Dynamic Variation and Prognostic Value of Weight Loss During Radiotherapy in Nasopharyngeal Carcinoma: A Large-Scale Cohort Study

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Abstract

Background: We aim to investigate the dynamic variation and prognostic value of weight loss among patients with nasopharyngeal carcinoma (NPC).

Methods: A total of 1149 newly diagnosed NPC patients who received radical radiotherapy (RT) were retrospectively analyzed. Patients' weights were measured at initiation of RT and every week during RT. Recursive partitioning analyses (RPAs) were utilized to determine cut-off value for rate of weight loss (RWL). Disease-free survival (DFS) was our primary endpoint. Secondary endpoints included locoregional relapse-free survival (LRRFS), distant metastasis-free survival (DMFS), and overall survival (OS).

Results: RWLs were 0%, 0%, -1.54%, -2.86%, -4.11%, -5.98%, -6.56% at 1st, 2nd, 3rd, 4th, 5th, 6th, and 7th week of RT, respectively. RWL optimal threshold with respect to DFS was -5.3% based on RPAs. Thus, a consistent threshold of -5% (> -5% versus ≤ -5%) was selected to classify NPC patients into low RWL and high RWL groups for survival analysis. Compared to high RWL (≤-5%), patients with low RWL (> -5%) had significantly better ten-year DFS (78.6% versus 61.2%; P< 0.001), OS (86.6% versus 70.1%; P< 0.001), and DMFS (88.5% versus 80.2%; P = 0.007). However, no difference was observed between LRRFS groups (91.7% versus 94.3%; P= 0.173). In multivariate analysis, high RWL was an independent risk factor for DFS (HR, 1.56; 95% CI, 1.19-2.03; P= 0.001), OS (HR, 1.54; 95% CI, 1.11-2.15; P= 0.011) and DMFS (HR, 1.47; 95% CI, 1.03-2.10; P= 0.033) in patients with NPC. Additionally, chemotherapy and old age were attributed to the development of high RWL.

Conclusions: Weight loss during RT was significantly associated with decreased survival among NPC patients. Clinicians should continuously inform patients on the health impact of minimizing weight loss under 5%.

Background

Nasopharyngeal carcinoma (NPC), an epithelial malignancy that is distinguished from other head and neck cancers, is highly prevalent in southern China [1]. The main treatment for NPC is radiotherapy (RT) due to anatomical restrictions and radio-sensitivity. Over the past decade, advances in imagining techniques, chemotherapy, and radiation technology contributed to the improved NPC survival. However, 20–30% of patients still die as a result of NPC recurrence [2–3]. Therefore, efforts to identify modifiable risk factors can potentially provide new insights on developing clinical intervention for increasing long-term survival.

Patients diagnosed with head and neck cancers often experience weight loss during treatment due to acute toxicity, such as mucositis, dysgeusia, xerostomia, and nausea [4–7]. Previous studies [8, 9] have estimated weight loss to range from 40–90%, especially among NPC patients where rates are high. Substantial weight loss during treatment was associated with poor survival in NPC [10–13]. Monitoring the decreasing weight during RT will allow for clinicians to evaluate the current treatment plan effectiveness for NPC [14]. Moreover, knowing the dynamic variation of patients' weight loss during

treatment is helpful in selecting the optimal time for nutritional intervention and altering RT treatment. However, bodyweight was only obtained at baseline visit and again at the end of treatment in previous studies [10–12], without considering the dynamic weight loss during treatment.

To fill the current gaps in knowledge and limitations of previous studies, we conducted a large-scale retrospective study of NPC patients treated with radical RT. The present study sought to (1) draw a dynamic map of weight variation during RT; (2) identify the weight loss prognostic value on survival outcomes; (3) demonstrate risk factors for weight loss; and (4) provide insight on individualized nutritional intervention and the timing of RT replanning for NPC patients.

Methods

Patient characteristics

The present study was a retrospective cohort study utilizing in-patient medical records from Sun Yat-Sen University Cancer Center consisting of first diagnosis of histologically confirmed, non-disseminated NPC from January 2006 to October 2014. We included patients if they met the following criteria: (1) newly diagnosed non-disseminated NPC; (2) Karnosfky performance score ≥ 70; (3) no indication of distant metastases; (4) absent of secondary malignancy; (5) treated with radical intensity-modulated radiation therapy (IMRT); and (6) weekly assessment of weight. This study was conducted in compliance with institutional policy to protect patients' private information, and was approved by the Institutional Review Board of our center.

