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Pretreatment weight status and weight loss among head and neck cancer patients receiving definitive concurrent chemoradiation therapy: implications for nutrition integrated treatment pathways

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Abstract

Purpose—The purpose was to examine the effect of pretreatment weight status on loco-regional progression for patients with squamous cell carcinoma of the head and neck (SCCHN) after receiving definitive concurrent chemoradiation therapy (CCRT).

Methods—In an expanded cohort of 140 patients, we retrospectively reviewed weight status and loco-regional progression of SCCHN patients treated with CCRT between 2004 and 2010.

Results—Pretreatment ideal body weight percentage (IBW%) was statistically significantly different for patients with disease progression than for those without progression ($p=0.02$) but was not an independent predictor of progression. Median pretreatment IBW% was 118 (72–193) for the progression-free group and was 101.5 (73–163) for the group with progression. Both groups suffered clinically severe weight loss of approximately 9 % from baseline to end treatment.

Conclusions—Pretreatment weight status, a very crude indicator of nutrition status, may have prognostic value in patients with SCCHN undergoing definitive CCRT. Inadequate nutritional status in these patients has been associated with poor clinical outcomes and decreased quality of life. Based on this report and others, the best next steps include routine validated malnutrition screening and the testing of evidence-based nutrition care protocols with the goals of minimizing weight loss and improvement of quality of life.

Keywords

Head and neck cancer; Nutrition; Nutrition status; Radiation therapy; Weight loss; Quality of life

Introduction

Approximately 43,000 cases of head and neck cancer and 12,000 deaths due to these cancers are estimated to occur in the USA during 2012 [1]. Concurrent chemoradiation therapy (CCRT) is a standard treatment for those with advanced head and neck disease. The major cause of death in patients with squamous cell carcinoma of the head and neck (SCCHN) is loco-regional progression, though CCRT provides loco-regional control in most patients who receive it [2, 3].

Treatment interruption has been associated with loco-regional progression in patients receiving radiation alone [4] and in those receiving radiation combined with chemotherapy [5]. We reported that treatment duration was a significant independent predictor of loco-regional progression in a cohort of 78 SCCHN patients who received CCRT between 2004 and 2007 at Roswell Park Cancer Institute (RPCI) [6, 7]. Additionally, using a multivariate model, we showed that weight status prior to treatment was a significant independent

predictor of loco-regional progression [6]. Weight status has been negatively associated with outcomes for SCCHN patients undergoing CCRT [8, 9].

Starting in October 2007, efforts were made to limit prolongation of CCRT in our SCCHN patients. The purpose of this analysis was to examine pretreatment weight status as an indicator of progression in an updated and expanded patient cohort.

Methodology

This retrospective examination of SCCHN patients was reviewed and approved by the institutional review board at Roswell Park Cancer Institute. Definitively treated patients who received intensity-modulated radiation therapy (IMRT) and concurrent chemotherapy between the years of 2004 and 2010 were eligible for this review. Patients who were treated at RPCI from August 2004 and September 2007 were entered into analysis as cohort 1. Following September 2007, measures were initiated to minimize treatment interruption and limit prolongation of therapy beyond 7 weeks. Patients who were treated between October 2007 and June 2010 were entered into analysis as cohort 2.

Treatment

Previous reports of the original cohort provide detailed description of the treatment for cohort 1 [6, 7]. Briefly, all patients received CCRT, which included IMRT to 70 Gy in 35 daily fractions to the high-dose target volume and 56 Gy to the elective target volume. Cisplatin 100 mg/m² on radiotherapy days 1, 22, and 43 or cisplatin 30–40 mg/m² weekly were the most commonly prescribed chemotherapy regimen.

For all patients in cohort 2, treatment measures were initiated to avoid interruptions and included beginning all treatments on a Monday, reducing optimal total treatment time from 49 to 47 days and providing twice daily treatments up to a total of six fractions per week enabling a patient to make up for any missed treatments. Additionally, supportive care was provided and included early initiation of social work support to assist in transportation matters, aggressive counseling for smoking and alcohol cessation, and standardizing supportive care with the use of preprinted sheets explaining general nutritional goals, proper use of prophylactic salt/baking soda rinses, and recommended use of pain medications.

