Impact of weight loss on treatment interruption and unplanned hospital admission in head and neck cancer patients undergoing curative (chemo)-radiotherapy in Hong Kong

Ying-Chu Choi[1] · Po-Chung Chan[2] · Ka-Wai Alice Cheung[2] · Jia-Jie Huang[3] · Kwok-Leung Aray Wong[2] · Johannes Doescher[4] · Tai-Chung Lam[5]

Abstract

Purpose Malnutrition is highly prevalent in head and neck cancer (HNC) patients, with weight loss being one of the major nutritional indicators. The objective of this study was to investigate the impact of weight loss on treatment interruptions and unplanned hospital admissions in HNC patients undergoing radiotherapy (RT) with or without chemotherapy.

Methods In this retrospective cohort study, consecutive HNC patients who started RT between January 2011 and December 2019 were included. Data from a total of 1086 subjects with 747 (68.8%) nasopharyngeal carcinomas (NPCs) and 31.2% (N=339) non-NPC patients were analysed. Body weight (BW) was measured before, during, and after RT treatment. Factors associated with ≥10% weight loss, treatment interruption, and unplanned admissions were analysed using multivariate logistic regression.

Results The prevalence of ≥10% weight loss was 26.8% (N=288), with 32.7% (N=243) in NPC and 13.5% (N=45) in non-NPC patients. The prevalence of RT delay in patients with ≥10% vs. <10% weight loss was 6.2% vs. 7.0% (p=0.668) in NPC patients and 42.2% vs. 50.5% (p=0.300) in non-NPC patients. The prevalence of unplanned admissions in patients with ≥10% vs. <10% weight loss was 51.9% vs. 25.3% (p<0.001) in NPC patients and 68.9% vs. 27.0% (p<0.001) in non-NPC patients.

Conclusion In our study, ≥10% weight loss was found to be associated with a higher rate of unplanned admissions but not with RT delay or chemotherapy interruption. Clinical implications: With the knowledge of the impact of weight loss on hospital admissions and the characteristics of patients with weight loss, nutritional intervention can be effectively focused on the stratification of patients for intensive nutritional support to reduce weight loss.

Keywords Head and neck cancer · Weight loss · Treatment interruption · Unplanned hospital admission · Nutrition · NPC · Non-NPC

Introduction

Head and neck cancers (HNCs) represent the sixth most common cancer category worldwide, with 93,193 new cases and 418,982 deaths in 2020 [1]. HNC treatment includes a single modality of surgery or radiotherapy (RT) alone with a disease eradication and organ preservation approach and, for locally advanced disease, multimodality treatment with a combination of surgery and RT with or without chemotherapy [2–4]. Patients who receive radical RT frequently experience difficulties in eating and drinking, leading to inadequate fluid and nutrition intake and consequently resulting in malnutrition and weight loss. Weight loss >5% has been defined as critical weight loss and was found to be a major prognostic factor for inferior treatment outcomes and

✉ Ying-Chu Choi
choipenny628@gmail.com

1 Department of Dietetics, Tuen Mun Hospital, Hong Kong, China

2 Department of Clinical Oncology, Tuen Mun Hospital, Hong Kong, China

3 Quality and Services Department, Tuen Mun Hospital, Hong Kong, China

4 Department of Otolaryngology, Augsburg University Hospital, Augsburg, Germany

5 Department of Clinical Oncology, University of Hong Kong, Hong Kong, China

poor survival in HNC patients [5–11]. Studies have shown that the prevalence of >5% weight loss ranges from 14 to 32% before and 32 to 54% after HNC treatment [11–14]. Critical weight loss was also found to be associated with adverse outcomes, including increased treatment toxicities and decreased treatment response [15, 16], increased enteral feeding dependence [17], unplanned hospital admissions [18], and worse survival outcomes [19].

Studies have demonstrated that treatment interruptions detrimentally impact treatment outcomes, including increased loco-region failure, increased relapse rate, and poor survival [12, 20–22]. Meng et al. showed that weight loss was correlated with treatment interruption in locally advanced nasopharyngeal carcinoma (NPC) patients [23].

In cancer care, unplanned hospital admissions during and after treatment are common, particularly in HNC patients [24]. Unplanned hospital admissions impose a heavy economic burden on the health care system and negatively impact patients' quality of life. The impact of nutritional support on reducing unplanned hospital admissions in HNC patients has been reported in several studies [25–28]. High weight loss during RT was associated with increased hospital admission [9]. Therefore, knowledge of the prevalence of weight loss and its association with treatment interruption and unplanned hospital admissions should be evaluated for HNC patients undergoing (chemo)RT. This knowledge is necessary for developing strategies to improve the treatment outcomes of HNC patients.