We included 1149 patients, and the baseline assessment included full physical examination, fiberoptic nasopharyngoscopy, neck and nasopharyngeal magnetic resonance imaging (MRI), computed tomography (CT), abdominal ultrasonography, biochemistry profiling and hematology, whole body bone scan (ECT) or ^{18}F-fluorodeoxyglucose positron emission tomography and CT (PET-CT). Real-time quantitative polymerase chain reaction was used to measure Epstein-Barr virus (EBV) DNA concentrations as previously described in detail [15]. Patients were staged based on the 7th edition of the American Joint Commission on Cancer staging system [16].

Radiotherapy and chemotherapy

All patients received radical IMRT in the current study. Dose prescribed to patients were (1) 66–70 Gy at 2.12–2.27 Gy/fraction to planning target volume (PTV) of nasopharyngeal gross tumor volume (GTVnx); (2) PTV of GTV of the metastatic lymph nodes (GTVnd) received 64–70 Gy; and (3) high-risk clinical target volume (CTV1) received 60–63 Gy to PTV and (4) low-risk clinical target volume (CTV2) received 50–56 Gy to PTV. Concurrent chemotherapy comprised of cisplatin (80 or 100 mg/m^2) given in weeks one, four, and seven of radiotherapy, or cisplatin (40 mg/m2) given weekly during radiotherapy. Induction chemotherapy (IC) included cisplatin (60 mg/m^2), docetaxel (60 mg/m^2), and 5-fluorouracil (600 mg/m^2/day over 120 h), or cisplatin (80 mg/m^2) plus 5-fluorouracil (800 mg/m^2/day over 120 h) or cisplatin (80 mg/m^2) plus docetaxel (80 mg/m^2) every three weeks for three cycles.

Data collection

Patients' age, height, weight, sex, pre-therapy laboratory counts of serum lactate dehydrogenase (LDH), high sensitivity C-reactive protein (hs-CRP), plasma EBV DNA, pathological types, clinical stage, and treatment type were extracted from medical records. Digital electronic scale (XiangShan, EB9871) was used to measure bodyweight to the nearest 0.1 kg in light garment and without shoes. We measured patients' bodyweight at initiation of RT and every week during RT. Bodyweight before RT (W_{Pre-RT}) was measured at initiation of RT, and $W_{RT1,2,3,4,5,6,7}$ (body weight at 1st, 2nd, 3rd, 4th, 5th, 6th, and 7th week of RT) was measured at each week of RT. $RWL_{1,2,3,4,5,6,7}$ was calculated using the following equation: $(W_{RT1,2,3,4,5,6,7} - W_{Pre-RT})/W_{Pre-RT} \times 100\%$. At time of study, all patients were on 100% oral intake, where no type of enteral feeding tube or total parental nutrition were used.

Follow-up and endpoints

Patients were examined every three months during the first two years, and every six months for years three through five, and annually thereafter until death. Disease-free survival (DFS) was our primary endpoint, defined as time from diagnosis to documented recurrence of disease (either distant metastasis or locoregional disease recurrence) or mortality from any cause, whichever occurred first. Secondary endpoints consisted of (1) distant metastasis free survival (DMFS) (no documented distant metastasis); (2) locoregional relapse free survival (LRRFS) (no documented locoregional recurrence); and (3) overall survival (OS).

Statistical methods

In this study covariates included host factors (e.g. age, gender, tobacco smoking status, hs-CRP, LDH, and plasma EBV DNA), treatment factors (e.g. treatment modality), and tumor factors (e.g. histology, T stage, and N stage). We classified categorical variables based on clinical findings. Determined by routine cutoff points and findings from prior studies, continuous variables were converted to categorical variables [17–19]. χ^2 test or Fisher's Exact test were used to compare clinicopathologic characteristics groups.

Kaplan-Meier method was used to calculate actuarial rates, where we compared differences by the log-rank test. Optimal RWL threshold was identified by performing recursive partitioning analyses (RPAs) for the cohort. Univariable with a $P < 0.05$ was used to include covariates in the multivariable model. Multivariate Cox proportional hazards model was applied to evaluate the impact of RWL on survival outcomes. Statistical tests were two-tailed and $P < 0.05$ was considered statistically significant. All statistical analysis and generate figures were performed by the rms package in R version 3.3.2 (http://www.r-project.org/).