All patients in both cohorts were offered a percutaneous endoscopic gastrostomy (PEG) tube as routine supportive care near the initiation of CCRT. Nutrition assessment and consultation with a dietitian was referral based only with some patients not having any contact with a dietitian. Following treatment, all patients underwent a complete head and neck examination that included flexible fiber optic laryngoscopy every 2 months for year 1, every 3 to 4 months for year 2, every 6 months for years 3 to 4, and then annually thereafter. At the 8-to 12-week visit following treatment completion, a positron emission tomography or computed tomography scan was used to evaluate the initial response to therapy.

Outcomes collected

Retrospective patient information was collected from the electronic medical record which included the following: age at diagnosis, gender, tumor site, tumor stage, lymph node stage,

duration of radiotherapy, height and weight, pretreatment hemoglobin levels, date of last follow-up, and loco-regional progression diagnosis at last follow-up.

Measurements of body weight were collected for the time period directly before initiation of CCRT (within 4 weeks) and directly after the completion of therapy (within 4 weeks). Ideal body weight (IBW) was calculated using the Hamwi formula [10] as follows:

IBW for men=106 lbs for 5 ft tall and 6 lbs/in. for each inch over 5 ft

IBW for women=100 lbs for 5 ft tall and 5 lbs/in. for each inch over 5 ft

Additionally, body mass index was calculated as weight in kilograms divided by height in meters squared.

Any proven disease in the primary disease site or neck not eradicated by CCRT was defined as loco-regional progression. This definition included both recurrent disease (viable disease noted beyond 6 months of CCRT completion) and persistent disease (viable disease noted within 6 months of CCRT completion). Progression was histopathologically confirmed for all cases.

Statistical analysis

The statistical package for the Social Sciences (Version 19, SPSS Inc. Headquarters, Chicago, IL) was used for all statistical analyses. The Chi square or Fisher exact test was used to examine categorical variables and the Mann–Whitney *U* was used to examine continuous variables. Variables were examined for the cohorts combined and between cohorts. Additionally, differences for pretreatment weight and weight status, determined by IBW or BMI, between cohorts and by loco-regional progression in the combined group were examined.

Duration of radiation therapy was examined in terms of days from initiation of therapy to the end of therapy. Percentage of pretreatment IBW (IBW%) was calculated and the variable was examined as a continuous variable and as a categorical variable. Pretreatment IBW% was dichotomized into adequate and inadequate status based on clinical significance as follows: 90 % IBW (adequate) and <90 % IBW (inadequate) [11]. BMI was examined as a continuous variable and as a dichotomous variable with a BMI of 20 as a cutoff for inadequate status [12].

Odds ratios (OR) and 95 % confidence intervals (CI) were estimated using unconditional logistic regression for the main effect of pretreatment weight status on loco-regional progression. Potential confounders that met the inclusion level of $p=0.10$ were examined for inclusion in the multivariate model. The final model included age of the patient, pretreatment hemoglobin level, radiation therapy duration in days, and stage. All statistical tests were two-sided and a p value of <0.05 was considered statistically significant.

Results

At RPCI, 140 patients with SCCHN were definitely treated with CCRT from 2004 to 2010. There were 78 patients in cohort 1 (treated between 2004 and 2007) and 62 patients in

cohort 2 (treated between October 2007 and 2010). Table 1 provides descriptive statistics for the cohorts combined and for comparisons between cohorts 1 and 2. The median age of the combined cohorts was 59.50 years with a median follow-up for those still alive ($n=104$) of 35 months. The majority of tumors were oropharyngeal tumors, 49% had a primary tumor staged at 3 or 4 and 66% had nodal positive disease. Eighteen of the 140 patients (13 %) experienced loco-regional progression. These included nine primary site failures, four regional neck failures, and five failures in both the primary site and regional lymph nodes. Out of the 18 patients with loco-regional progression, 4 were recurrent disease and 13 were persistent disease.

Approximately 14 % of the cohort was at an inadequate pretreatment weight status based on IBW calculation (<90 % IBW) and 8.6 % were at inadequate weight status based on BMI calculation (<20). Median pretreatment IBW% and BMI were 116 % (72–193) and 26.53 (16.58–45.10), respectively.

Characteristics that were statistically significantly different between cohorts 1 and 2 were follow-up time, median duration of radiation therapy, and loco-regional progression ($p<0.01$). Follow-up time for cohort 2 was a median of 26 months in comparison to 54 months for cohort 1. All cases of loco-regional progression were known or suspected by imaging within 12 months of completion of treatment in our institutional experience (data not shown).