Materials and methods

Study subjects

This retrospective cohort study included consecutive newly diagnosed adult HNC patients who were started on curative-intent RT with or without chemotherapy during the period of 1 January 2011 to 31 December 2019. These HNC patients were referred to the dietitian for nutrition support under the blanket referral policy in our centre. Patients with metastatic disease, double primary, cancer recurrence or progressive disease, cancer of unknown primary, cancer of the ear, thyroid cancer, and lymphoma; patients who did not complete the planned treatment; and patients who died during treatment were excluded. Approval was obtained from the ethics committee of New Territories West Cluster Hospital Cluster Research Ethics Committee/Institutional Review Board of Hospital Authority in Hong Kong. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Data collection

Data were collected retrospectively. Demographic data, including age, sex, social history, smoking, and drinking habits, were collected from dietetic records. Clinical characteristics and treatment outcomes, including diagnosis, staging, treatment modality, chemotherapy and RT regimen, and hospital admissions, were collected from electronic medical records. Nutrition data, including BW, height, number of dietitian outpatient consultations, and feeding tube placement, were obtained from dietetic and oncology records. In our centre, feeding tube placement was mainly proactive in our non-NPC patients as most of these patients already had their feeding tube placed at diagnosis or after surgery, and reactive in our NPC patients. Feeding tube placement was defined as patient once had a feeding tube placed during their treatment regardless of whether it was used for supplementing oral feeding or solely tube feeding. In addition, a new nutrition program was implemented in 2013 where all HNC patients received intensive nutrition support with weekly or bi-weekly dietitian contact before and during treatment.

Outcome variables

The primary outcomes were weight loss <10% and ≥10% at the end of RT treatment, RT delay for more than 2 days of the prescribed schedule, and unplanned hospital admissions from the beginning of concomitant chemoRT or RT until 1 month after the end of RT.

BW in kilograms (kg) and height in metres (m) were routinely measured and recorded in our oncology and dietetic clinics before, during, and after treatment. Weight loss was defined and calculated as the difference between the weight before treatment and the weight at the end of treatment. The calculation is given as follows:

Percentage weight loss at the end of RT treatment = [(BW at the end of RT treatment − BW at the beginning of treatment) ÷ BW at the beginning of treatment × 100]

Weight loss ≥10% at the end of RT treatment was chosen as the cut-off of high weight loss according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5 [29]. Weight loss 5–10% during treatment was also included as a variable as in our clinical practice it was considered as moderate weight loss and in our experience patients with early weight loss was commonly prone to high weight loss as the treatment progressed. Body mass index (BMI) was calculated as BMI = BW (kg)/Height (m)^2. BMI cut-offs were categorized as underweight when BMI was < 18.5 kg/m^2, normal weight when BMI was between 18.5 and 24.9 kg/m^2, and obese when BMI was ≥ 25 kg/m^2 [30]. The mean imputation method was used for missing BW data to provide consistent data. The time points for BW data were pretreatment, weekly during RT, and at the end of RT treatment. BW and BMI were recorded to the nearest 0.1 kg/m^2.

Treatment interruption: RT delay

Patients were treated with radical RT using volumetric modulated arc therapy (VMAT) with or without chemotherapy. The total dose ranged from 50 to 74 Gy and consisted of 5–6 fractions per week of 2–2.5 Gy per fraction administered to the primary tumour and, if needed, to neck nodes either bilaterally or unilaterally. RT treatment duration was the time from the first day to the last day of RT. RT delay was defined as delay for more than 2 days of the originally planned treatment time according to the guidelines from the Royal College of Radiologists [31].

Unplanned hospital admissions

Unplanned hospital admissions were defined as any unplanned hospital admission requiring inpatient care for more than 24 h, from the beginning of concomitant chemoRT until 1 month after the end of RT treatment. Reasons for admission were categorized as nutrition-related and nonnutrition-related. Nutrition-related admissions included rehydration, poor oral intake, dysphagia, insertion of feeding tube, feeding tube-related causes, and management of eating- or nutrition-related symptoms. In our centre, feeding tube placement was reactive for NPC patients and mostly prophylactic for non-NPC patients, as non-NPC patients often had feeding tubes placed during surgery or at the time of diagnosis and kept until completion of RT treatment.

Statistical methodology

Categorical variables were compared using the chi-square test. Univariate logistic regression was performed to test the association between each independent variable and adverse outcomes, including treatment interruption and unplanned hospital admissions. Independent variables included RT delay, chemotherapy as planned, and unplanned hospital admissions. Variables with a significant association shown in univariate analysis were entered into multivariate analysis logistic regression. A p value of <0.05 was considered to indicate statistical significance. Statistical Package for the Social Sciences (SPSS) software version 27 was used for the statistical analysis.

Results

Patient characteristics

A total of 1086 patients were included, with 747 (68.8%) NPC and 339 (31.2%) non-NPC patients. There were five missing data where BW was not available in our NPC patients for unknown reason. The demographics and characteristics of the patients are shown in Table 1. Locally advanced stage III and IV diseases comprised 67.3% of the cohort. The mean ages of the NPC and non-NPC patients were 54.2 and 61.9 years, respectively (p<0.001). There were significantly more young patients <45 years in the NPC group than in the non-NPC group (20.6% vs. 6.8%, p<0.001). More NPC than non-NPC patients received a combined modality of chemoRT (69.6% and 36.9%, p<0.001), with an RT dose ≥65 Gy (98.3% and 65.8%, p<0.001), and underwent a cisplatin regimen (63.7% and 30.4%, p<0.001). Given significant differences in the characteristics of NPC and non-NPC patients, subgroup analysis was conducted.

