Original Article

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Scenario of Palliative Radiotherapy at a Cancer Centre in Kashmir

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Abstract

Background: Almost two-third cancer patients who present to hospitals in developing countries have either locally advanced or metastatic disease. Palliative radiotherapy (PRT) is an indispensable modality for control of cancer symptoms in advanced stages and approximately one-half of prescribed radiotherapy is given for palliation of symptoms.

Materials and Methods: Scenario of PRT was analyzed in 125 patients with various malignancies, who either needed radiotherapy at presentation or later sometime after disease progression. We analyzed the data with respect to (i) socio-demographic status, (ii) site or indication of palliation, (iii) dose prescribed, and (iv) response rate. Descriptive statistics were evaluated in terms of frequencies and percentage to allow comparisons.

Results: About 70% (*n* = 87) of the patients were males; median age of the patients receiving PRT was 55 years (range: 18-70); 28% (*n* = 37) patients received PRT at the primary site, whereas the rest (72%) received PRT at the metastatic site. Pain was the most common indication of PRT in 60% patients, followed by brain metastasis (raised Intra Cranial Tension), hemostatic PRT, and cord compression. The median dose prescribed was 20 Gy (range 8-30 Gy) delivered in 1-10 fractions. Overall response rate after 2 weeks of completion of PRT was 65%; the median follow-up of the patients was 109 days (range 7-280 days). The overall long-term symptom control was 20%.

Conclusion: Radiotherapy is a successful, time-efficient, cost-effective, and safe modality to palliate the symptoms of cancer patients in their advanced stages. The optimal use of PRT requires accurate survival prognostication, judicious enrolment of patients on need basis and, choosing regimens that best suit the patients in terms of toxicity and treatment duration.

Key words: Cancer, Metastasis, Pain, Palliative radiotherapy, Survival

INTRODUCTION

Radiotherapy has been used for palliating cancer symptoms soon after its discovery in the 1800's.[1] It is a cost-effective and time-efficient intervention that is associated with a low toxicity profile and can relieve symptoms, such as pain, obstruction, bleeding, and neurologic symptoms due to the primary or metastatic tumor. While the complexity of palliative radiotherapy (PRT) has increased with the advent of newer technologies, the common sense goals of its delivery remain a good chance for symptom relief with a limited risk of side effects.[2]

In developed nations, radiation therapy is a potentially valuable, but under-utilized tool in end-of-life care programs that could greatly enhance the quality of life (QoL) in appropriately selected patients with advanced cancer who still have more than a few weeks or months to live.[3,4]

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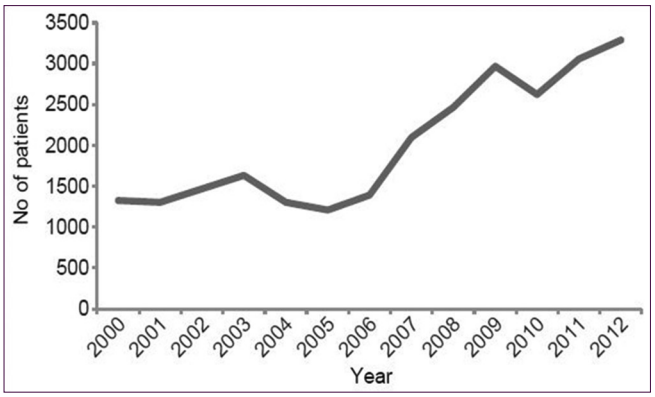

In developing nations like India where advanced cancer presentations are more common,[5] radiotherapy is used as much with a curative intent as is being used for palliation.

Over the last one decade, Kashmir valley has witnessed increase in incidence of cancer.[6]

More than half of patients present as locally advanced or metastatic disease[7] requiring PRT at some point during disease course. In this study, we tried to outline the indications for PRT, the selection of appropriate dose-fractionation schemes, the response to PRT, and long-term symptom control.

MATERIALS AND METHODS

We conducted a retrospective, analytical study in the Department of Radiotherapy SMHS Hospital - a tertiary care hospital of Jammu and Kashmir, from January 2012 to July 2014. All the patients who were selected for the analysis had received PRT either at presentation for a locally advanced or metastatic disease or later after disease progression during follow-up. Written consent was taken from all the enrolled patients before starting PRT. Dose and fractionation were chosen keeping in view the performance score (PS), expected survival, and comorbid medical ailments. PS was calculated via Eastern Cooperative Oncology Group (ECOG) scoring system.[8] Adjuvant supportive measures were instituted as and when required in the form of corticosteroids, analgesics, antidepressants, and psychotherapy. Symptomatic pain relief and clinical improvement were observed over a period of 2 weeks and above. Differences in pain improvement, time to improvement of symptoms, the durability of symptom control, improvement in QoL were analyzed with respect to demography, dose and fractionation of radiation, and, site of metastasis. Dose and fractionation of radiotherapy were determined by (i) histology of the primary tumor, (ii) duration of neurodeficit, (iii) PS, (iv) expected survival, and (v) feasibility of attending hospital. Endpoints considered for response were pain control, reversal of neuro-deficit, improvement in QoL.