Efforts made to decrease radiation therapy duration time resulted in a decrease in radiation duration by 5 days for cohort 2 with an accompanied decreased incidence of loco-regional progression from 15 cases in cohort 1 to 3 cases in cohort 2. Efforts to prevent treatment interruption did not result in a statistically significant difference between cohorts for median weight loss during treatment period.

Significant differences for the cohorts combined based on loco-regional progression include duration of radiotherapy ($p<0.01$) and pretreatment hemoglobin ($p<0.02$) and are shown in Table 2. The median duration of therapy in days for those without progression versus those with progression was 50 and 53 days, respectively. The median value of pretreatment hemoglobin for those without progression was 13.9 g/dl (8.60–19.40) and was 12.45 g/dl (9.50–15.50) for those with progression. Primary tumor stage, nodal stage, and disease site were not significantly different for those with progression and those without.

An examination of pretreatment weight status and changes in weight during treatment for the combined cohorts based on loco-regional progression resulted in a statistically significant difference for pretreatment IBW% as both a continuous and a categorical variable (Table 3). Median pretreatment IBW% was 118 (72–193) for the progression-free group and was 101.5 (73–163) for the group with loco-regional progression. This was a statistical difference of $p=0.02$. When distributed categorically by adequate (≥ 90 % IBW) and inadequate status (<90 % IBW), the difference between progression groups remained statistically significant ($p<0.02$). Pretreatment weight status defined by BMI did not show significant differences although those with progression had a pretreatment BMI that was lower than those without progression (24.70 and 26.78, respectively). Median weight loss

during RT was not statistically significant between groups. Both groups suffered weight loss that is clinically severe at a level of approximately 9 % in 7 weeks.

A multivariate logistic regression model was developed to examine pretreatment weight status as an independent predictor of loco-regional progression. The weight status variable used for the exposure was categorized IBW% (≥ 90 % IBW vs. <90 % IBW) since differences by BMI were not statistically significant based on loco-regional progression. The developed model included the following confounders: radiation therapy duration, pretreatment hemoglobin, and age. An additional model including tumor stage was evaluated since the significance level of primary tumor stage was $p=0.11$ on univariate analysis and the cutoff for confounders to include was set at $p=0.10$. The final model therefore included age, pretreatment hemoglobin, duration of radiation therapy, and tumor stage.

The crude and adjusted estimates for the multivariate logistic regression models developed are shown in Table 4. Compared to patients with adequate weight status (≥ 90 % IBW), patients with inadequate status (<90 % IBW) had an almost fourfold increase in the odds for loco-regional progression in the crude model (OR=3.86, CI=1.25–11.91; $p=0.02$). In the adjusted model, this increase in odds was reduced to 2.08 (CI=0.55–7.91) and was further attenuated to 1.89 (CI=0.49–7.25) in the model including primary tumor stage. The adjusted odds ratios were not statistically significant.

Discussion

In this updated and expanded cohort of patients treated with CCRT for SCCHN, inadequate pretreatment weight status as defined by IBW% was not an independent predictor of loco-regional progression. Patients in both cohorts did suffer severe weight loss during treatment. Substantial weight loss related to treatment has been reported elsewhere [13–16]. Weight loss that is ≥ 20 % has been correlated with not only treatment interruptions, infection, and hospital readmissions but also with early mortality [9, 17–19]. Additionally, weight loss has been associated with deterioration of quality of life (QOL) scores both during treatment and up to 3 years following treatment [19–22].

Pretreatment weight status based on IBW or BMI

Inadequate nutritional status decreases treatment response and increases treatment complications and toxicities resulting in poor cancer prognosis [23]. In this analysis, pretreatment IBW% along with treatment duration and pretreatment hemoglobin was associated with progression and thus poor prognosis. Classification of pretreatment weight status by BMI did not. IBW describes an adequate weight for a given height and gender and is a valid measure to consider along with other measures when classifying nutritional status as being severely malnourished to morbidly obese [24]. BMI provides similar information, with values less than 18.5 kg/m^2 , typically interpreted as malnourished. There is concern that this cutoff for BMI is too low and may not capture all who are malnourished. A cutoff point of less than 20.0 kg/m^2 has been suggested [12] and was used in this analysis. In a recent report of the effect of BMI on outcomes of head and neck patients treated with chemoradiation, patients with a BMI of 25 or less had a statistically significantly increased hazard ratio for recurrence (HR=4.4, CI=1.2–15.9, $p=0.026$) and shorter overall survival

($p=0.043$) [8]. In a post hoc analysis using 25 or less as a BMI cutoff for inadequate status, we found no difference with our initial results (data not shown). We did not have wrist circumference measurements for the patients in our study and therefore we were not able to adjust IBW for frame size. It is possible that this accounts for the different results between IBW% and BMI.