Prevalence of weight loss and predictive factors

A total of 288 patients (26.8%) had ≥10% weight loss at the end of RT. The prevalence of ≥10% weight loss increased from 2.8% before treatment to 32.7% after treatment in NPC patients and from 6.2% pretreatment to 13.5% after treatment in non-NPC patients (Table 2). In the NPC group, patients with ≥10% weight loss, when compared with <10% weight loss, had a significantly higher proportion of men (80.2% vs. 71.3%, p=0.009), patients at a younger age <45 years old (26.3% vs. 17.8%, p=0.018), patients who lived alone (12.0% vs. 7.0%, p=0.023), patients with stage III–IV disease (75.7% vs. 62.5%, p<0.001), N+ (95.8% vs. 88.4%, p<0.001), chemoRT (87.2% vs. 60.7%, p<0.001), and cisplatin regimen (43.1% vs. 20.5%, p=0.004). In non-NPC, patients with ≥10% weight loss contained a significantly higher proportion of men (88.9% vs. 73.4%, p=0.024), patients at an age of ≥75 years (2.2% vs. 11.8%, p=0.018), with stage III–IV disease (86.4% vs. 65.2% p=0.005), N+ (83.7% vs. 43.6%, p<0.001), chemoRT (86.7% vs. 29.1%, p<0.001), RT >65 Gy (97.8%, vs. 61.6% p<0.001), and patients with no surgery (80.0% vs. 45.0%, p<0.001).

In NPC patients, multivariate logistic regression analysis yielded factors that were significantly associated with ≥10% weight loss at the end of RT: age, living alone, use of cisplatin regimen, tube feeding, unplanned admissions, pretreatment BMI, and >5% weight loss at week 2 (Table 3). In non-NPC patients, multivariate logistic

Table 1 Demographic and patient characteristics of HNC patients undergoing RT with or without chemotherapy from 2011 to 2019 in Tune Mun Hospital

	Total		NPC		Non-NPC		*p* value
	N	%	*N*	%	*N*	%	
N	1086	100.0%	747	68.8%	339	31.2%	
Age (mean, SD)	56.6	12.1	54.2	11.9	61.9	10.8	0.000
Age (*N*, %)							
<45 years	177	16.3%	154	20.6%	23	6.8%	0.000
45–64 years	644	59.3%	464	62.1%	180	53.1%	
65–74 years	194	17.9%	94	12.6%	100	29.5%	
≥75 years	71	6.5%	35	4.7%	36	10.6%	
Smoking							
Smoker or ex-smoker	532	50.2%	323	44.6%	204	60.9%	0.000
Non-smoker	527	49.8%	401	55.4%	131	39.1%	
Alcohol consumption							
Drinker or ex-drinker	643	61.1%	235	32.7%	174	52.1%	0.000
Non-drinker	409	38.9%	483	67.3%	160	47.9%	
Living situation							
Live with family	958	88.6%	672	91.4%	286	86.9%	0.024
Live alone	106	9.8%	63	8.6%	43	13.1%	
Tumour site							
NPC	747	68.8%	747	100.0%			
Oropharynx	64	5.9%			64	18.9%	
Hypopharynx	31	2.9%			31	9.1%	
Larynx	99	9.1%			99	29.2%	
Oral cavity	90	8.3%			90	26.5%	
Sinus	9	0.8%			9	2.7%	
Salivary gland	37	3.4%			37	10.9%	
Nasal cavity	9	0.8%			9	2.7%	
Stage of disease							
Stage I–II	346	32.7%	247	33.1%	99	31.7%	0.673
Stage III–IV	713	67.3%	500	66.9%	213	68.3%	
T classification							
T1–2	526	49.9%	373	49.9%	153	49.7%	0.093
T3–4	529	50.1%	374	50.1%	155	50.3%	
N classification							
N0	281	26.7%	127	17.0%	154	50.2%	0.000
N+	773	73.3%	620	83.0%	153	49.8%	
Treatment modality							
RT alone	441	40.6%	227	30.4%	214	63.1%	0.000
ChemoRT	645	59.4%	520	69.6%	125	36.9%	
RT dose							
<65 Gy	129	11.9%	13	1.7%	116	34.2%	0.000
≥65 Gy	957	88.1%	734	98.3%	223	65.8%	
Induction chemotherapy							
No	861	79.3%	541	72.4%	320	94.4%	0.000
Yes	225	20.7%	206	27.6%	19	5.6%	
Chemotherapy regimen							
No cisplatin	66	10.2%	44	8.5%	22	17.6%	0.002
Cisplatin	579	89.8%	476	91.5%	103	82.4%	
Pretreatment BMI (mean, SD)	23.9	4.0	24.2	4.0	23.3	4.1	0.003
Pretreatment BMI							
<18.5 kg/m^2	67	6.2%	33	4.4%	34	10.0%	0.001