Eastern Cancer Oncology Group: Classification[8]

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work and office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled cannot carry on any self-care. Totally, confined to bed or chair
5	Dead

Statistical Analysis

The data were analyzed by an experienced statistician using Student's *t*-test and Chi-square test wherever appropriate. $P < 0.05$ was considered significant.

Table 1: Demographic profile of study population

Demographic profiles	Number of patients (%)
Males	87 (70)
Females	38 (30)
Rural	90 (72)
Urban	35 (28)

Table 2: Site specific dose- fractionation

Site	Number of patients	Symptoms	Dose/ fractions
Esophagus	8	Dysphagia, pain	30 Gy/10#: 6 20 Gy/5#: 2 (recurrence)
Lung	6	Pain, collapse, dyspnea	30 Gy/10#: 3 45 Gy/20#: 3
Skin	4	Pain	8 Gy/1#: 1 15 Gy/3#: 3
Rectum	3	Pain	15 Gy/3#: 1 30 Gy/10#: 2
Head and neck	2	Pain	15 Gy/3#
Sarcoma	2	Pain	30 Gy/10#
GBM (recurrence)	2	Headache, vomiting	15 Gy/3#

GBM: Glioblastoma-multiforme

Table 3: Proportion of metastasis in study group

Site	Number of patients (%)
Bone metastasis	30 (24)
Brain metastasis	25 (20)
Hemostatic	16 (13)
Cord compression	15 (12)
Svc obstruction	12 (9)
Primary site	27 (21)

RESULTS

The outcome of 125 patients were analyzed. The majority of the patients were males (70%) and from rural background (72%) shown in Table 1.

The median age of the patients receiving PRT was 55 years (range: 18-70); pain was the most common symptom (90%) for which PRT was given (Table 2).

Although liver was the most common site of metastasis, bone and brain metastases were the most common sites (24% and 12%, respectively) for which PRT was sought (Table 3).

About 30% of the patients who required PRT had presented in a locally advanced stage who eventually progressed to metastatic disease. Breast and lung were the most common primaries which metastasized to bones, other primaries were prostate, nasopharynx, urinary bladder, and melanoma (Table 4). The most ommon fractionation used in bone metastasis was 8 Gy single fraction.

Brain metastasis constituted the second most common site of metastasis with lung as primary in 7 patients. Two patients with small cell carcinoma lung (SCLCa) and one with melanoma had multiple metastases and succumbed after 2 months of RT (Table 5). The most commonest fractionation used was 30 Gy/10#.

Exactly 16 patients had received hemostatic radiotherapy of which 8 had hemoptysis and 5 had hematuria. Other indications were bleeding from fungating squamous cell carcinoma skin which has recurred locally and were not amenable to surgical intervention. Fractionation used was 20 Gy/5#. One patient received PRT for bleeding per rectum with underlying advanced rectal cancer (Table 6).

Around 15 patients had clinical and radiological evidence of cord compression of whom four each was secondary to myeloma and prostatic cancer (Table 7). Three patients had breast as their primary, two had lung, and one each had non-Hodgkin's lymphoma (NHL) and carcinoma unknown primary site (CUPs).

Hypo-fractionation schedule of 8 Gy/1# was chosen for two patients with prostate cancer because of poor performance status and complicated cord compression (compression with fracture) which was not amenable to neurosurgical stabilization. One patient each with CUPs and myeloma received 8 Gy/1# as both had disseminated visceral metastasis and paraplegia of more than 1 week. One patient each with prostate, breast and myeloma who received 15 Gy/3# had multiple sites of cord compression.

