

Assessment of treatment tolerance and response of elderly head and neck cancer patients: A single institution retrospective study

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ABSTRACT

Background: Head and neck (H and N) cancers are the leading cancer in elderly Indian population especially in Central India. Poor socioeconomic (SE) factors, lack of knowledge, and that of proper facilities is responsible for delayed presentation in advanced stages of the disease. Management of such patients is challenging for an oncologist. **Aim:** The present study evaluated the pattern of tolerance and response to treatment in elderly (>65 years) H and N cancer patients. **Materials and Methods:** Medical records of elderly H and N cancer patients presenting from January to December 2014 to the Department of Radiotherapy, Gandhi Medical College, Bhopal were reviewed, and data were collected from the departmental case files. **Results:** A total 112 patients were selected for this study. The mean age of presentation was 70 years. There was a marked male preponderance, with male to female ratio of 5.22:1. 102 patients presented in advanced stages (stage III and IV). The mean duration of symptoms was 6.5 months. Records of 99 patients were available and further analyzed. 59 patients were advised three courses of induction chemotherapy (CT) out of which 44 patients completed the treatment. 28 of these patients showed a positive response to the treatment while 16 showed no response (NR)/progression. Similarly, 24 patients were advised concurrent chemoradiotherapy out of which 17 patients completed the treatment. 13 of these patients showed a positive response while 04 showed NR/progression. On subgroup analysis, the difference between tolerance, response and overall treatment time between the two arms was not statistically significant. **Conclusions:** Treating elderly H and N cancer patients is a major therapeutic challenge for a clinician because of its poor prognosis, aggressive clinical behavior, associated co-morbidities, and SE factors. However, it is possible to achieve a quality outcome in select patients with basic CT and radiation.

Key words: Chemotherapy, elderly, head and neck cancers, radiotherapy

INTRODUCTION

Head and neck (H and N) cancer is the sixth most common type of cancer in the world, representing about 6% of all cancer cases.^[1] It has a higher incidence in older people, primarily due to its relationship with chronic exposure to tobacco smoking and alcohol intake.^[2] More than 40% of H and N cancers occur in patients older than 65 years^[3]

and with increasing life expectancy, there is an increased likelihood of the elderly population being diagnosed with this malignancy. It is estimated that by 2030, nearly 70% of the cancer cases would be diagnosed in adults with age 65 years or older.^[4]

Overall, 57.5% of global H and N cancers occur in Asia, especially in India for both sexes. In India, Bhopal has the world's highest age-standardized incidence of both tongue (10.9) and mouth cancers (9.6) in males.^[5] Overall, the comprehensive management of H and N cancer in the elderly population has not been adequately addressed, and these patients have also been under-represented in clinical trials of new cancer treatments.^[6] Advancing age may be associated with adverse factors like decline in functional reserve of multiple organ systems, a high prevalence of co-morbid conditions and limited socioeconomic (SE)

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support. Compliance and tolerance of elderly patients to intensive multimodality cancer therapy can be challenging due to significant treatment-related toxicities, the logistic demands prevalent in developing countries, and unplanned treatment gaps introduced between the treatments.^{16]} The present study is a retrospective analysis of elderly (>65 years) H and N cancer patients who presented to the Department of Radiotherapy (RT) in a Medical College of Central India. This institution caters to the population with a high incidence of H and N cancers.

MATERIALS AND METHODS

Hundred and twelve elderly (>65 years) H and N cancer patients presenting to the Department of Radiotherapy, Gandhi Medical College, Bhopal from January to December 2014 were selected. The presentation of cases was studied from the outpatient registration. Records of 99 patients (88.4%) were retrievable and analyzed with respect to the duration of symptoms, stage at presentation, treatment advised, and tolerance to the same. Tolerance was defined as all those patients who were able to complete the advised treatment that was either induction chemotherapy (CT) for 3 courses at 21 days interval or upfront chemoradiation (CTRT). RT was delivered on telecobalt using conventional fractionation with concurrent weekly injection cisplatin. Treatment duration was calculated from the 1st day of starting the therapy to the date of completion. Incomplete treatment (<3 cycles of induction CT or incomplete CTRT) constituted nontolerance. Response was assessed clinically and subjectively at completion of the advised treatment and at first follow-up in terms of response being present (<50% or > 50%) or absent (no response [NR]/progressive disease [PD]). Statistical analysis was done with the online Graph Pad software (GraphPad Software Inc., 7825 Fay Avenue, Suite 230 La Jolla, CA 92037 USA) using Fisher's exact test and unpaired *t*-test (*P* < 0.05) was considered significant.

