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Radiotherapy and geriatric cancer patients: A single institute experience

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ABSTRACT

Objectives: The aim of this study was to study patient, disease, and treatment related characteristics in geriatric patients 65 years and older treated by Radiotherapy (RT).

Material and methods: A retrospective observational and descriptive study was conducted in a tertiary care government institute with academic and research potential. The electronic medical records, medical documents, and Radiotherapy treatment charts were retrieved and studied.

Results: 247 patients aged 65 years and older were included over 2-year study period. Mean age was 70.3 years and the oldest patient treated was of 94 years. 66% patients were males. 82 patients (33%) had metastatic disease. The common sites of origin were head and neck (28%), lung (23%), genitourinary (20%), and gastrointestinal malignancies (15%). 125 patients (51%) were having one or more co-morbidities. 135 patients (55%) were treated with radical intent. 66 patients (27%) received chemotherapy in concurrent setting. 89 patients (36%) were hospitalized for some duration of their RT course. In 58 patients (23%), RT was interrupted briefly. 46 patients (19%) could not complete the prescribed RT. 8 patients (3%) developed Grade 3 and 4 hematological toxicities. 57% patients developed Grade 2,3 mucocutaneous toxicities. 53% patients developed Grade 2,3 GI toxicities. Mortality rate while on treatment was 4%.

Conclusion: Geriatric patients, though more prone to develop systemic and site-specific toxicities warranting supportive care in indoor or outdoor setting, can be offered Radiotherapy either alone or concurrently with chemotherapy. Such patients present with heterogeneous spectrum of entities often posing a therapeutic challenge to clinicians; but proper selection of cases and diligent supervision may allow these patients to be treated with Radiotherapy with radical or palliative intent as indicated.

Keywords: Radiotherapy, Cancer, Geriatric, Symptomatic care, Toxicities, Medical comorbidities

INTRODUCTION

Cancer is a disease of aging; approximately 60% of all cancers and 70% of cancer mortality occur in persons aged 65 years and above.[1] The number of cancer patients over the age of 65 is projected to significantly increase over the next 20 years. In India, 11% of its population will include geriatric population (>60 years age) by 2020.[2] The incidence of cancer increases with age and more than 12–23% of all cancers occur after the age of 65 years.[3] It is estimated that by 2020 prevalence of cancer will be more than one million in Indian geriatric population. The increased risk of cancer in this age can be explained by telomere shortening, defective DNA repair mechanism,

immune-system alteration, variable expression of oncogenes, exposure to carcinogens in early life, and hormonal alterations or exposure.[2,4,5]

Despite increasing prevalence of cancer in this age group, these patients have received less attention in terms of investigation and appropriate treatment. Aging is a highly individualized process, characterized by physiologic and psychosocial changes that can affect tumor biology, decision-making for cancer treatment, tolerance to treatment, and ultimately outcomes.[1] Usually, the elderly cancer patients are considered not suitable for a curative treatment approach and a large proportion of patients are denied the benefit of aggressive treatment. Historically, clinical trial enrollment of older adults has not reflected the more general population of older patients with cancer due to the low overall numbers of older patients enrolled and overly strict inclusion criteria. It is very difficult to extrapolate clinical trial data to inform treatment decisions of older patients with cancer who are more vulnerable to adverse outcomes due to underlying health issues.[3]

Although the commonly-used Karnofsky Performance Status (KPS) and Eastern Cooperative Oncology Group (ECOG) performance status (PS) measures do correlate with treatment toxicity, these tools alone do not reliably predict toxicity in the older adult. The geriatric population is a heterogeneous group and a patient's chronologic age does not always correlate with underlying physiologic status.[1,6] Comprehensive Geriatric Assessment (CGA), a compilation of standardized tools to assess geriatric domains such as comorbidity, functional status, nutrition, physical function, cognitive performance, and social support, can help to define the "stage of the aging." CGA is defined as a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long-term follow-up.[7] With the use of CGA, geriatricians and oncologists can tailor treatment to their patients based on inputs from physical therapist, occupational therapist, pharmacist, social worker, and nutritionist.[8–10]

In view of paucity of information available on cancers in geriatric population in India, we envisaged the present study to evaluate various characteristics of geriatric patients attending Oncology centre in tertiary-care setup. Selected published Indian studies on elderly cancer patients are also discussed.

MATERIAL AND METHODS

It was a retrospective observational analytical study where the electronic medical records, medical documents, radiotherapy treatment charts, and indoor files in case of hospitalized patients were retrieved and studied. The study was conducted over a two year period in a tertiary care government institute with a dedicated oncology centre and all allied specialties. All these patients had been registered in hospital's central registry as well as oncology department during 2016–18.