Results

Patient characteristics

Clinicopathological characteristics of the 1149 patients are shown in Table 1. Among all patients, 892 (77.6%) were male and majority (1058, 92%) of patients experienced weight loss during RT. The percentage of patients at stage I, II, III, and IVA-B were 2.1%, 9.9%, 53.7%, and 34.3%, respectively. Additionally, 140 (12%) received RT alone and 1009 (88%) received chemotherapy. Of these patients receiving chemotherapy, 549 (48%; 549/1009) received IC plus CCRT and 460 (40%; 460/1009) received CCRT alone. The median follow-up time was 72.6 months (54.8, 6–85.8 months).

Table 1
Baseline patient characteristics according to rate of weight loss (RWL).

Characteristic	Total (N = 1149)[a]	No. (%) of patients by RWL		*P* value
		>-5% (n = 402, 35%)	≤-5% (n = 747, 65%)	
Gender				0.826
Male	892 (77.6)	314 (78.1)	578 (77.4)	
Female	257 (22.4)	88 (21.2)	169 (22.6)	
Age, y				0.006
<30	68 (5.9)	28 (7.0)	40 (5.4)	
30–39	263 (22.9)	96 (23.9)	167 (22.4)	
40–49	447 (38.9)	143 (35.6)	304 (40.7)	
50–59	227 (19.8)	67 (16.7)	160 (21.4)	
≥60	144 (12.5)	68 (16.9)	76 (10.2)	
Histology (WHO)				0.732
Type I-II	35 (3.1)	11 (2.7)	24 (3.2)	
Type III	1114 (96.9)	391 (97.3)	723 (96.8)	
Smoking history				0.996
No	807 (70.2)	282 (70.2)	525 (70.3)	
Yes	342 (29.8)	120 (29.9)	222 (29.7)	
T stage (7th edition)				0.031
T1	71 (6.2)	32 (8.0)	39 (5.2)	
T2	185 (16.1)	69 (17.2)	116 (15.5)	
T3	627 (54.6)	226 (56.2)	401 (53.7)	
T4	266 (23.2)	75 (18.7)	191 (25.6)	
N stage (7th edition)				< 0.001
N0	128 (11.1)	59 (14.7)	69 (9.2)	

Abbreviations: RWL, rate of weight loss; WHO, World Health Organization; hs-CRP, high sensitivity C-reactive protein; LDH, lactate dehydrogenase; EBV, Epstein-Barr virus;

[a] Percentages may not add up to 100 due to rounding.

[b] All variables were measured before treatment.

Characteristic	Total (N = 1149)[a]	No. (%) of patients by RWL		*P* value
N1	448 (39.0)	177 (44.0)	271 (36.3)	
N2	399 (34.7)	118 (29.4)	281 (37.6)	
N3	174 (15.1)	48 (11.9)	126 (16.9)	
Overall stage				0.001
Stage I	24 (2.1)	13 (3.2)	11 (1.5)	
Stage II	114 (9.9)	53 (13.2)	61 (8.2)	
Stage III	617 (53.7)	223 (55.5)	394 (52.7)	
Stage IVA-B	394 (34.3)	113 (28.1)	281 (37.6)	
hs-CRP, g/mL[b]				0.536
<1.0	363 (31.6)	133 (33.1)	230 (30.8)	
1.0–3.0	370 (32.2)	132 (32.8)	238 (31.9)	
≥3.0	416 (36.2)	137 (34.1)	279 (37.4)	
LDH, U/L[b]				0.095
<245	1058 (92.1)	378 (94.0)	680 (91.0)	
≥245	91 (7.9)	24 (6.0)	67 (9.0)	
EBV DNA, copy/mL[b]				0.043
<1,000	500 (43.5)	193 (48.0)	307 (41.1)	
1,000–9,999	266 (23.2)	96 (23.9)	170 (22.8)	
10,000–99,999	268 (23.3)	82 (20.4)	186 (24.9)	
≥100,000	115 (10.0)	31 (7.7)	84 (11.2)	
Treatment				< 0.001
RT alone	140 (12.2)	81 (20.2)	59 (7.9)	
CCRT alone	460 (40.0)	126 (31.3)	334 (44.7)	

Abbreviations: RWL, rate of weight loss; WHO, World Health Organization; hs-CRP, high sensitivity C-reactive protein; LDH, lactate dehydrogenase; EBV, Epstein-Barr virus;

[a] Percentages may not add up to 100 due to rounding.