Table 1 (continued)

	Total		NPC		Non-NPC		p value
	N	%	N	%	N	%	
18.5–24.9 kg/m^2	628	57.9%	431	57.8%	197	58.1%	
≥25 kg/m^2	390	35.9%	282	37.8%	108	31.9%	

regression analysis demonstrated that factors significantly associated with ≥10% weight loss were RT dose ≥65 Gy, chemoRT, unplanned admissions, and weight loss >5% at week 2. In both NPC and non-NPC patients, weight loss >5% in week 2 of treatment was the strongest predictor of ≥10% weight loss at the end of treatment (OR 10.8, 95% CI 5.05–23.1 in NPC and OR 9.7, 95% CI 2.5–38.3 in non-NPC).

Weight loss and unplanned admissions

The prevalence of unplanned admissions in patients with ≥10% vs. <10% weight loss was 51.9% vs. 25.3% (p<0.001) in NPC patients and 68.9% vs. 27.0% (p<0.001) in non-NPC patients, respectively (Fig. 1, Appendix, Table 6). In both the NPC and non-NPC groups, unplanned admission was significantly higher in patients with ≥10% weight loss. A univariate analysis was conducted to assess the association between weight loss and unplanned admission.

In the NPC group, a significantly higher rate of unplanned admissions was observed in the following patients: those with stage III–IV disease, those who received induction chemotherapy, those on a cisplatin regimen, those with chemotherapy not given as planned, those who received a cisplatin dose of <200 mg/m^2, those with feeding tube placement, and those with weight loss of 5–10% at week 2. In the non-NPC group, there was a significantly higher prevalence of unplanned admissions in the following patients: those with stage III–IV disease, those with chemotherapy added, those with chemotherapy not given as planned, those with tube feeding, those with ≥2 dietitian consultations, and those with no surgery (Table 4).

These statistically significant factors in univariate analysis were entered into a multivariate analysis (Table 5). In NPC patients, multivariate logistic regression analysis showed that factors significantly associated with unplanned admissions were stage III–IV disease (OR 1.73, 95% CI 1.0–3.0, p=0.049), chemotherapy as planned (OR 0.61, 95% CI 0.39–0.97, p=0.036), feeding tube placement (OR 30.35, 95% CI 7.15–128.72, p<0.001), and ≥10% weight loss at the end of RT (OR 1.9, 95% CI 1.24–2.89, p=0.003). In non-NPC patients, multivariate logistic regression analysis showed that factors significantly associated with unplanned admissions were treatment modality of chemoRT (OR 6.34, 95% CI 3.04–13.22, p<0.001), chemotherapy as planned (OR 0.34, 95% CI 0.13–0.89, p=0.034), feeding tube placement (OR 11.42, 95% CI 5.21–25.01, p<0.001), and weight loss >5% at week 2 (OR 2.67, 95% CI 1.09–6.55, p=0.032). In both NPC and non-NPC patients, feeding tube placement was the strongest independent predictor of unplanned hospital admissions.

Discussion

Our study aimed to investigate the association of weight loss and treatment interruptions, including RT delay, chemotherapy given as planned, cisplatin dose of ≥200 mg/m^2, and unplanned hospital admissions. Our study found that patients with weight loss of ≥10% had a significantly higher rate of unplanned hospital admissions but had no significant association with treatment interruptions.

Weight loss and treatment interruption (RT delay)

In our study, the prevalence of RT delay was 20.2% (N=219) for the whole cohort. The prevalence of RT delay ranged from 11.8 to 67% in previous studies [21, 32, 33]. This variation among studies might be related to the different definitions of RT delay and different disease entities included in various studies. In the subgroup analysis, we found that NPC patients had a significantly lower prevalence of RT delay than non-NPC patients (6.8% vs. 49.6%, p=0.05). This could likely be explained by the practice of RT schedule compensation for our NPC patients. In our centre, the RT schedule and progress of HNC patients were closely monitored. However, due to historical and logistical reasons, the facility was only able to accommodate special arrangements for NPC patients to catch up on any delays. It was not until 2019 that compensatory measures could also be arranged for non-NPC HNC patients.

Our study showed no significant association between weight loss and RT delay in either NPC or non-NPC patients. Previous studies investigating the association of weight loss and RT delay yielded conflicting results. Lindberg et al. reported that patients with HNC primary sites had the highest rate of RT interruptions among all cancer sites [34]. Likewise, patients with greater weight loss had significantly more RT interruptions and lower RT completion rates, as observed by another research group [35]. Studies have shown that weight loss with a change in body contour was one of the independent predictors for replanning