Value of validated nutrition screening and assessment

Identification of poor nutritional status by means of IBW% is a crude, non-validated method. Factors other than body weight are important when screening for poor nutritional status and more than one factor should be considered [25, 26]. Screening and assessment tools, such as the patient-generated subjective global assessment, have been validated for use with cancer patients in the clinic setting [27–29]. A major limitation of our retrospective review is the use of body weight, with no ability to adjust for frame size, as our only means of determining nutritional status.

Weight loss during treatment: can it be minimized and does it matter?

Patients in cohort 2 received interventions to prevent treatment interruption resulting in a median decrease in treatment duration of 5 days [30]. As a consequence, these patients may have sustained increased acute effects of treatment, but no significant difference on total weight loss during treatment was observed between the cohorts. In fact, despite the use of prophylactic PEG tubes and enteral nutrition support initiated at the beginning of treatment, both cohorts lost approximately 9% of their bodyweight during treatment. Based on published criteria, this percentage of weight loss in a short period of time is classified as clinically severe weight loss [31, 32]. Since neither cohort was provided regular nutrition assessment, counseling, and follow-up by a nutrition professional, some of the weight loss sustained may be a consequence of inefficient use of tubes and/or compliance issues.

There is evidence that despite dietary intervention, weight will be lost during treatment as a result of dysphagia, xerostomia, radiation-induced mucositis, and other CCRT-related toxicities. It should be noted that radiation dose to the pharyngeal constrictors through analysis of dose volume histograms is also being used by some investigators to identify patients who are at high risk of dysphagia [33, 34]. It is generally accepted that less radiation dose to normal tissues including the pharyngeal constrictors is preferred. Newer techniques such as IMRT and VMAT make this normal tissue sparing more feasible. However, even with these techniques in experienced hands, tumor size and location often prevent aggressive sparing of the normal tissues.

Nutrition counseling and support, however, can minimize the amount of weight lost [35, 36]. Recently, a prospective non-randomized study compared the effect of intensive nutritional intervention on weight loss, daily setup variations, and planning target volume margins among head and neck cancer patients undergoing radiation therapy [37]. Nutrition intervention included enteral nutrition support via PEG tube and weekly nutrition assessment by a dietitian. Criteria for PEG tube included the following: pre-existing dysphagia, inadequate oral intake resulting in a 10 % weight loss, CCRT, and bilateral neck irradiation. Patients in the intensive nutritional support group lost statistically significantly

less weight ($p=0.04$) and had decreased setup variation in the superior–inferior and anterior–posterior planes. The authors concluded that intensive nutritional intervention for patients at risk for weight loss during radiation therapy promotes weight stability throughout treatment and is associated with reduced setup variation [37].

It must be noted that in the current analysis, human papillomavirus (HPV) status was not available on most tumors and this is a potential confounding factor. Patients with HPV-associated tumors demonstrate improved long-term survival [38, 39] and other better clinical outcomes including less weight loss [40] than patients with HPV-negative tumors.

The importance of quality of life

Survival for the head and neck cancer patient continues to improve making QOL increasingly important. Through the application of validated tools such as the European Organization for Research and Treatment of Cancer Questionnaire (EORTCQLQ-Cx30 version 3), patient quality of life has been measured at baseline, through treatment and up to 3 years following radiation treatment. Analysis of QOL includes examination of therapeutic symptom scores as well as functional status of the patient, perception of health and disease, and psychosocial well-being. QOL may impact nutritional status and/or be influenced by malnutrition [41, 42]. Unintentional weight loss, malnutrition, and dysphagia can impair QOL beginning at diagnosis and affect physical and social functions for at least 3 years following treatment of head and neck cancer [19–22]. Nutrition intervention has been shown to improve QOL scores in these patients [43].