[b] All variables were measured before treatment.

Characteristic	Total (N = 1149)[a]	No. (%) of patients by RWL		*P* value
IC + CCRT	549 (47.8)	195 (48.5)	354 (47.4)	

Abbreviations: RWL, rate of weight loss; WHO, World Health Organization; hs-CRP, high sensitivity C-reactive protein; LDH, lactate dehydrogenase; EBV, Epstein-Barr virus;

[a] Percentages may not add up to 100 due to rounding.

[b] All variables were measured before treatment.

Identification of the optimal cut-off value for defining RWL as high or low

Five- and ten-year DFS, OS, DMFS, and LRRFS rates were 76.3% and 66.8%, 86.0% and 75.3%, 85.9% and 83.1%, and 93.2% and 92.7%, respectively. For the RWL, the optimal cutoff point for DFS among the entire group was − 5.3% based on RPAs. Thus, a uniform cutoff point was selected at -5% (>-5% versus ≤-5%) to classify patients into groups low RWL and high RWL for survival analysis. 63% (725/1149) of patients suffered ≥ 5% weight loss. When comparing survival between groups, our findings showed patients with high RWL had poorer ten-year DFS (61.2% versus 78.5%; P < 0.001; Fig. 1A), OS (70.1% versus 86.6%; P < 0.001; Fig. 1B), and DMFS (80.2% versus 88.5%; P = 0.007; Fig. 1C) compared to low RWL patients. However, no associated difference between groups for ten-year LRRFS (91.7% versus 94.3%; P = 0.173; Fig. 1D) was observed. Further analysis revealed that high RWL was an independent unfavorable prognostic factor for DFS (HR, 1.56; 95% CI, 1.19–2.03; P = 0.001), OS (HR, 1.54; 95% CI, 1.11–2.15; P = 0.011) and DMFS (HR, 1.47; 95% CI, 1.03–2.10; P = 0.033) in multivariate analysis (Table 2).

Table 2
Multivariate analysis of prognostic factors for patients with NPC (n = 1149).

Endpoint	Variable	HR	95% CI for HR	P[a]
DFS				
	RWL status	1.56	1.19–2.03	0.001
	Age	1.36	1.08–1.71	0.010
	Gender	0.83	0.63–1.08	0.157
	Pathology	0.44	0.26–0.72	0.001
	T stage	1.62	1.16–2.27	0.005
	N stage	1.54	1.20–1.97	0.001
	EBV DNA	1.50	1.12–2.01	0.007
	Treatment strategy	0.84	0.54–1.32	0.455
OS				
	RWL status	1.54	1.11–2.15	0.011
	Age	1.57	1.17–2.10	0.002
	Pathology	0.37	0.21–0.66	0.001
	T stage	1.84	1.20–2.81	0.005
	N stage	1.72	1.26–2.81	0.001
	Smoking history	1.26	0.93–1.70	0.131
	LDH	1.27	0.80–2.03	0.308
	EBV DNA	1.54	1.08–2.21	0.018
DMFS				
	RWL status	1.47	1.03–2.10	0.033
	Age	1.43	1.04–1.96	0.026
	Pathology	0.55	0.27–1.13	0.104
	T stage	1.41	0.92–2.18	0.118

Abbreviations: RWL, rate of weight loss; HR, hazard ratio; 95% CI, 95% confidence interval; DFS, disease-free survival; OS, overall survival; DMFS, distant metastasis-free survival; LRRFS, locoregional relapse-free survival; LDH, lactate dehydrogenase; EBV, Epstein-Barr virus.

[a] *P* values were calculated using an adjusted Cox proportional hazards model.