Table 4: Profile of patients receiving radiotherapy for bone metastasis

Dose/ fractionation	Primary site	Number of patients	Total (%)
8 Gy/1#	Lung	5	11 (36)
	Breast	2	
	Prostate	3	
	Nasopharynx	1	
15 Gy/3#	Lung	2	4 (13)
	Breast	2	
20 Gy/5#	Nasopharynx	3	7 (23)
	Breast	3	
	Urinary bladder	1	
30 Gy/10#	Prostate	3	8 (26)
	NHL	2	
	Breast	2	
	Melanoma	1	

The most common fractionation used in bone metastasis was 8 Gy single fraction
NHL: Non-Hodgkin's lymphoma

Table 5: Profile of patients receiving radiotherapy for brain metastasis

Dose/ fractionation	Primary site	Number of patients	Total
30 Gy/10	Lung	5	12
	Breast	4	
	Anaplastic thyroid	2	
	Melanoma	1	
25 Gy/05	Lung	2	03
	Choriocarcinoma	1	

The most common fractionation used was 30 Gy/10#

Table 6: Profile of patients receiving hemostatic radiotherapy

Primary site	Number of patients	Dose/ fractionation	Total patients
Lung (hemoptysis)	05	20 Gy/5#	8
Urinary bladder (hematuria)	03		
Lung (hemoptysis)	03		
Urinary bladder (hematuria)	02	15 Gy/3#	8
Skin (fungation)	02		
Rectal cancer (advanced)	01		

Table 7: Profile of patients receiving radiotherapy for cord compression

Primary site	Number of patients	Total	Dose/ fractionation
Myeloma	2	08	30 Gy/10#
Lung	2		
NHL	1		
Breast	2		
Prostate	1		
Breast	1	03	15 Gy/5#
Myeloma	1		
Prostate	1		
CUPs	1	04	8 Gy/1#
Prostate	2		
Myeloma	1		

CUPs: Carcinoma unknown primary site, NHL: Non-Hodgkin's lymphoma

Eight patients received protracted course of PRT of 30 Gy/10# for cord compression, had reasonable PS (ECOG of 1-2), had bone as the only site of metastasis, NHL patient had two sites of nodal disease and presented with a paraspinal mass), had expected survival of more than 6 months, primary diseases under remission and none of them had any neuro-deficit. The dose in NHL patient was later escalated to 45 Gy as the patient had contraindication to chemotherapy.

About 12 patients were irradiated for superior vena cava obstruction (SVCO), of which six (2 Hodgkin's disease [HD], 2 NHL, 1 thymoma and 1 small cell lung cancer [SCLCa]) presented with SVCO while as six developed later during the course of treatment and relapse. Fractionation used was 15 Gy/5# (Table 8).

Of the six patients, one each with SCLCa and NHL had rapid worsening of clinical symptoms in the form of deteriorating sensorium, whereas one each with HD and SCLCa had impending airway obstruction for which radiotherapy was started upfront. One patient with NHL had a medical contraindication to chemotherapy, and another with HD had refused chemotherapy. All these patients had received corticosteroids as adjunctive treatment.

PRT as a primary treatment modality was given in 27 patients of whom esophageal cancer constituted approximately one-third (29%). Dysphagia and pain were the prime indications. PRT of 30 Gy/10# was used in six patients whereas two patients who had recurred after radical radiotherapy received 20 Gy/5#. Six patients of primary lung cancer received PRT for pain, dyspnea and collapse. 30 Gy/10# and 40 Gy/20# were two schedules used; former used for infirm and low expected survival patients. Four recurrent skin cancer (squamous cell) patients received PRT at the primary site (thigh in three and abdominal wall in one) for fungating and infiltrating large volume disease not amenable for resection. Pelvic pain due to unresectable rectal cancer was another indication for PRT in three patients one of whom had recurrent disease after radical RT. 30 Gy/10# was given in two patients whereas the one with recurrent disease was given 15 Gy/3#. Four patients, two each, with recurrent retroperitoneal sarcoma with distant metastasis and recurrent glioblastoma-multiforme (GBM) received PRT for pain, obstruction and raised intra-cranial pressure, respectively (Table 2).

We observed that complete relief of pain (CRP) from bone metastasis was observed in 40% of patients, partial relief in 90% and no response was seen in 20% of patients. Overall response rate (ORR) was 70-80% (Table 9).

CRP was seen in patients who had (i) breast and NHL as primary, (ii) solitary metastatic site, (iii) ECOG score of 0 or 1, and (iv) age less than 50 years and male sex. No difference in pain relief and survival was seen as regards to dose and fractionation, but retreatment rates were high in single fraction group.

All patients with brain metastasis except those with primaries as melanoma and anaplastic thyroid cancer showed overall improvement 60-70% of symptoms (Table 10).

While the improvement lasted 2-3 months, most of them succumbed to their primary disease. Different "dose-fractionation" did not alter the outcome nor did the sex and age of the patient.

