Clinical Oncology xxx (2013) 1–7

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Predictors of Weight Loss during Conformal Radiotherapy for Head and Neck Cancers – How Important are Planning Target Volumes?

I. Mallick [*], S.K. Gupta [*], R. Ray [†], T. Sinha [†], S. Sinha [‡], R. Achari [*], S. Chatterjee [*]

[*] Department of Radiation Oncology, Tata Medical Center, Kolkata, India
[†] Department of Clinical Nutrition, Tata Medical Center, Kolkata, India
[‡] Department of Biostatistics, Tata Medical Center, Kolkata, India

Received 30 September 2012; received in revised form 22 February 2013; accepted 12 March 2013

Abstract

Aims: Nutritional compromise is common during high dose radiotherapy (RT) or chemoradiotherapy (CRT) for head and neck cancers. We aimed to identify the factors that determine nutritional outcome for head and neck cancer patients during radiotherapy.
Methods: Data from 103 patients with head and neck cancer treated with highly conformal radiotherapy to doses of 60 Gy or more in 30–33 fractions in the adjuvant or definitive setting was analyzed. All patients received complex 3D conformal radiotherapy (3DCRT) or intensity modulated radiotherapy (IMRT). Patients received regular nutritional counseling and need-based interventions. Their weight was recorded at the beginning and end of radiotherapy. Using univariate and multivariate models we tested possible predictors of weight loss of >5% and NG tube requirement.
Results: The mean weight loss was 3.8%. The incidence of weight loss >5% was 37.9% and NG tube placement was 24.3%. The factors significantly associated with >5% weight loss in the univariate analysis were tumor site (oro-hypopharyngeal vs. others), definitive vs. adjuvant RT; prescription dose of >60 Gy vs. 60 Gy; CRT vs. RT alone; prescription dose planning target volume (PTV) volume >235 cc and total PTV volume >615 cc. Age, sex, T stage, N stage and modality (3DCRT/IMRT) were not significant. In multivariate analysis, the total PTV volume, prescription dose PTV volume and use of chemotherapy were significant after controlling for other factors. Patients could be risk stratified based on the use of CRT and large PTV volumes. Patients with none, one or both factors had a likelihood of >5% weight loss of 0%, 30.3%, and 56.9% ($p < 0.001$) and likelihood of NG tube placement of 5.3%, 15.2% and 37.3% ($p = 0.007$).
Conclusions: It is possible to predict weight loss and NG tube requirements from disease and treatment related factors. PTV volumes are important predictors of nutritional compromise. Risk stratification may enable more focused counseling and identification of patients who require preventive interventions.

Key words: Chemoradiation; enteral nutrition; head and neck cancer; PTV; radiotherapy; weight loss

Introduction

Curative radiotherapy or chemoradiotherapy (CRT) for head and neck cancers is known to cause substantial acute nutritional compromise. Radiotherapy leads to odynophagia and dysphagia secondary to acute mucositis; platinum-based chemotherapy together with radiotherapy results in dysgeusia, anorexia, nausea and vomiting, leading to further malnutrition and dehydration. Caloric intake reduces during radiotherapy [1]. Reported literature in head and neck cancer suggests that weight loss during a course of curative radiotherapy or CRT may be substantial, with greater than 10% weight loss occurring in 30–50% of patients undergoing CRT and in 10% of those treated with radiotherapy alone [2–4].

Weight loss is significant not only in terms of weakness and general well-being, it is often a surrogate for dehydration. It is one of the determinants for introducing enteral nutrition via the nasogastric or gastrostomy route [4]. Severe weight loss has been implicated as a cause of treatment interruption, infections and hospital admission [5]. Substantial weight loss could alter the anatomical contour of the neck and lead to dosimetric changes in the volumes treated with radiotherapy.

Nutritional counselling is an integral part of a co-ordinated head and neck radiotherapy service. There is evidence to show that planned nutritional counselling before and through a course of radiotherapy leads to less weight loss and

Author for correspondence: I. Mallick, Department of Radiation Oncology, Tata Medical Center, 14 MAR (EW), Newtown, Kolkata 700156, India. Tel: +91-33-66057103; Fax: +91-33-66057578.
E-mail address: indranil.mallick@tmckolkata.com (I. Mallick).

0936-6555/$36.00
http://dx.doi.org/10.1016/j.clon.2013.04.003

a shorter rehabilitation period [6,7]. Prophylactic percutaneous endoscopic gastrostomy/jejunostomies (PEG) is also used in some centres, especially before radical intent CRT, as this approach has been shown to reduce weight loss and hospitalisation during radiotherapy [8,9]. However, PEG may lead to prolonged tube dependence and a higher incidence of oesophageal strictures [10,11] and, therefore, may not be an ideal prophylaxis for all patients.