The study population consisted of patients with histopathological confirmation of malignancy, who were aged 65 years or more, and willing to get radiotherapy (RT). The patient and the family members were explained the malignant nature of disease, treatment options, survival benefit, and potential complications.

The patients had undergone complete work-up for primary and metastatic disease according to standard guidelines. All the coexisting medical conditions were noted, and the cases were discussed with allied specialists to determine their fitness to undergo RT with or without chemotherapy. The patients received RT either by 2-D technique on Telecobalt Unit or 3D-conformal RT on a linear accelerator (Primus, Siemens, with 15 MV photons) without any major difference in the toxicity profile. There is no institutional protocol to provide blanket cover to geriatric patients with cancer, and the treatment was individually tailored according to disease characteristics, patient's performance status, medical co-morbid conditions, willingness to undergo treatment, and logistic concerns of the patient and families.

A record was made of patient-related, disease-related, and treatment-related attributes. The patients were reviewed twice-weekly by the treating radiation oncologist for tolerance and for therapy-induced complications. Age alone was not a criterion to offer admission, and the patients were hospitalized for supportive care whenever clinically indicated. Inferences were drawn of these various attributes and data from previously-published similar studies was perused for comparison and discussion.

RESULTS

Data from total of 247 patients was analyzed during the 2 year study period. Out of these, 154 (63%), 55 (22%), 30 (12%), and 8 (3%) patients belonged to age brackets of 65–70, 71–75, 76–80, and more than 80 years, respectively. The mean age was 70.3 years and the oldest patient was 94 years old. The number of males was 164 (66%) while the rest 83 (34%) were females. 165 patients (67%) presented with non-metastatic disease. Remaining 82 patients (33%) had metastatic disease, of whom 7 (3%) had single site of metastasis while 75 (30%) had multiple sites of metastasis. Performance-wise, 82 (33%), 95 (38%), 51 (21%), and 19 (8%) patients had ECOG status 1, 2, 3, and 4, respectively.

The site of primary origin is given in Table 1. Overall, the common sites of origin were head and neck (70 patients, 28%), lung (57 patients, 23%), genitourinary (49 patients, 20%, of whom 24 were cancer cervix), and gastrointestinal malignancies (36 patients or 15%, mostly carcinoma of the

esophagus comprising of 28 patients of primary Ca esophagus, followed by carcinoma of anorectum).

All patients had histopathological confirmation of malignancy before being offered oncological management. The histopathological profile of tissue biopsied from primary or metastatic site and the operative specimen is given in Table 2. The most common pathology was squamous cell carcinoma (150 patients, 61%) , followed distantly by adenocarcinoma (54 patients, 22%). 122 patients were not having any existing medical comorbid condition, while the rest 125 (51%) were having one or more morbidities. The most common of these were hypertension, COPD, diabetes mellitus, and CAD, as seen in 26%, 12%, 11%, and 6% patients, respectively. The details of comorbid conditions are given in Table 3.

135 patients (55%) were treated with radical intent, 82 patients (33%) were offered palliative radiotherapy in metastatic setting while the remaining 30 patients (12%) were offered palliative RT in non-metastatic setting due to unfavorable performance status. In curative setting, 55 received definitive concurrent chemoradiotherapy (CCRT), 43 received definitive RT, 2 received neoadjuvant RT, 7 received neoadjuvant CCRT, 24 received adjuvant RT, and 4 received adjuvant CCRT. Amongst these, 32 patients (13%) received 70 Gy, 40 patients (16%) received 60–69 Gy, 37 patients (15%) received 51–59 Gy while remaining 26 patients received ≤50 Gy. In palliative setting, 23 patients (9%) received <10 Gy, 31 patients (12.5%) received 15–20 Gy, 5 patients received 25 Gy, and remaining 53 patients received 30 Gy.

179 patients (72%) did not undergo any oncological surgery. Of the remaining 28%, 51 patients (21%), 15 patients (6%), and 2 patients (1%) underwent definitive surgery, palliative resection, and emergency surgeries. The most common site of surgery was head and neck, followed by pelvis, as seen in 16 and 13 patients, respectively. 66 patients (27%) received chemotherapy in concurrent setting. The most commonly chemotherapy regimen was Inj Cisplatin based, exhibited in 41 patients (17%), of whom 35 patients received weekly and the rest 6 patients received 3-weekly schedule. 89 patients (36%) were hospitalized for some duration of their RT course, while 158 patients (64%) were able to complete the prescribed course of RT in outdoor setting. Out of the 36% patients hospitalized, 72, 9, and 8 patients were admitted for <7 days, 8–10 days and >11 days, respectively.