Table 2 Prevalence and characteristics of patient with weight loss

	NPC					Non-NPC				
	<10%		≥10%		*p* value	<10%		≥10%		*p* value
	N	%	*N*	%		*N*	%	*N*	%	
N	499	67.3%	243	32.7%		289	86.5%	45	13.5%	
% weight loss at week 7 (mean, SD)	−5.4	3.1	−13.1	2.8	0.000	−3.0	3.9	−12.9	2.4	0.000
Sex										
Male	356	71.3%	195	80.2%	0.009	212	73.4%	40	88.9%	0.024
Female	143	28.7%	48	19.8%		77	26.6%	5	11.1%	
Age										
<45 years	89	17.8%	64	26.3%	0.018	22	7.6%	1	2.2%	0.018
45–64 years	313	62.7%	147	60.5%		144	49.8%	33	73.3%	
65–74 years	69	13.8%	25	10.3%		89	30.8%	10	22.2%	
≥75 years	28	5.6%	7	2.9%		34	11.8%	1	2.2%	
Smoking										
Smoker	205	42.4%	115	48.7%	0.111	172	59.9%	27	62.8%	0.721
Nonsmoker	278	57.6%	121	51.3%		115	40.1%	16	37.2%	
Alcohol consumption										
Drinker	147	30.7%	86	36.8%	0.105	144	50.2%	26	61.9%	0.155
Non- or ex-drinker	332	69.3%	148	63.2%		143	49.8%	16	38.1%	
Living situation										
With family	454	93.0%	213	88.0%	0.023	243	87.1%	41	91.1%	0.447
Alone	34	7.0%	29	12.0%		36	12.9%	4	8.9%	
Stage of disease										
Stage I–II	187	37.5%	59	24.3%	0.000	92	34.8%	6	13.6%	0.005
Stage III–IV	312	62.5%	184	75.7%		172	65.2%	38	86.4%	
T classification										
T1–2	264	52.9%	108	44.4%	0.031	131	50.4%	21	48.8%	0.851
T3–4	235	47.1%	135	55.6%		129	49.6%	22	51.2%	
N classification										
N0	106	21.2%	20	8.2%	0.000	146	56.4%	7	16.3%	0.000
N+	393	78.8%	223	91.8%		113	43.6%	36	83.7%	
Treatment modality										
RT alone	196	39.3%	31	12.8%	0.000	205	70.9%	6	13.3%	0.000
ChemoRT	303	60.7%	212	87.2%		84	29.1%	39	86.7%	
Induction chemotherapy										
No	188	62.0%	132	62.3%	0.960	75	89.3%	30	76.9%	0.071
Yes	115	38.0%	80	37.7%		9	10.7%	9	23.1%	
Chemotherapy regimen										
No cisplatin	35	11.6%	9	4.2%	0.004	14	16.7%	8	20.5%	0.605
Cisplatin	268	88.4%	203	95.8%		70	83.3%	31	79.5%	
RT dose										
<65 Gy	10	2.0%	3	1.2%	0.453	111	38.4%	1	2.2%	0.000
≥65 Gy	489	98.0%	240	98.8%		178	61.6%	44	97.8%	
Surgery										
No surgery						130	45.0%	36	80.0%	0.000
Surgery						159	55.0%	9	20.0%	
Pretreatment BMI (mean, SD)	23.6	3.8	25.3	4.2	0.000	23.2	4.1	23.9	4.0	0.328
Pretreatment BMI										
<18.5	29	5.8%	4	1.6%	0.000	31	10.7%	3	6.7%	0.633
18.5–24.9	316	63.5%	112	46.1%		169	58.5%	26	57.8%	

Table 2 (continued)

	NPC					Non-NPC				
	<10%		≥10%		*p* value	<10%		≥10%		*p* value
	N	%	*N*	%		*N*	%	*N*	%	
≥25	153	30.7%	127	52.3%		89	30.8%	16	35.6%	
Pretreatment weight loss										
<5%	451	90.4%	214	88.1%	0.013	221	76.5%	37	82.2%	0.549
5–10%	40	8.0%	16	6.6%		51	17.6%	5	11.1%	
≥10%	8	1.6%	13	5.3%		17	5.9%	3	6.7%	
Weight loss 2 weeks										
<5%	479	97.8%	186	77.8%	0.000	278	97.2%	35	77.8%	0.000
5–10%	11	2.2%	50	20.9%		8	2.8%	10	22.2%	
≥10%	0	0.0%	3	1.3%		0	0.0%	0	0.0%	

Table 3 Multivariate logistic regression analysis of weight loss ≥10% at the end of RT

	B	S.E.	Wald	df	Sig.	Exp(*B*)	95% CI	
							Lower	Upper
a. NPC								
Age (<45 years as ref)			9.7	3	0.021			
Age (45–64 years)	−0.7	0.2	9.4	1	0.002	0.49	0.3	0.8
Age (65–74 years)	−0.7	0.4	4.1	1	0.042	0.49	0.2	1.0
Lives alone	0.7	0.3	4.6	1	0.032	1.97	1.1	3.7
Cisplatin regimen	1.2	0.2	24.6	1	0.000	3.37	2.1	5.5
Tube feeding	1.4	0.4	13.9	1	0.000	3.86	1.9	7.8
Unplanned admissions	0.5	0.2	5.1	1	0.024	1.60	1.1	2.4
BMI ≥25	2.1	0.7	10.8	1	0.001	8.52	2.4	30.7
Pretreatment weight loss ≥10%	1.3	0.5	6.1	1	0.014	3.55	1.3	9.7
>5% weight loss at week 2	2.4	0.4	37.6	1	0.000	10.81	5.1	23.1
Constant	−3.1	0.7	20.8	1	0.000	0.05		
b. Non-NPC								
RT dose ≥65 Gy	0.2	0.1	5.6	1	0.017	1.18	1.0	1.3
Chemotherapy added	1.8	0.5	11.2	1	0.001	6.24	2.1	18.3
>5% weight loss at week 2	2.3	0.7	10.5	1	0.001	9.70	2.5	38.2
Constant	−14.3	4.6	9.5	1	0.002	0.00		