RESULTS

Patient characteristics

Total number of cases registered during the period 01/01/2014–31/12/2014 was 1649 [Table 1]. Total number of elderly (>65 years) patients with H and N cancers was 112 (6.79%). Mean age of this subgroup was 70.04 years (range: 65–107 years). Of these, male patients accounted for 94 cases (83.92%) while the number of female patients was 18 (19.14%). Majority (102/112) of the elderly patients presented in locoregionally advanced stage (III and IV). The most common site of malignancy was oral cavity (34/112), followed by oropharynx (32/112), larynx (20/112), metastasis of unknown primary with secondary neck (11/112) and 15 cases of other H and N cancers. With regard to the age

distribution, 70% (84/112) of the patients were between the age group of 65–70 years, whereas 30% (28/112) were aged > 70 years. The average duration of symptoms was 6.5 months (Range: 1–24 months).

Treatment characteristics [Table 1]

In accordance with the Department Protocol, patients were advised either induction CT for tumor down-staging (3 courses) or upfront concurrent CTRT.

Induction CT was taxol and platinum-based (32 cases) or methotrexate, cisplatin, and bleomycin (27 cases) depending on the hospital drug supply. 24 patients were planned for upfront CTRT. 16 patients were either found to be unfit for any therapy or defaulted for the advised treatment.

Treatment outcome [Table 2]

Of the 59 cases planned to receive induction CT, 44 patients (74.57%) completed the prescribed course (28 patients receiving taxol + platinum and 16 receiving methotrexate, cisplatin, and bleomycin). 28 patients (63.63%) out of these showed disease regression (<50% in 20 cases and >50% in 8 cases). NR/PD was seen in 16 cases. Of the 24 patients planned for upfront CTRT, 17 patients (70.8%) completed the prescribed course. Of these, 17 patients, 12 patients (70.58%) showed disease regression (<50% in

Table 1: Patient and treatment characteristics

Characteristics	Sub groups	n (%)
Total number of patients		1649 (100)
	Elderly (>65 years)	112 (6.79)
	Males	94 (83.92)
	Females	18 (19.14)
Age distribution (years)	65-70	84/112 (70)
	>70	28/112 (30)
Stage	I-II	10/112 (8.92)
	III-IV	102/112 (91.07)
Site	Oral cavity	34/112 (30.35)
	Oropharynx	32/112 (28.57)
	Larynx	20/112 (17.85)
	Metastasis of unknown primary with secondary neck	11/112 (9.82)
	Others	15/112 (13.39)
Treatment advised	Taxol+cisplatin	32/59 (54.23)
	Methotrexate+cisplatin+bleomycin	27/59 (45.76)
	Chemoradiation	24
	Patients defaulted/supportive care	16

Table 2: Treatment outcome

Characteristic	Subgroups	n (%)
Patients completing treatment	Induction CT	44/59 (74.57)
	Chemoradiotherapy	17/24 (70.8)
Good response to treatment	Induction CT	28/44 (63.63)
	<50%	20/28 (71.42)
	>50%	08/28 (28.57)
	Chemoradiotherapy	12/17 (70.58)
	<50%	09/12 (75)
	>50%	03/12 (25)

CT: Chemotherapy

9 cases and > 50% in 3 cases). NR/PD was seen in 5 cases. Treatment completion and response of the two treatment modalities were compared using the Fisher’s exact test, and the two-tailed *P* value was found to be 0.8257 that was not statistically significant [Table 3].