The common indications of hospitalization [Table 4] were for supportive care during deteriorating performance status (25 patients), mucositis (14 patients), SVC obstruction (10 patient), raised ICT (10 patients), bleeding (9 patients), febrile neutropenia (7 patients), and dysphagia (6 patients). The most common intervention planned was nasogastric tube placement (71 patients, 29%), followed by PEG placement (5 patients) and esophageal stenting (4 patients). Less common indications were DJ stenting and embolization for which patient was referred to interventional radiologist.

In 58 patients (23%), RT was temporarily interrupted, the common causes being mucositis (29 patients, 12%), poor PS (10 patients, 4%), and febrile neutropenia (7 patients). Other indications were raised intracranial tension, skin reactions, and dysphagia, as seen in 3, 4, and 5 patients, respectively. The gap in RT was for <10 days in 47 patients (19%), while 7 and 4 patients had gap of 11–20 days and >20 days, respectively. 8 patients (3%) were initially planned for hypofractionated RT for palliative relief and later switched

Table 1: Primary site of origin (n = 247).

Primary site of origin	Number of patients	Percentage
Head and neck	70	28%
Lung	57	23%
Genito-urinary	49	20%
Gastro-intestinal	36	14%
Hematolymphoid	10	4%
Bone and soft tissue	9	4%
Breast	9	4%
CUPS	4	2%
Brain	3	1%
Total	247	100%

CUPS: carcinoma of unknown primary site.

Table 2: Histopathological distribution (n = 247).

Histopathology	Number of patients
SCC	150
Adenocarcinoma	54
IDC	9
PDCA	7
Lymphoma	6
Multiple myeloma	4
Bone/STS	4
Glioma	3
Small cell carcinoma	4
TCC	2
Neuroendocrine carcinoma	2
RCC	1
Melanoma	1

IDC: infiltrating ductal carcinoma, RCC: renal cell carcinoma, STS: soft tissue sarcoma, TCC: transitional cell carcinoma, SCC: squamous cell carcinoma, PDCA: poorly differentiated carcinoma.

Table 3: Comorbid medical conditions.

Comorbidity	Number of patients
Nil	122
Hypertension	63
COPD	30
Diabetes mellitus	26
CAD	14
TB	8
Old Fracture/Arthritis	6
Hypothyroidism	4
Hepatitis	1
Others	6

CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease (Some patients had more than 1 comorbidity).

Table 4: Indications for hospitalization.

Indication	Number of patients
Poor PS	25
Muco-cutaneous reactions	14
SVCO	10
Raised ICT	10
Bleeding	9
Febrile neutropenia	7
Dysphagia	6
Pain	3
Renal toxicity	2
Miscellaneous	3

SVCO: superior vena cava obstruction, ICT: intracranial tension, PS: performance status.

to conventional radical dose in view of improved performance status. 46 patients (19%) who were initially planned for conventional or palliative RT could not complete the planned dose, of whom 2 patients were switched to extremely hypofractionated RT, 26 (11%) had RT stopped due to poor tolerance, 7 patients (3%) developed aspiration pneumonitis, and 11 (4%) succumbed to disease while on RT.

Hematological toxicities were noted in 69 patients (28%), of whom 29, 32, 7, and 1 patient developed Grade 1, 2, 3, and 4 toxicities, respectively. Thus a total of 8 patients (3%) developed Grade 3, 4 hematological toxicities. Amongst the muco-cutaneous toxicities, no patient developed Grade 4 toxicity, while 13, 92, and 50 patients developed Grade 1, 2, and 3 toxicities. Thus a total of 57% patients developed Grade 2, 3 toxicities of skin and mucosa during RT, manageable in majority cases by supportive care in outdoor setting. Amongst the gastrointestinal (GI) toxicities, no patient developed Grade 4 toxicity, while 15, 74, and 57 patients developed Grade 1, 2, and 3 toxicities. Thus a total of 53% patients developed Grade 2, 3 GI toxicities during RT with or without chemotherapy, manageable by supportive care.