Hemostatic PRT appeared to be very effective in controlling bleeding in lung cancer and urinary bladder cancer patients with complete cessation of hemoptysis and hematuria in over 60% of patients.

The effect was more pronounced in small cell histology in lung cancer. Overall response was 60%, but patients with skin and rectal cancer had only partial control. The two fractionation schedule appeared to be equally effective (Table 11).

Six patients out of 12 who received PRT for SVCO had over 90% response and included NHL, HD and SCLCa as primary disease. Two patients one with non-small cell lung cancer (NSCLCa) and other thymoma had 50% response. All patients with HD, NHL and SCLCa and one patient with NSCLa received radical dose of RT later. All of them received same dose of PRT of 15 Gy/5#. All patients were below 50 years of age except one SCLCa and one NSCLCa. All patients had ECOG PS of 1 or 2. ORR was 75% (Table 11).

Table 8: Profile of patients receiving radiotherapy for SVCO

Primary site	Number of patients	Dose/ fractionation
Non-small cell Ca	5	15 Gy/5#
Small cell Ca	2	
Non-Hodgkin's lymphoma	2	15 Gy/5#
Hodgkin's disease	2	15 Gy/5#
Thymoma	1	15 Gy/5#

SVCO: Superior vena cava obstruction, Ca: Cancer

Table 9: Response rate of treated patients

Symptom	Complete response	Partial response	No response
Bone pain (%)	40	90	20

Table 10: Response rate in various malignancies

Brain metastasis	Primary lung cancer	Primary breast cancer	Primary choriocarcinoma	Malignant melanoma	Anaplstic thyroid cancer
Response (%)	70	65	75	15	10

Table 11: Response rate of various treated malignancies

SVCO	Lung (NSCLCa)	Lung (SCLCa)	NHL	HD	Thymoma
Response (%)	50	95	95	92	50

SVCO: Superior vena cava obstruction, NSCLCa: Non-small cell lung cancer, SCLCa: Small cell lung cancer, NHL: Non-Hodgkin's lymphoma, HD: Hodgkin's disease

Table 12: Response rate of patients with cord compression

Primary	100%	50%	Stable/no progression	No response/ progression
Prostatic	-	-	1	2
CUPs	-	-	-	1
Breast	1	1	1	-
NHL	1	1	-	1
Myeloma	1	1	1	-
Lung	1	1	-	-

CUPs: Carcinoma unknown primary site, NHL: Non-Hodgkin's lymphoma

Table 13: Overall response rate with PRT

Disease	Symptom	Percentage
Ca esophagus	Pain, dysphagia	70
Ca lung	Pain, dyspnea	65
Ca skin	Pain	50
Ca rectum	Pain	50
GBM	Pain	50
Sarcoma	Pain	50
Head and neck	Pain	50

PRT: Palliative radiotherapy, GBM: Glioblastoma multiforme, Ca: Cancer

Two patients with complicated cord compression due to metastatic carcinoma prostate who received single fraction showed the progression of neurodeficit, whereas the patients with CUPs and myeloma with more than 1 week paraplegia did not show any improvement. One patient each with prostate, breast and myeloma as primaries had stable disease and no progression in neurodeficit was observed. Of the eight patients who received 30 Gy/10# one each with NHL, breast, myeloma and lung as primaries had complete recovery whereas four had over 50% recovery of neurodeficit (Table 12).

Overall response to dysphagia was 70% in patients receiving PRT for cancer esophagus, though median survival did not improve in these patients and none survived beyond 6 months. Fractionation did not seem to affect the time to improvement, neither sex nor age. All the patients were more than 60 years of age.

Pain and dyspnea improved in four of the six lung cancer patients; all the four were small cell variant. Response lasted for an abbreviated period of average 2-month after which patients progressed and were put on supportive care only. Two non-responders had non-small cell histology, had ECOG of 3 and were more than 60 years age.

About 50% pain improvement was seen in 3 out of 4 skin cancer patients irrespective of dose-fractionation schedule. Two rectal cancer patients who had 70% response with 30 Gy/10 fractions (30 Gy/10#) schedule were below 60 years and were receiving RT for the first time, and concurrent chemotherapy was used in these set of patients. Recurrent rectal cancer patient showed 30% response. Of the six patients two each with sarcoma, GBM and head and neck cancer showed up to 50% relief. All had recurrent disease (Table 13).

