

Compliance to Therapy—Elderly Head and Neck Carcinoma Patients



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DOI: <http://dx.doi.org/10.5770/cgj.17.101>

ABSTRACT

Background

Treatment compliance of elderly patients to intensive multimodality cancer therapy can be challenging and has not been adequately addressed in developing countries. The present study evaluated compliance of elderly head and neck carcinoma patients to cancer-directed therapy.

Methods

Forty-seven elderly HNSCC patients were evaluated in the present study. Patients were assessed as per stage and site of disease, general condition, performance status, and any pre-existing co-morbidities. Compliance was defined as patients who were able to complete cancer therapy as intended at primary clinic. Non-compliance to therapy was stratified as early, mid- and late-course non-compliance. Statistical analysis was done using STATA 9.1 software, chi-square/Fischer's exact test to see strength of association between two categorical variables that could possibly affect compliance in elderly patients.

Results

Sixty-eight per cent of elderly patients were subjected to radical treatment, majority (42/47) presented in loco-regionally advanced stage (III-IV), most common site of malignancy was oropharynx (21/47). Sixty-two per cent of elderly HNSCC patients were compliance to cancer therapy. Median overall treatment time for patients subjected to radical radiation therapy was 52 (range 47–99) days, and for radical surgery and adjuvant radiotherapy was 109 (95–190) days. Compliance to therapy for elderly HNSCC patients was not significantly associated with advanced stage, poor general condition, intent of treatment or presence of co-morbidity. As regards to

non-compliance, majority (14/18) of elderly patients showed mid-course treatment non-compliance.

Conclusions

Nearly two-thirds of elderly head and neck carcinoma patients were compliant to cancer-directed therapy.

Key words: compliance, HNSCC, elderly patients, overall treatment time

INTRODUCTION

Head and neck cancer is the sixth most common type of cancer in the world, representing about 6% of all cancer cases. (1) Worldwide, more than half a million head and neck cancer cases and 320,000 deaths due to head and neck cancer are estimated to occur each year, and it is the eighth cause of cancer mortality in the world. (2) Head and neck cancer has a higher incidence in older people, primarily due to its relationship with chronic exposure to tobacco smoking and alcohol drinking. (3) Fifty-seven per cent of all newly diagnosed malignancies and 71% of all cancer deaths occur in those ≥ 65 years of age. (4) More than 40% of head and neck cancers occur in patients older than 65 years. (5) With increasing life expectancy, there is increased likelihood of elderly population being diagnosed with malignancy. It is estimated that by 2030, nearly 70% of the cancer cases would be diagnosed in adults with age 65 years or older. (6) In India, 30,831,190 males and 33,998,613 females are in the age group of 65 years and above, accounting for 5.5% of the nation's population. (7)

One of the most challenging tasks for the practicing oncologist today is the care of the elderly cancer patient. In recent years, management of cancer in elderly population has not been adequately addressed as these patients have often been under-represented in clinical trials of new cancer treatments (8-11) and most clinical cancer trials have had arbitrary upper age limits. Majority of elderly cancer patients are

less likely to receive definitive or adequate cancer-directed therapy. This has been seen not only for head and neck cancers, but also for other common malignancies.⁽¹²⁻¹³⁾ Advancing age may be associated with progressive loss of stress tolerance, decline in functional reserve of multiple organ systems, high prevalence of co-morbid conditions, limited socioeconomic support, reduced cognition, and higher prevalence of depression. However, aging is highly individualized, and chronologic age may not reflect the functional reserve and life expectancy of an individual. Compliance of elderly patients to intensive multimodality cancer therapy can be challenging due to significant treatment-related toxicities, the logistical demands involved in treatments, and unplanned treatment gaps introduced between the treatments. All these factors can decrease treatment compliance and prolong overall treatment time, which is known to be a detriment to therapeutic outcomes to cancer directed therapy.⁽¹⁴⁻¹⁶⁾ Treatment compliance of elderly patients has not been adequately addressed in developing countries. The present study evaluated compliance of elderly HNSCC to cancer-directed therapy. To our knowledge this study is one of the first studies evaluating compliance and overall treatment time of elderly HNSCC patients to cancer-directed therapy from a developing nation.

METHODS

Our study included a total of forty-seven elderly HNSCC patients (age 65 years or older) referred for radiotherapy from the various multi-disciplinary clinics at our institute in one unit of Department of Radiotherapy from July 2010 to June 2011. The patients were assessed per stage and site of the disease, general condition, performance status, and any pre-existing co-morbidities. For the purpose of study, compliance was defined as all patients who were able to complete the stipulated treatment as intended at the primary clinic. The key factors evaluated for compliance and overall treatment time included date of registration at cancer centre, radiotherapy registration date, surgery date, radiation start and completion date, and treatment completion date. Compliance was evaluated with regard to age, stage, general condition, performance status, presence of co-morbidity, and intention of treatment.