DISCUSSION

247 patients aged 65 years and above were enrolled in this study, forming about 18% of total patients receiving Radiotherapy during the study period. Data from five Indian Hospital based cancer registries (HBCR) also shows that roughly 20.3% of all malignancies occur in the population above 65 years.[11] Geriatric cancer patients contribute substantially to the workload of radiation oncology facilities. Treatment decisions for elderly patients should not simply rely on biological age. Rather, comprehensive assessments of organ function, comorbidity, and patients' ability to function independently are needed to provide individualized care.[12]

Pang A carried out a questionnaire-based survey on attitudes of cancer physicians towards management of the elderly cancer patient in a developed Asian country. The treatment decisions of oncologists to treat elderly patients are mainly based on performance status (95%), co-morbidities (75%), cancer stage (75%), cancer type (75%), patient's decision (53%), and age (51%). More than 60% of treating clinicians never engage a geriatrician's help in treatment decisions.[13] There is a need to incorporate valid CGA tools in Indian scenario of geriatric oncology. International Society of Geriatric Oncology (SIOG) recommendations on geriatric assessment include evaluation of functional status, comorbidity, cognition, mental health status, fatigue, social status and support, nutrition, and presence of geriatric syndromes. [9,10]

In an Indian study , Sarkar and Shahi[3] compared the profile of 104 cancer patients of age ≥60 years and 121 patients of 45–59 years. The median age was 65 years in elderly and 50 years in younger group. Elderly had higher proportion of gastrointestinal and genito-urinary tract malignancies. Younger group had higher proportion of breast, lymphoma, and brain tumor. 13% had co-morbidity, 50% received treatment, 27% were treated with radiotherapy with or without surgery, and two-third of these cases belonged to elderly group. Majority tolerated treatment well. 10% had significant grade of toxicity. 57% of elderly patients did not accept and one-fourth of all cases did not complete the prescribed treatment. 88% cases were responders of which 70% showed complete response. At 12 months 35% of treated patients came for follow-up. The authors concluded that elderly patients deserve same opportunity as younger patients for treatment and survival options from the oncologist.

Patil *et al.*[14] conducted a study to determine the patterns of care in elderly patients above age 70 years treated at a tertiary rural cancer center in India. A total of 761 patients

were evaluable. The median age of this cohort was 75 years (70–95 years). The most frequent primary sites of malignancies in 451 males were head neck (32.4%), lung (23.3%), and gastrointestinal (23.3%). In 310 females, the most common sites were head, neck (31.6%), gynecological (18.4%), and gastrointestinal (24.5%). 228 (30%) of the patients had localized disease, 376 (49.4%) had loco-regionally advanced disease, and 145 (19.1%) had distant metastases at presentation. 334 (46.32%) of patients were treated with curative intent. The factors that predicted use of curative intent treatment were age <75 years, performance status 0–1, primary site and clinical extent of disease. The authors concluded that routine CGA needs to be implemented in our setting as almost 50% of our geriatric patients undergo curative intent treatment.

In this study, the common sites of origin were head and neck (28%), lung (23%), genitourinary (20%), and gastrointestinal malignancies (15%). In a similar hospital based observational, analytic study, Goyal *et al.*[2] evaluated patients above 60 years of age. Total 1800 patients attended cancer OPD during the study period, out of them 489 patient were >60 years old (age range 61–91 years). The male:female ratio was 5:3. Ca lung was the most prevalent malignancy with prevalence of 30.9% (151/489). Ca breast and Ca ovary were next common malignancy with prevalence of 9.4% (46/489) each. Ca gall bladder, Ca oral cavity and Ca colon were 7%, 5.5%, and 3.5 prevalent, respectively. In male cancer patients, Ca lung was the most prevalent (41.3%) and Ca oral cavity (7.4%) was second most common malignancy. Ca gall bladder was third common malignancy with prevalence of 6.8 %. In female cancer patients, Ca breast was the most frequent malignancy with prevalence of 25.2% (45 /179). Ca ovary was the second prevalent malignancy (prevalence 24%) and Ca lung was the third common (12.8%).

The maximum age noted in our study was 94 years, a patient of urothelial malignancy who received palliative RT for bony metastasis and tolerated it well. Chargari *et al.*[15] studied the feasibility of radiation therapy in patients 90 years of age and older in a French multicentre analysis. 308 pts receiving 318 RT courses were identified, mean age was 93.2 years. Treatment was given with curative and palliative intent in 44% and 56%, respectively. Factors associated with a curative treatment were performance status (PS), place of life, previous surgery, and tumor stage. Hypofractionation and split course were used in 88% and 7.3%, respectively. Most toxicities were mild to moderate. RT could not be completed in 23 pts (7.5%). Median overall survival was 22.9 months. Cancer was the cause of death in 8.7% and 46% of pts treated with curative and palliative intent, respectively. This study showed that RT is feasible for patients aged 90 years or more.