DISCUSSION

Radiotherapy is an indispensable treatment modality in cancer care being administered with palliative intent in up to 40% to 50% of the patients of any radiation oncology department.[9] The goal of PRT is to achieve durable symptom relief at the shortest expense of time and resources while inflicting the least possible toxicity.[10] Palliative RT is based on the principles of maximizing symptom relief with minimal consumption of time and resources, and causing the least possible concern to the patient with regards to span of treatment and toxicities afforded. Lower total time as well as lower total dose is the hallmark of palliative RT.[11]

Although painful bone metastasis is the most common reason for the delivery of PRT, approximately 66% of PRT is delivered for the management of other symptoms.[12] Bone metastases are a very common manifestation of malignancy, and radiotherapy provides partial (50%) pain relief in 60-80% and complete pain relief in 30-50% of patients within days to weeks after the initiation of therapy.[13] As is evident in our analysis, pain relief was equivalent with fractionation regimens of 30 Gy/10#, 20 Gy/5#, or a single 8 Gy/1#.[14] As per literature retreatment rates may be higher in those who receive a single fraction and a second course of therapy can be expected to provide a reasonable rate of pain relief.[15] Pain relief secondary to bone metastasis seems to be independent of dose-fractionation, whereas response

in symptoms of cord compression due to lymphomas, small cell cancer appear to correlate with histology and dose. Moreover, female patients seemed to have a more prolonged survival as compared to men presumably due to higher number of breast cancer patients who have a long survival even with bone metastasis.

PRT has traditionally been used as a non-invasive means of palliating dysphagia in patients with incurable esophageal cancer.[16] Options of palliating esophageal cancer for dysphagia are stenting, brachytherapy or feeding jejunostomy. Brachytherapy was not available at our center and stenting was not elected in view of low PS. However, overall survival seems to be unaffected by PRT and PS and comorbid conditions play a role in overall survival. SVCO is a life threatening sequelae of advanced cancer. Most of the cancers causing SVCO are sensitive to chemotherapy as well as radiotherapy; however for cancers less radio-responsive to chemotherapy, radiotherapy is an efficacious tool of management. We analyzed in this study that patients with SVCO secondary to lymphoma and SCLCa had more than 90% response and that RT doses were escalated to definitive dose levels following good clinical response. Many patients with metastatic lung cancer, and selected patients with locally advanced disease, are routinely treated with thoracic radiotherapy with palliative intent to relieve tumor-related symptoms (hemoptysis, bronchial obstruction, cough, shortness of breath, and chest pain) and to improve health-related QoL.[17] We saw age, PS and histology were variables which affected the response in our study. Poor outcome in low PS patients may be due to use of a low-dose, hypofractionated regimen and omission of chemotherapy. Rectal cancer is prone to recur locally[18] and the outcome of a recurrent rectal cancer is even post adjuvant treatment is dismal. We saw more radiological and symptomatic improvement in RT naive unresectable rectal cancer compared to the re-irradiation cohort; this might in part be due to use of concurrent chemotherapy in newly diagnosed advanced unresectable cancer. In cord compression, complete recovery of neurodeficit in NHL, breast, myeloma and lung as primaries suggest a radio-responsive primary, single site of compression, compression without fracture and a protracted fractionation, good prognostic indicators for response. Short fractionation was chosen in patients with low PS and poor chances of recovery as corroborated with literature.[19]

Hemostatic PRT appears to be effective in controlling bleeding in advanced cancers of lung, urinary bladder, rectum and skin and improving QoL. Our results of greater than 60% overall response are corroborated in various studies.[20] Short fractionation schedules should be preferred. Single or reduced fraction regimens appear to be as effective as multiple fractions in controlling bleeding.[21] Brain metastasis is the terminal event in most malignancies and survival does not exceed beyond 6-7 months in most cases even after palliative RT or drugs like temozolomide. Radio surgery is a relatively promising intervention for patients with solitary metastasis, reasonable PS but patients in our study who fulfilled the criteria did not afford due to financial constraints. Some less well-recognized favorable parameters seem to be a response to steroid treatment, serum lactate dehydrogenase, age, sex in lung primaries, and site and histology of primary tumor.[22]

CONCLUSION

Poor health awareness, quackery, late referral to a tertiary care centre and financial constraints, all play an important role in advanced presentation of cancer in developing nations like India. PRT seems to be an important tool in improving QoL and pain relief albeit without an improvement in long-term survival. PS and age independently affect the outcome in all settings of palliative care, but long-term outcome to PRT in all demographic settings is same. To conclude PRT should be considered at all stages of advanced cancer as it is least invasive, cost-efficient, and associated with minimum toxicities.

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