Next steps: nutrition protocols for radiation medicine clinics

Despite the lack of high-quality evidence to support intensive dietary counseling and/or nutrition support for head and neck cancer patients undergoing multimodal radiation therapy, there is clearly a role for nutrition intervention provided by trained nutrition professionals within the setting of multidisciplinary care. New foci for investigation rightly include the establishment of prognostic indicators and development of predictive models for the identification of patients who will benefit most from integrated nutrition therapy. Along with pretreatment weight status, other indicators identified include tumor location and stage, expectation of high grade mucositis, 60 Gy total radiation dose, radiotherapy field comprising swallowing structures, pretreatment diet consistency, and multimodal therapy [13, 18, 36, 44, 45]. Wermker et al. developed two prediction models with a prognostic accuracy of 90 % [46]. Kiss et al. recently reported on a dietitian-led clinic for head and neck cancer patients undergoing (chemo)radiotherapy [47]. Outcomes included increased first contact for high-risk patients, significantly decreased nutrition-related hospital admissions, improved transition back to oral diets, and reduced unplanned insertions for tube feeding. Overall, patient acceptance was high, quality of care was improved, and a substantial cost savings was realized [47].

Conclusion

Inadequate nutritional status of head and neck cancer patients undergoing CCRT has been associated with poor clinical outcome and decreased quality of life. Inadequate pretreatment

weight status, a crude proxy for poor nutritional status, might be considered a prognostic indicator among less controlled patient cohorts who have longer treatment duration than the patient cohort included in this analysis. Moving forward, accurate assessment of nutritional status and of quality of life through the application of validated tools is required. Additionally, there is a pressing need to integrate routine, evidence-based nutritional intervention into care plans. Based on the information that we have gained from prognostic indicators and prediction models, best next steps may include the development and testing of nutrition care protocols, with goals of minimizing weight loss and improving patient quality of life, in multicenter longitudinal studies.

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Table 1

Descriptive characteristics of cohort 1 (original) and cohort 2 (new)

Characteristics	Combined cohorts	Individual cohorts		<i>p</i> value ^a
	Cohorts 1 and 2 (<i>n</i> =140) no (%) median	1 (<i>n</i> =78) no (%) median	2 (<i>n</i> =62) no (%) median	
Median age in years at diagnosis (range in years)	59.50 (37–82)	62 (37–81)	59 (38–82)	0.15
Follow-up time in months (range in months)	35 (1–85)	54 (1–85)	26 (5–54)	<0.01
Gender, male/female	107 (76)/33 (24)	56 (72)/22 (28)	51 (82)/11 (18)	0.15
Lymph node stage treated (<i>n</i> =129)				
N0/N+	37 (29)/92 (71)	25 (32)/53 (68)	12(24)/39(76)	0.30
Primary tumor stage (<i>n</i> =135)				
1 or 2 / 3 or 4	69 (51)/66 (49)	38 (49)/40 (51)	31(54)/26(46)	0.52
Disease site condensed (<i>n</i> =134)				
Oral cavity	4 (3)	4 (5)	0 (0)	
Oropharynx	79 (59)	42 (54)	37 (66)	
Hypopharynx	9 (7)	4 (5)	5 (9)	
Larynx	42 (31)	28 (36)	14 (25)	0.13
Median RT duration in days	50 (38–83)	51 (39–83)	46 (38–67)	<0.01
Median pretreatment Hgb (g/dl) (range)	13.80 (8.60–19.40)	13.50 (9–17.10)	14 (8.60–19.40)	0.17
Median pretreatment weight (kg) (range)	80.05 (42.60–141)	79.75 (46.80–141)	81.75 (42.60–125.50)	0.39
Median pretreatment IBW % (range)	116 (72–193)	113.5 (73–193)	120 (72–190)	0.24
Pretreatment weight status by IBW%				
<90 % IBW	20 (14)	14 (18)	6 (10)	
90 % IBW	120 (86)	64 (82)	56 (90)	0.23
Median pretreatment BMI (range)	26.53 (16.58–45.10)	25.89 (16.58–45.10)	27.37 (16.90–41.55)	0.24
Pretreatment weight status by BMI				
20 BMI	12 (8.6)	8 (10.3)	4 (6.5)	
>20 BMI	128 (91.4)	70 (89.7)	58 (93.5)	0.43
Median weight loss during RT (kg) (range)	6.90 (–5–26)	6.50 (–5–26)	7 (–2.90–20.10)	0.86
Median weight loss % during RT (range)	8.56 (–5.95–24.07)	9.08 (–5.95–24.07)	8.30 (–5.58–20.30)	0.35
Loco-regional progression: no/yes	122 (87)/18 (13)	63 (81)/15 (19)	59 (95)/3 (5)	0.01