In our study, the most common site of origin was head and neck cancer (HNC, 28%). Bahig *et al.*[16] reported outcomes and predictive factors of overall survival, hospitalization, and treatment completion rates in 129 elderly patients with locally advanced HNC treated with CCRT. Completion rate of combined CRT was 84%. Using competing risks, KPS ⩽ 80 and weight loss >5% were predictive of cancer mortality. The authors concluded that CCRT may be a feasible treatment option for healthier older patients at the cost of high hospitalization rates. VanderWalde *et al.*[17] performed a comprehensive literature review on therapeutic recommendations that are particular to HNC patients 65 years and older. Evidence from this study suggests that older patients have similar survival outcomes compared with their younger peers; however, they may experience worse toxicity and may require more supportive care. Moye *et al.*[18] in a retrospective study designed to characterize HNC in geriatric patients, found that older patients were nearly twice as likely to die within 5 years as their younger counterparts (hazard ratio: 1.92).

In our study, 28 patients of Ca esophagus were irradiated, of whom 50% (13 patients) received concurrent chemotherapy. Servagi-Vernat *et al.*[19] evaluated the acute toxicities, and efficacy of CCRT comprising a single platinum-based agent combined with radiotherapy in elderly patients with esophageal cancer. Dysphagia was the only grade 4 toxicity to occur during the study; no grade 5 toxicities were observed. Six weeks after the completion of treatment, 16 patients (53.3%) were in complete response. Three-year overall survival was 22.2%. The authors concluded that selected elderly patients with esophageal cancer and adequate functional status should not be excluded from CCRT and may be able to tolerate the treatment with acceptable acute toxicities. Similar promising results were reported by Song *et al.*[20] who assessed the efficiency and safety of CCRT using paclitaxel plus cisplatin in elderly patients (age ≥70 years) with esophageal cancer which resulted in encouraging survival outcomes and tolerable toxicities.

In our study, 125 patients (51%) were having some form of preexisting medical comorbid conditions. Jørgensen *et al.*[21] reviewed the prevalence of comorbidity in newly diagnosed elderly cancer cases compared with the background population and found a high prevalence of comorbid conditions among elderly cancer patients. Comorbidity potentially affects the development, stage at diagnosis, treatment, and outcomes of people with cancer. There is limited consensus on how to record, interpret, or manage comorbidity in the context of cancer, with the result that patients who have comorbidity are less likely to receive treatment with curative intent.[22] Evidence in this area is lacking because of the frequent exclusion of patients with comorbidity from randomized controlled trials.[23] There is evidence that some patients with comorbidity have potentially curative treatment unnecessarily modified, compromising optimal care. Patients with comorbidity have poorer survival, poorer quality of life, and higher health care costs. Strategies to address these issues

include improving the evidence base for patients with comorbidity, further development of clinical tools to assist decision making, improved integration and coordination of care, and skill development for clinicians.[24]

In our study, 89 patients (36%) were hospitalized for some duration of their RT course for supportive care. This data is in concurrence with findings of Bahig *et al.*[16] who reported similar hospitalization rate in elderly patients with locally advanced HNC treated with CCRT. Literature shows that elderly patients are especially likely to experience febrile neutropenia, complications from chemotherapy-induced nausea, anemia, osteoporosis (especially in patients diagnosed with breast or prostate cancer), depression, insomnia, and fatigue. These issues are often complicated by other chronic conditions related to age, such as diabetes and cardiac disease.[25]

In our study, only 1 patient developed Grade 4 hematological toxicity and no patient developed Grade 4 cutaneous, renal, and GI toxicity. RT could not be completed in 11% due to poor tolerance; and mortality rate was 4%. Thus our patients tolerated prescribed RT well. This was feasible by individually tailored treatment plan, meticulous periodic supervision, timely intervention to manage toxicities and continuous supportive care. Data supports utilization of PRT irrespective of age for most patients with PS 0-3 but care should be taken in selecting the right fractionation regimen in order to avoid lengthy palliative RT courses when survival is limited.[26]

There are certain drawbacks of our study. It is a retrospective study from a single institute. The study period spanned for 2 years. Patients reporting to Radiotherapy department were included and not from allied departments. Though the study shows promising results regarding tolerance of Radiotherapy in elderly patients without significant toxicities, the results cannot be generalized over entire population.

CONCLUSION

There will be a progressive increase in the number of geriatric oncology patients reporting to oncology centers for management in the years to come. Age alone should not be the criteria to deny aggressive multimodal treatment to these patients. All such patients should be subjected to comprehensive assessment and should be offered an individualistic treatment plan best suited to their performance status. A significant number of these cases can complete the curative treatment by continuous supervision, timely supportive care, and management of co-morbidities. It is high time that every institute incorporates the concept of geriatric oncology in their treatment protocols and academic programs.

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Conflicts of interest

There are no conflicts of interest.

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