The mean treatment duration for the patients completing 3 courses of induction CT (*n* = 44) was 64 days (range: 50–103 days) while those completing concurrent chemoradiotherapy (CCRT) (*n* = 17) was 66 days (range: 55–77 days). This difference was also found to be statistically not significant with a *P* = 0.4894 [Table 4].

DISCUSSION

Central India contributes to a sizable proportion of the country’s H and N cancer cases. Tobacco consumption, either smoked or smokeless is widely prevalent in this region. Most common presentation seen is that of elderly patients with a long history of tobacco abuse with advanced disease. The general and SE condition of these patients is often poor and completing the advised treatment is a challenging task. About two-thirds of H and N cancer patients present with loco-regionally advanced disease, commonly involving cervical lymph nodes. Metastatic disease at initial presentation is reported in about 10% of patients.^[7] Mountzios^[8] in his review article regarding optimal management of the elderly H and N cancer patients (comprising of 886 original articles) concluded that, it is well recognized that elderly patients with H and N cancers tend to receive suboptimal treatment, mainly due to fears of poor adherence and/or tolerance, excessive toxicity or lack of support from their environment. Nevertheless, it becomes increasingly apparent that medical intervention in the elderly should be guided by the benefit/risk ratio and that elderly patients affected by H and N cancers

should be treated on the basis of a curative intent, as long as comprehensive preoperative evaluation of existing co-morbidities is performed and optimal management of concomitant morbidities is completed. Age itself should never guide therapeutic decision, but a holistic, multidisciplinary approach addressing the real needs of the patient, as well as her/his wishes, should be implemented and maintained throughout the whole therapeutic process.

Patient compliance is a major obstacle in delivering definitive care to the elderly H and N cancer patients.^[9] The treatment options in H and N cancers can be surgery if the primary tumor can be excised with an appropriate margin without causing major functional compromise. However, the choice of definitive local therapy must take into account the likely functional outcome of treatment, resectability of the tumor, comprehensive geriatric assessment, and the patient’s wishes. In advanced stages, and with the usual associated co-morbidities, the elderly patients are usually poor candidates for surgery.

Radiotherapy for H and N cancers can be delivered with curative intent (radical RT), in order to improve local control following surgery (adjuvant RT) or to provide symptomatic relief (palliative RT). RT for H and N cancers is extremely complex and anatomic, tumor and clinical circumstances govern the use of radiation as primary treatment or as an adjuvant setting for H and N cancers.^[10] Both acute and late complications induced by RT can be very severe when treating H and N cancers and some researchers support the idea of not delivering palliative RT in elderly patients due to the disproportionately high toxicity induced in order to achieve a clinical response.^[11] The indications for RT in elderly cancer patients should take into account multiple parameters and should be based on a thorough geriatric assessment. Chronological age itself is seldom a contraindication for RT and it can be safely administered to an elderly population aged 80 years and older with both curative and palliative intent with the expectation of completion in more than 80% of patients.^[11]

Derks *et al.*^[12] in their analysis of quality-of-life (QOL) comparing elderly (>70 years) and young (45–60 years) H and N cancer patients found out that treatment did not affect QOL differently in older and younger patients and that standard treatment should always be considered, irrespective of the patient’s age.

In the present study, the patients who were offered RT were selected based on a good performance status and early disease. Despite that we had 7 mid-treatment dropouts defaulting primarily to radiation-induced side effects. Nevertheless, 12/17 (70.58%) patients showed disease regression.

Table 3: Statistical analysis for comparison of treatment completion and response using Fisher’s exact test

	Treatment completion	Positive response
Induction CT	44	28
Chemoradiotherapy	17	12
Two-tailed <i>P</i> =0.8257		

CT: Chemotherapy

Table 4: Comparison of treatment duration (days) using unpaired *t*-test

Group	Induction CT	Chemoradiotherapy
Mean	64.36	66.41
SD	11.23	6.67
SEM	1.69	1.62
<i>n</i>	44	17
<i>P</i> =0.48, 95% CI between -7.87 and 3.78 <i>t</i> =0.7036, <i>df</i> =59, <i>SED</i> =2.911		