For possible factors affecting compliance, statistical analysis was done using STATA 9.1 software, chi-square/Fischer's exact test were used to see the strength association between the two categorical variables. A *p* value of less than .05 was taken as significant. For all compliant patients, overall treatment time was calculated from the day of initiation of cancer-directed therapy to completion of treatment. Further, to study the pattern of non-compliance, patients were divided into early non-compliance (patients that were non-compliant during the investigation and staging work up period), mid-course non-compliance (patients non-compliant after complete diagnostic work up and treatment decision, but before radiation delivery), and late non-compliance (patients non-compliant during radiation delivery).

RESULTS

In this cohort of 47 patients, treatment decision taken at the multi-disciplinary clinic was for radical treatment in 68% (32/47 patients), whereas the remaining 32% (15/47 patients) were planned to receive palliative treatment. Radical treatment included either radical radiation with or without chemotherapy in 55% (26/47) of the patients or surgery followed by post-operative radiotherapy in 13% (6/47) of the patients. In this retrospective analysis, patient and treatment characteristics have been highlighted in Table 1. The salient features were that majority (42/47) of the elderly HNSCC presented in loco-regionally advanced stage (III-IV), the most common site of malignancy was oropharynx (21/47), followed by oral cavity (11/47), larynx (9/47), and hypopharynx (6/47). With regard to age distribution, 72% (34/47) of the patients were between the age group of 65–74 years, whereas (13/47) 28% were 75 or older. General condition was fair in most of the elderly patients (38/47); only (5/47) of the elderly patients were in good general condition, while the remaining (4/47) were in poor general condition.

Out of the 47 elderly patients, analysis of compliance to treatment decision revealed that 62% (29/47) of the elderly HNSCC patients were compliant to cancer-directed therapy, whereas 38% (18/47) of the patients were not able to complete the stipulated treatment. For all compliant patients, overall treatment time was calculated from the day of initiation of cancer directed therapy to completion of treatment. The median overall treatment time for patients subjected to radical radiation therapy was 52 (range 47–99) days, and for

TABLE 1.
Patient & treatment characteristics

<i>Characteristic</i>	<i>Sub-Group</i>	<i>Percentage</i>
Age	65-74.9 yrs	(34/47) 72%
	> 75 yrs	(13/47) 28%
KPS	90-100	—
	80	(26/47) 55%
	70	(21/47) 45%
General condition	Good	(5/47) 10%
	Fair	(38/47) 81%
	Poor	(4/47) 9%
Stage	I-II	(5/47) 11%
	III-IV	(42/47) 89%
Site	Oral cavity	(11/47) 23%
	Oropharynx	(21/47) 45%
	Larynx	(9/47) 19%
	Hypopharynx	(6/47) 13%
Treatment intention	Radical	(32/47) 68%
	Palliative	(15/47) 32%
Radical treatment	Radiotherapy±Chemotherapy	(26/47) 55%
	Surgery-PORT	(6/47) 13%

radical surgery and adjuvant radiotherapy was 109 (95–190) days. Twenty-two per cent of the elderly patients had one or more associated co-morbidities. Factors affecting compliance and the association between the categorical variables using statistical analysis by chi-square/Fischer Exact test are mentioned in Table 2. Compliance to treatment decreased as the stage of disease increased (80% for early stage versus 62% in loco-regionally advanced stage). Compliance was better for elderly patients with good to fair general condition (63% versus 50% patients with poor general condition). However, neither was statistically significant. Fifty-seven per cent of the patients having one or more co-morbidity were compliant to treatment, whereas compliance increased to 63% when patients had no co-morbidity (*p* value NS). Compliance was similar with regard to intention of treatment (radical 63% vs. palliative 60%), advancing age (age group 65-74years 62% vs. 75 or older 62%). A further analysis on pattern of non-compliance revealed that early non-compliance to therapy was seen in 5% (1/18) of the patients, whereas majority (14/18) of elderly patients showed mid-course non-compliance. Only 17% (3/18) of the patients were non-compliant to treatment during the course of radiation delivery.

DISCUSSION

Compliance to cancer-directed therapy is a key factor in the treatment outcomes. Non-compliance to treatment has been reported to determent all parameters of disease control and survival. The assessment of patients receiving definitive concurrent chemoradiation for either locally advanced or medically inoperable NSCLC treated in RTOG studies revealed that prolongation of OTT was associated with significantly poorer survival, with a 2% increase in the risk of death for each day of treatment prolongation.⁽¹⁷⁾ Interruptions more than one week during post-operative irradiation of breast

cancer adversely affected overall survival in these patients.⁽¹⁸⁾ For head and neck cancer analysis of treatment compliance in all Radiation Therapy Oncology Group (RTOG) prospective randomized trials between 1978 and 1991, reported a significantly reduced three-year loco-regional control (13% vs. 27%) and three-year absolute survival (13% vs. 26%) in patients with prolongation of treatment by 14 days or more.⁽¹⁹⁾ Similarly, numerous studies have demonstrated non-compliance to treatment protocols impedes local control of head and neck cancers.⁽¹⁹⁻²³⁾ These studies describe a loss of local control of 0.4% to 2.9% for each day the treatment course is prolonged, with an average of 1.7% per day. A recent analysis of critical impact of radiotherapy compliance in treatment of advanced head and neck cancers, the Trans-Tasman Radiation Oncology Group (TROG 02.02) trial,⁽²⁴⁾ revealed that patients with major deficiencies in their treatment plans had a markedly inferior outcome (i.e., for deviations versus compliance as regards the treatment results—2 years overall survival 50% vs. 70% and freedom from loco-regional failure, 78% vs. 54%).