RT radiation therapy, *Hgb* hemoglobin, *g/dl* grams per deciliter, *kg* kilogram, *IBW* ideal body weight

^a *p* value is for comparison between cohort 1 and 2; Chi square (two-tailed) was used to examine differences for categorical variables and Mann–Whitney *U* (two-tailed) was used to examine differences for continuous variables; statistical analysis compares cohort 1 to cohort 1

Table 2

Characteristics by loco-regional progression for cohorts 1 and 2 combined

Characteristics	Subjects		<i>p</i> value ^a
	Loco-regional progression		
	No (<i>n</i> =122) no (%) or median	Yes (<i>n</i> =18) no (%) or median	
Median age in years at diagnosis (range)	59 (37–82)	63 (47–81)	0.17
Gender, male/female	92 (75)/30 (25)	3 (17)/15 (83)	0.46
Lymph node stage treated (<i>n</i> =129)			
N0/N+	30 (27)/81 (73)	7 (39)/11 (61)	0.30
Primary tumor stage (<i>n</i> =135)			
1 or 2 / 3 or 4	63 (54)/54 (46)	6 (33)/12 (67)	0.11
Disease site condensed (<i>n</i> =134)			
Oral cavity	3 (3)	1 (6)	
Oropharynx	72 (61)	7 (41)	
Hypopharynx	8 (7)	1 (6)	
Larynx	34 (29)	8 (47)	0.37
Median RT duration in days (range)	50 (38–79)	53 (49–83)	<0.01
Median pretreatment Hgb (g/dl) (range)	13.9 (8.60–19.40)	12.45 (9.50–15.50)	0.02

RT radiation therapy, *Hgb* hemoglobin, *g/dl* grams per deciliter

^a Fisher exact test or Chi square (two-tailed) was used to examine differences for categorical variables and Mann–Whitney *U* (two-tailed) was used to examine differences for continuous variables

Table 3

Weight status of cohorts 1 and 2 combined by loco-regional progression

Characteristics	Subjects		<i>p</i> value ^a
	Loco-regional progression		
	No (<i>n</i> =122) no (%) or median	Yes (<i>n</i> =18) no (%) or median	
Median pretreatment weight (kg) (range)	80.55 (42.60–140.50)	74.50 (46.80–141)	0.26
Median pretreatment IBW % (range)	118 (72–193)	101.5 (73–163)	0.02
Pretreatment weight status			
<90 % IBW	14 (11)	6 (33)	
90 % IBW	108 (89)	12 (67)	0.02
Median pretreatment BMI (range)	26.78 (16.90–45.10)	24.70 (16.58–41.65)	0.10
Pretreatment weight status by BMI			
20 BMI	9 (7.4)	3 (16.7)	
>20 BMI	113 (92.6)	15 (83.3)	0.19
Median weight loss during RT (kg) (range)	7 (–3.7–26)	5.5 (–5–18.3)	0.48
Median weight loss % during RT (range)	8.67 (–5.78–24.07)	8.23 (–5.95–22.5)	0.96

kg kilograms, *IBW* ideal body weight

^aFisher exact test or Chi square (two-tailed) was used to examine differences for categorical variables and Mann–Whitney *U* (two-tailed) was used to examine differences for continuous variables

Table 4

Risk of loco-regional progression estimated by pretreatment IBW status

Exposure	Loco-regional progression no/yes	Crude OR (95 % CI)	Adjusted OR (95 % CI) ^a	Adjusted OR (95 % CI) ^b
Pretreatment IBW status				
90 % IBW (reference)	108/12	1.00	1.00	1.00
<90 % IBW	14/6	3.86 (1.25–11.91), <i>p</i> =0.02	2.08 (0.55–7.91), <i>p</i> =0.28	1.89 (0.49–7.25), <i>p</i> =0.36

OR odds ratio, *CI* confidence interval, *IBW* ideal body weight^aOR was adjusted by age, pretreatment hemoglobin, and radiation therapy duration (days)^bOR was adjusted by age, pretreatment hemoglobin, radiation therapy duration (days), and stage of disease