CI: Confidence interval, *df*: Degrees of freedom, *SED*: Standard error of deviation, *SEM*: Standard error of mean, *SD*: Standard deviation, *CT*: Chemotherapy

The role of CT in H and N cancers is expanding. For patients with metastatic or incurable locoregional disease, CT is palliative. In contrast, for patients with potentially curable locoregional disease, it is an integral component of the multimodality approach, particularly when the disease is unresectable, or organ preservation is one of the goals of therapy.^[13] The addition of CT to locoregional treatment for patients with nonmetastatic H and N cancers significantly improves survival, with absolute survival benefit of 8% at 2 and 5 years.^[14] Induction CT followed by concurrent CRT results in excellent locoregional control and lower distant recurrence rates^[15] and combination CT with either cisplatin/5 fluorouracil or a platinum/taxane combination has become the standard of care in patients with incurable or recurrent H and N cancers.^[16]

As per departmental policy, patients were either prescribed cisplatin/taxol or methotrexate/cisplatin/bleomycin. Of the 59 cases, 44 completed the prescribed course of 3 cycles, 6 patients received 2 cycles while 5 patients did not return after the first cycle. For our analysis, only the patients completing 3 cycles were assessed.

Completion of the prescribed treatment is of paramount importance in the treatment outcome of cancer. Noncompliance to treatment has been reported to determent all parameters of disease control and survival.^[6] Studies have linked delay/interruption in treatment causing prolongation of overall treatment time to a significantly poorer overall survival in lung and breast cancers.^[17,18]

For H and N cancer analysis of treatment compliance in all radiation therapy oncology group prospective randomized trials between 1978 and 1991, reported a significantly reduced 3 years loco-regional control (13% vs. 27%) and 3 year absolute survival (13% vs. 26%) in patients with prolongation of treatment by 14 days or more.^[19]

Patel *et al.*^[20] in their study of 40 patients with node-positive stage III/IV H and N cancers concluded that poorly compliant patients are at significantly higher risk of persistent neck disease.

In our analysis, there was no significant difference between induction CT and CCRT in terms of treatment tolerance, response or treatment duration. An interesting observation was that the overall treatment time was increased in the induction CT arm mainly due to the delay in procurement of the CT drugs through the hospital supply rather than morbidity due to CT itself. However, treatment time increased in the CCRT arm chiefly due to the acute radiation toxicities leading to treatment breaks and the need for supportive management.

We were not able to systematically analyze the prominent reasons for noncompliance to therapy. However, the probable causes were chiefly lack of SE support and treatment side effects. The response assessment ideally should have an objective demarcation between total/near total or partial response based on clinical as well as imaging findings but could not be done in a dedicated manner due to logistical reasons.

We aimed at providing an initial analysis to highlight the presentation of elderly H and N cancer patients to a government institution in a high prevalence region, and an attempt to provide the best possible care in the available basic facilities. However, in light of these initial findings, we recommend the need to formulate exact hypothesis of noncompliance, the reasons causing it and means to secure the same. In general, CT seems to be feasible in elderly patients with H and N cancers, although its side effects may be exaggerated. However, a reduction in the administered dosage based purely on chronological age may seriously affect the efficacy of treatment. Effective management of CT associated toxicity with appropriate supportive care is crucial in the elderly population to give them the best chance of cure and survival, or to provide palliation.^[16]

Sizable proportions (61/83) of our patients were able to complete the prescribed treatment and showed satisfactory tolerance and results. We hope to further follow-up these patients in terms of providing data for long-term disease control and associated variables.

CONCLUSIONS

Age alone should not be considered a contraindication to management for advanced H and N cancer. Older patients require more careful multidisciplinary assessment of their supportive care needs to ensure successful completion of treatment and avoid further treatment-related toxicity.^[21]

Appropriate geriatric tools should be used to identify elderly patients who are eligible for optimal locoregional treatment.^[22]

We also propose an immediate need to address the factors responsible for causing intolerance in the elderly H and N cancer patients. The presence of associated co-morbidity, treatment toxicity, logistic reasons, and their apt solution warrants further studies.

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