Head and neck squamous cell carcinoma may have geographical variation with regard to site and stage at presentation, treatment compliance, and survival.⁽²⁵⁾ Amidst the pre-existing geographical variation with inferior treatment compliance and survival in the Asian population, compliance of elderly HNSCC patients is of utmost importance, as advancing age may be construed (i) with progressive loss of stress tolerance, (ii) decline in functional reserve of multiple organ systems, (iii) high prevalence of co-morbid conditions, (iv) limited socioeconomic support, (v) reduced cognition, and (vi) higher prevalence of depression—all of which may be the reasons for poor treatment compliance. In the present study, 62% of elderly HNSCC patients were compliant to treatment protocol. Elderly HNSCC patient compliance in our study is comparable to overall treatment compliance for HNSCC patients previously reported from the subcontinent.⁽²⁵⁾ Overall treatment time was prolonged for patients subjected to radical surgery and adjuvant radiotherapy (median OTT 109 days), whereas there were no such delays for patients receiving radical radiotherapy (median OTT 52 days). Properly selected elderly HNSCC patients seem to be equally compliant to treatment protocols.

Elderly patients with cancer may often have other pre-existing medical co-morbidities especially related to chronic exposure to tobacco smoke and alcohol. The secondary aim of the study was to see the burden of co-morbidities in elderly HNSCC patients. Associated co-morbidities were present in 23% of the elderly HNSCC patients, and this burden of co-morbidity was less when compared to those reported in literature.⁽²⁶⁻²⁷⁾ Presence of co-morbidity in these patients was associated with decreased compliance; however, the difference in compliance was not statistically significant. Similarly, the study did not find a statistical significant association of compliance with age, stage, performance condition, general condition, and intent of treatment. The factors influencing

TABLE 2.
Factors affecting compliance

Factor	Subset	Compliance (%)	P value
Age (years)	65-74	(21/34) 62%	.98
	> 74	(8/13) 62%	
Stage	Early (I-II)	(4/5) 80%	.64
	Advanced (III-IV)	(26/42) 62%	
General condition	Good-fair	(27/43) 63%	.63
	Poor	(2/4) 50%	
Performance status (KPS)	KPS 80	(14/26) 54%	.46
	KPS 70	(15/21) 71%	
Intention of treatment	Radical	(20/32) 63%	.87
	Palliative	(9/15) 60%	
Associated co-morbidity	Absent	(23/36) 64%	.97
	Present	(6/11) 55%	

compliance in elderly patients remain complex and need to be further elucidated.

The highlights of this study can be:

1. The pattern of elderly HNSCC patient non-compliance revealed that majority of the elderly patients (83%) were non-compliant to treatment before the initiation of radiation therapy. This was a bit surprising result as elderly patients were expected to be non-compliant to treatment during the course of radiation therapy because of development of increased acute radiation morbidity, worsening of performance status, and poor tolerance.
2. To our knowledge the present study is the first study to report early to mid-course non-compliance to cancer-directed therapy in elderly HNSCC patients. As per available records, the reasons for this early to mid-course non-compliance finding could not be evaluated. The probable explanation could be a long median radiation waiting of two months at our cancer center, during which some elderly patients may have preferred early cancer-directed therapy at some other cancer centers. Further the possibility of upstaging and disease progression during the radiation waiting period cannot be ignored (majority of the patients were already in a loco-regionally advanced stage). This aspect of early to mid-course non-compliance to cancer-directed treatment that emerged as predominant factor in our study needs to be further evaluated, especially in developing countries where there is much load on the available machines and where the cancer patient population has probably outnumbered the available resources.

Limitations of our study include:

1. Retrospective nature of the study and small number of patients.
2. In view of the retrospective nature of the study, all factors for non-compliance could not be elicited. Other factors which could influence non-compliance and were not available include (a) poor socio-economic status, (b) lack of social or family support, (c) distance from the treatment centre.
3. Elderly patients were not subjected to comprehensive geriatric assessment before treatment decisions.
4. While the medical record documented non-compliance, the underlying reasons behind non-compliance could not be determined.

CONCLUSION

In recent years, the improvements in treatment modalities and techniques have made the delivery of cancer-directed therapy safe and feasible in elderly HNSCC patients. Carefully selected elderly HNSCC patients seem to be equally compliant to treatment protocols. Non-compliance to treatment in these patients could pose an obstacle to delivery of effective health care. Our

findings from India in a small cohort of elderly HNSCC patients showing the issues of early mid-course non-compliance pattern need to be evaluated further. A larger prospective study, performing a comprehensive geriatric assessment and evaluating the role of comprehensive interventions combining cognitive, behavioural, and affective components to improve compliance in elderly patients, is warranted.

CONFLICT OF INTEREST DISCLOSURES

The authors declare that no conflicts of interest exist.

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