[36, 37]. Significant weight loss could lead to anatomical changes and alter the external contour and position. This can potentially result in significant dosimetric changes in planning target volumes, and it can negatively affect treatment accuracy and increase toxicity [38–40].

Weight loss and unplanned admissions

A study showed that the rate of unplanned admissions in HNC patients was 65% [41]. Among studies performed on NPC patients, the incidence of unplanned admissions was between 20 and 36% [42, 43]. Our study revealed a significantly higher rate of unplanned admission in patients with ≥10% weight loss. These findings generally aligned with other studies. Duffy et al. reported that critical weight loss of >5% was associated with a higher number of unplanned admissions in HNC patients undergoing chemoRT [9]. Capuano et al. reported a significantly higher rate of unplanned admissions in HNC patients with >20% weight loss, and weight loss was positively correlated with hospital admissions [44]. In a large cohort study on HNC surgical patients, Gourin et al. found that weight loss was significantly associated with postoperative complications, morbidities, and hospital length of stay [45]. In our non-NPC patients with >5% weight loss at week 2 of RT treatment, we found a significantly higher risk of unplanned admissions. We speculate that weight loss during the first few weeks of RT treatment predicts unplanned admissions, likely due to cumulative toxicity. If patients encounter symptoms early in their treatment journey, they are more likely to become intolerable to

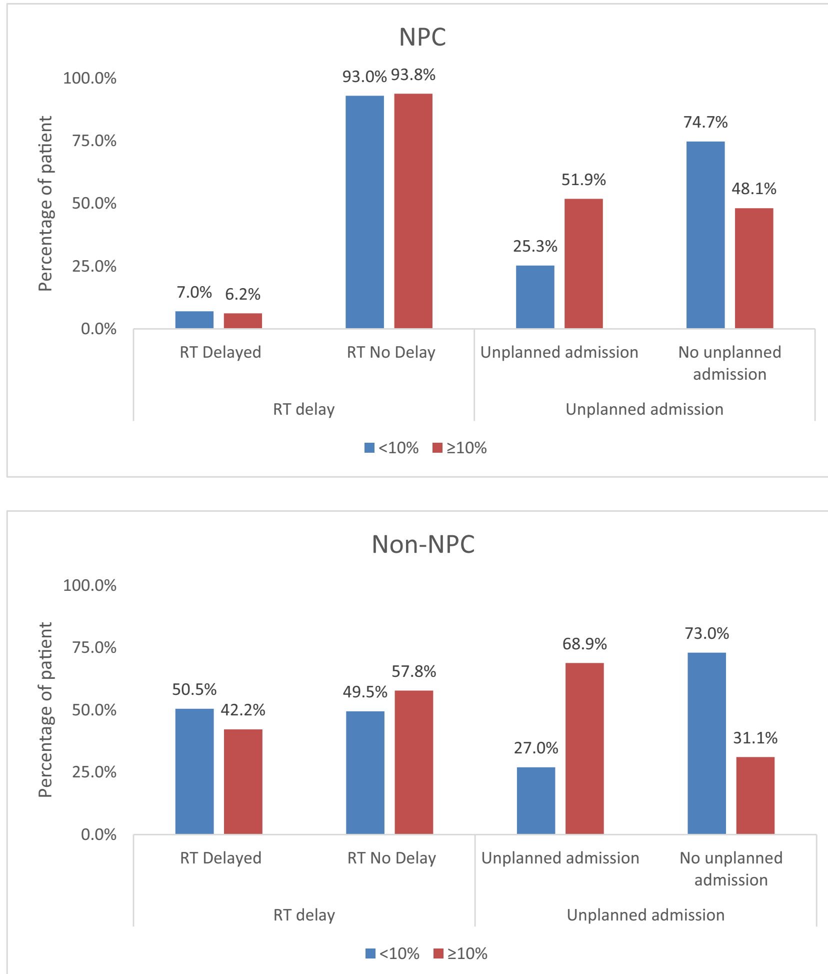

Fig. 1 Prevalence of weight loss at the end of RT treatment in NPC and non-NPC patients with treatment interruptions (RT delay) and unplanned admissions

subsequent side effects and require hospitalization for side effect management.