It would be beneficial to know the factors that predict for a higher likelihood of significant weight loss. This would help define an approach for nutritional counselling, screen patients who would benefit most from prophylactic interventions and potentially also alter treatment decisions and details in a vulnerable subgroup of patients.

There have been some retrospective analyses on factors predicting for severe weight loss [12–15]. However, treatment- related factors, especially the importance of planning target volumes (PTVs), have not been investigated in detail. We therefore undertook a study looking at factors predicting for weight loss in the setting of patients treated with intensity-modulated radiotherapy (IMRT) or complex three-dimensional conformal radiotherapy (c-3DCRT) in the curative setting.

Materials and Methods

This was a retrospective analysis of data from patients undergoing curative intent radiotherapy (either definitive or adjuvant) between June 2011 and July 2012 in a single tertiary care cancer hospital in Kolkata, India. In total, 113 patients completed a course of radiotherapy for head and neck cancers. We excluded patients who received hypofractionated radiotherapy in 4 weeks for T1/T2 glottic cancers. The data for the remaining 103 patients were used for this analysis.

Target Delineation

For definitive treatments, the gross tumour volume was identified on the basis of a clinical examination and a computed tomography/magnetic resonance imaging scan for all patients. A minimum expansion of 5 mm was taken and further expansion into areas suspected of harbouring clinical disease was included as a part of the high-dose clinical target volume, and prescribed a dose of 65 Gy/30 fractions/6 weeks on the PTV expansion. Clinically involved nodal levels were treated to a radical dose. Levels adjacent to involved levels received an intermediate dose of 60 Gy/30 fractions/6 weeks. Other nodal levels were treated to a dose of 54 Gy based on their risk of involvement as per guidelines by Gregoire *et al.* [16]. For adjuvant radiotherapy, pretreatment imaging was used as a reference for all patients. The tumour bed and operated nodal levels were treated to 60 Gy/30 fractions/6 weeks. Areas with close or positive margins or nodal levels with extracapsular extension were treated to 63 Gy/30 fractions/6 weeks or 66 Gy/33 fractions/6.5 weeks. All clinical target volumes were expanded by 5 mm geometrically to obtain the corresponding PTV.

Treatment Planning

All patients received highly conformal radiotherapy, either with c-3DCRT using multiple beams with forward planning or inverse-planned IMRT. Details of the planning procedure is beyond the scope of this article, but has been detailed elsewhere [17]. All treatment plans were single phase with simultaneous integrated boost.

Chemotherapy

Concurrent chemotherapy was administered with weekly cisplatin 40 mg/m^2 intravenously when indicated according to institutional protocol after discussion in a multidisciplinary meeting.

Nutritional Assessment and Interventions

All patients received nutritional assessment by a trained clinical nutritionist before and weekly during radiotherapy. The nutritional assessment was carried out at the radiotherapy department on a specific day of the week with weight and nutritional measurements, preparation of a diet chart and detailed counselling. None of the patients received prophylactic placement of PEG. If significant impairment of oral intake was observed, a nasogastric tube was placed and kept *in situ* until the patient was able to resume their oral intake to satisfy the daily caloric requirements. There was provision for hospital admission or intravenous fluid supplementation as a day care procedure. Body weight was measured at the start of radiotherapy, weekly during radiotherapy and at the end of radiotherapy. Nasogastric tube placements and hospital admissions were documented. Weight changes were recorded according to a preplanned schedule and entered into a database.

Data Collection and Statistical Analysis

For the purpose of this study, demographic, disease-related and treatment-related information was retrieved from electronic medical records. We planned an analysis of the following factors: age; gender; primary site; T stage; N stage; adjuvant or definitive radiotherapy; radiotherapy alone or CRT; prescription dose of 60 Gy or higher; c-3DCRT or IMRT; PTVs. For the last factor, we decided a priori to look at two specific volumes: the volume of the highest/prescription dose PTV (prescPTV) and the total PTV (totalPTV), which was generated by carrying out a Boolean summation of all PTVs.

A statistical analysis was carried out using the SPSS © v 17 software. Descriptive statistics were generated for percentage weight loss as well as patient-, disease- and treatment-related factors. Unpaired *t*-tests were carried out to compare weight losses between different treatment groups after testing for normality assumption using the Kolmogorov–Smirnov test. Using a cut-off of 5% weight loss, patients were divided into two groups. The optimal diagnostic threshold for the prescPTV and totalPTV were tested using receiver operating characteristic (ROC) curves. The chi-squared test was carried out to test the different

Please cite this article in press as: Mallick I, et al., Predictors of Weight Loss during Conformal Radiotherapy for Head and Neck Cancers – How Important are Planning Target Volumes? Clinical Oncology (2013), http://dx.doi.org/10.1016/j.clon.2013.04.003