted of chart review and may be prone to misclassification bias, may be subject to confounding variables, and may lack essential information. Selection bias may also be another disadvantage but was minimized by including all patients treated within the specified period. The prospective aspect of this study was also made to complement data from the retrospective review. However, this was also prone to recall bias. Given the limitations posed by the pandemic, interviews through phone calls allowed the most feasible method of gathering data. Since most of the mentioned biases are attributable to the retrospective nature of the study and its reliance on recollection, it is suggested to undertake a prospective study with objective measures for treatment response and an appropriate follow-up period to determine the clinical outcomes of patients treated with short-course palliative radiotherapy in our institution. It is also worthwhile to examine the rationale for choosing a particular palliative schedule when treating patients.

CONCLUSION

Due to the COVID-19 pandemic, short courses of palliative radiotherapy have been advocated. In this single institution review, a short course of palliative radiotherapy provides good symptom control with few side effects. Its use should be considered in the setting of a pandemic, especially in patients with poor performance status, transportation difficulties, and limited life expectancy.

Statement of Authorship

Both authors contributed in the conceptualization of work, acquisition and analysis of data, drafting and revising, and approval of the final version submitted.

Author Disclosure

Both authors declared no conflicts of interest.

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