Feeding tube placement and unplanned admissions In the present study, the strongest factor associated with unplanned admissions was feeding tube placement. Our non-NPC patients had a significantly higher rate of feeding tube placement (21.5%) than NPC patients (8.0%). This was likely related to the fact that many of our non-NPC patients already had their feeding tube placed after surgery or before treatment due to the early onset of eating-related symptoms prior to diagnosis. Studies on feeding tube placement and hospital admissions had mixed results. Brown et al. showed a lower incidence of unplanned admissions with prophylactic feeding tubes [46], and some reported no differences [47, 48]. Duffy et al. demonstrated a significantly higher risk of unplanned admissions with enteral feeding tube placement [9]. This variation in outcomes may be due to the timing of feeding tube placement and the availability of intensive supportive care. Nutrition status could be better preserved with prophylactic feeding tube placement, but admissions for feeding tube complications were frequently observed [48]. In our centre, feeding tube placements were all performed in inpatient settings, and the majority of patients had reactive feeding tube insertions. For the majority of our HNC patients, by the time tube feeding is needed, they may already have developed profound toxicities, including those resulting in severe weight loss and requiring hospital admission for symptom management.

Concomitant chemoRT, cisplatin regimen, and unplanned admissions In our study, non-NPC patients with concomitant chemoRT had a significantly higher risk of unplanned admissions than patients with RT alone. Similarly, a study reported that patients with concomitant chemotherapy had a 3.96 times higher risk of unplanned admissions [49]. Nugent et al. reported that tube feeding was required for 66–71% of HNC patients on a combined treatment modality compared to only 12% of patients on a single modality of RT treatment [50]. Chemotherapy was found to be a major contributing factor for more clinic visits, a higher rate of RT interruption, more chemotherapy incompletion, a greater need for tube

Table 4 Univariate analysis of weight loss and unplanned admissions (variables with $p<0.05$)

	No admission		Admitted		*p* value
	N	%	*N*	%	
a. NPC					
Stage of disease					
Stage I–II	200	40.5%	47	18.6%	0.000
Stage III–IV	294	59.5%	206	81.4%	
Treatment modality					
RT alone	197	39.9%	30	6.1%	0.000
ChemoRT	297	60.1%	223	45.1%	
Induction chemotherapy					
No	376	76.1%	165	33.4%	0.002
Yes	118	23.9%	88	17.8%	
Feeding					
Oral	490	99.2%	197	77.9%	0.000
Tube feeding	4	0.8%	56	22.1%	
Weight loss at week 2					
<5%	458	93.9%	211	85.8%	0.001
5–10%	29	5.9%	33	13.4%	
≥10%	1	0.2%	2	0.8%	
Weight loss at week 7					
<10%	373	76.1%	126	50.0%	0.000
≥10%	117	23.8%	126	50.0%	
b. Non-NPC					
Stage of disease					
Stage I–II	83	39.7%	16	15.5%	0.000
Stage III–IV	126	60.3%	87	84.5%	
Treatment modality					
RT alone	177	77.3%	37	33.6%	0.000
ChemoRT	52	22.7%	73	66.4%	
Feeding					
Oral	215	93.9%	51	46.4%	0.000
Tube feeding	14	6.1%	59	53.6%	
Total no. of dietitian outpatient contacts					
≤1	17	7.4%	17	15.5%	0.021
≥2	212	92.6%	93	84.5%	
Weight loss at week 2					
<5%	220	97.8%	96	88.1%	0.000
5–10%	5	2.2%	13	11.9%	
≥10%		0.0%		0.0%	
Weight loss at week 7					
<10%	211	93.8%	78	71.6%	0.000
≥10%	14	6.2%	31	28.4%	
Surgery					
No surgery	104	45.4%	63	57.3%	0.041
Surgery	125	54.6%	47	42.7%	

feeding, and higher rates of complications and hospitalizations [51, 52]. Our results were consistent with these studies and showed that concomitant chemotherapy was associated with an increased rate of unplanned hospital admissions, greater weight loss, and tube feeding needs. Specifically, our NPC patients given a cisplatin regimen had a significantly higher risk and rate of unplanned admissions. Bright et al. reported that 23% of unplanned admissions for adverse effects were found in patients who received cisplatin regimens in various cancer types [53].

Prevalence of weight loss and its predictive factors

In the present study, the prevalence of ≥10% weight loss at the end of RT was 26.8%, and the prevalence was significantly higher in NPC patients (32.7%) than in non-NPC patients (13.5%) ($p<0.001$).

Pretreatment weight loss Greater pretreatment weight loss in non-NPC patients can be explained partly by worse symptom exacerbation at the time of diagnosis. Non-NPC patients more often had a higher number of eating-related symptoms, including dysphagia, chewing difficulty, or airway obstruction, as their presenting symptoms. They commonly experienced issues with eating for a period of time, which already resulted in substantial pretreatment weight loss [54–56].

Posttreatment weight loss We observed less posttreatment weight loss in our non-NPC group. This might be due to the higher rate of feeding tube placement in these patients. In our practice, feeding tubes were often placed postoperatively in non-NPC patients and kept until the completion of adjuvant treatment. Patients with early commencement of tube feeding could have better preservation of nutrition status. In addition, more non-NPCs had a single modality of RT alone, and they commonly experienced less severe toxicities than those with concomitant chemoRT.

Age and weight loss Our results showed that younger patients had a significantly higher prevalence of ≥10% weight loss. This finding is consistent with previous studies [9, 57–62]. Some explanations include that younger patients often receive more aggressive treatment with substantially higher toxicities and are more physically active with higher energy expenditures. Interestingly, Monroe et al. reported that more nausea and vomiting were observed in younger patients, and the reason was not known [63].

BMI and weight loss Similar to other studies [58, 59, 64–70], our results showed that patients with higher BMI had significantly greater weight loss. Lønbro et al. reported a 5.1 times higher risk of >10% weight loss in HNC patients with BMI above 25 [58]. The reason for greater weight loss in patients

Table 5 Multivariate logistic regression analysis of weight loss and unplanned admissions

	B	S.E.	Wald	df	Sig.	Exp(*B*)	95% CI	
							Lower	Upper
a. NPC								
Stage III–IV	0.55	0.28	3.88	1	0.049	1.73	1.00	3.00
Chemotherapy as planned	−0.49	0.23	4.42	1	0.036	0.61	0.39	0.97
Tube feeding	3.41	0.74	21.43	1	0.000	30.35	7.15	128.72
≥10% weight loss at week 7	0.64	0.22	8.78	1	0.003	1.90	1.24	2.89
Constant	−1.05	0.28	13.78	1	0.000	0.35		
b. Non-NPC								
ChemoRT	1.85	0.38	24.26	1	0.000	6.34	3.04	13.22
Chemotherapy as planned	−1.08	0.50	4.79	1	0.029	0.34	0.13	0.89
Tube feeding	2.44	0.40	37.06	1	0.000	11.42	5.21	25.01
>5% weight loss at week 2	0.98	0.46	4.61	1	0.032	2.67	1.09	6.55
Constant	−2.32	0.28	67.13	1	0.000	0.10		

with high BMI might partly be due to the perception of better nutritional reserve, and consequently, reduced supportive care and less aggressive nutritional support were provided to these patients. de Oliveira Faria et al. reported that patients with obesity had been given less nutritional support when compared with that given to normal weight patients [70]. A study demonstrated that people with obesity experienced greater satisfaction from eating than normal weight adults [71]. When patients with obesity start to experience eating-related side effects, the joy of eating diminishes, and they become psychologically and emotionally distressed, eventually resulting in a substantial decrease in oral intake and subsequently causing significant weight loss.

Strengths and limitations

The main strength of this study is the large sample size with a representative sample of both NPC and non-NPC patients. This gives more reliable results with greater statistical power and precision. To the best of our knowledge, this is the first study investigating the association of weight loss with treatment outcomes and hospital admissions in an Asian population. This is also the first study that yielded differences in weight loss, treatment interruption, and unplanned hospital admissions between NPC and non-NPC patients.

This study has some limitations. First, there are intrinsic limitations of retrospective studies with potential selection bias. Second, both the methods and instruments used for the weight measurements were not standardized. This can affect measurement accuracy and affect the reliability and validity of the data. Third, some important confounding factors, including patient performance status, quality of life status, comorbidity, and HPV status in oropharyngeal cancer, were either unavailable or not included. Fourth, during the selected period of 9 years, many new practices and advances in treatment modalities developed. Last, using BW as the sole nutritional indicator might not truly reflect patients' nutritional status, and the cause of weight loss is often multifactorial.

Conclusions

In our study, ≥10% weight loss was shown to be associated with a higher rate of unplanned hospital admissions in both NPC and non-NPC patients. Significant weight loss was not associated with RT delay or chemotherapy interruption in the present study. In NPC patients, factors significantly associated with unplanned admissions were stage III–IV disease, chemotherapy as planned, tube feeding placement, and ≥10% weight loss at the end of RT. In non-NPC patients, factors significantly associated with unplanned admissions were treatment modality of chemoRT, chemotherapy as planned, feeding tube, and weight loss >5% at week 2.

Clinical implications: This weight loss information assists in stratifying patients for intensive nutritional support. Our findings also support more targeted strategies to prevent unfavourable outcomes due to unplanned hospital admissions.

Appendix

Table 6 Prevalence of weight loss at the end of RT treatment in patients with treatment interruptions and unplanned admission

	NPC					Non-NPC				
	N	%	N	%	p value	N	%	N	%	p value
	<10%		≥10%			<10%		≥10%		
RT delay										
No Delay	464	93.0%	228	93.8%	0.668	143	49.5%	26	57.8%	0.300
Delayed	35	7.0%	15	6.2%		146	50.5%	19	42.2%	
Unplanned admission										
No admission	373	74.7%	117	48.1%	0.000	211	73.0%	14	31.1%	0.000
Admitted	126	25.3%	126	51.9%		78	27.0%	31	68.9%	

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Declarations

Conflict of interest The authors declare no competing interests.

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