Endpoint	Variable	HR	95% CI for HR	*P*[a]
	N stage	1.99	1.41–2.80	< 0.001
	Smoking history	1.37	0.99–1.90	0.055
	LDH	1.33	0.82–2.16	0.247
	EBV DNA	2.01	1.23–3.30	0.006
LRRFS				
	Pathology	0.31	0.14–0.72	0.006
	Smoking history	0.56	0.31–1.01	0.056
	Treatment strategy	4.86	1.17–20.15	0.029

Abbreviations: RWL, rate of weight loss; HR, hazard ratio; 95% CI, 95% confidence interval; DFS, disease-free survival; OS, overall survival; DMFS, distant metastasis-free survival; LRRFS, locoregional relapse-free survival; LDH, lactate dehydrogenase; EBV, Epstein-Barr virus.

[a] *P* values were calculated using an adjusted Cox proportional hazards model.

Dynamic variation of body weight during RT

The dynamic variation of weight loss during RT was analyzed. We observed that RWL remained largely unchanged in the first two weeks of RT, and then began to drop at a relatively stable rate during weeks three to five of RT (from-1.54% to -4.11%; at a rate of -1.3% weight loss per week). At the 6th week of RT, the RWL dropped faster than the prior week (from − 4.11% to -5.98%; nearly 2% weight loss in this week). RWL then slowed in the last week of RT (from − 5.98% to -6.56%; approximately 0.5% weight loss in this week). The median weight loss during RT was − 4.0 kg (IQR, − 2.0 to -6.0 kg) and the percentage for median weight loss was − 6.7% (IQR, − 3.5 to -9.7%).

Correlation between RWL and clinicopathological characteristics

Table 1 presents the correlations between clinicopathological characteristics and RWL. High RWL patients were more likely to have advanced TNM stage (advanced T, N, and/or overall stage) ($P < 0.05$ for all). With respect to treatment strategy, the proportion receiving RT alone among the low RWL patient group was associated with higher receipt compared with high RWL (20.2% versus 7.9%; $P < 0.001$). Factors associated with development of high or low RWL were analyzed. After logistic regression analysis, treatment modality and age remained associated with high RWL ($P < 0.05$ for all; Table 3). Patients treated with RT alone had the lowest risk with development of weight loss during RT. In contrast, CCRT alone had a significantly strong correlation with the development of weight loss in comparison to RT alone or IC followed by CCRT (OR, 1.71; 95% CI, 1.23–2.31; $P < 0.001$). Moreover, patients older than 45 were more likely to suffer high weight loss than patients age ≤ 45 (OR, 1.35; 95% CI, 1.12–1.67; $P = 0.002$) during RT.

Table 3
Multivariate analysis of prognostic factors for the development of high RWL in patients with NPC.

Variable	HR	95% CI for HR	*P* value[a]
Age at diagnosis, y			
≤45	Reference		
>45	2.03	1.13–3.66	0.023
T stage			
T1	Reference		
T2	0.96	0.53–1.73	0.908
T3	0.87	0.50–1.51	0.625
T4	1.46	0.80–2.68	0.220
N stage			
N0			
N1	1.01	0.66–1.55	0.952
N2	1.52	0.95–2.44	0.075
N3	1.68	0.97–2.91	0.064
LDH, U/L[b]			
<245	Reference		
≥245	1.38	0.83–2.29	0.232
EBV DNA, copy/mL[b]			
<1,000	Reference		
1,000–9,999	0.91	0.65–1.28	0.604
10,000–99,999	1.11	0.78–1.57	0.586
≥100,000	1.30	0.79–2.12	0.315
Treatment			

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; LDH, lactate dehydrogenase; hs-CRP, high sensitivity C-reactive protein; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; IC + CCRT, induction chemotherapy plus concurrent chemoradiotherapy.

[a] *P* values were calculated using an adjusted Cox proportional hazards model.

[b] All variables were measured before treatment.

Variable	HR	95% CI for HR	*P* value[a]
RT alone	Reference		
CCRT alone	3.29	2.18–4.96	< 0.001
IC + CCRT	2.03	1.32–3.13	0.001

Abbreviations: HR, hazard ratio; 95% CI, 95% confidence interval; LDH, lactate dehydrogenase; hs-CRP, high sensitivity C-reactive protein; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; IC + CCRT, induction chemotherapy plus concurrent chemoradiotherapy.

[a] *P* values were calculated using an adjusted Cox proportional hazards model.

[b] All variables were measured before treatment.

Discussion

To the best of our knowledge, this study is the longest follow-up analysis for dynamic variation of weight loss during RT. Results of this present study revealed body weight remained largely unchanged during RT for the first two weeks, and dropped fastest at the sixth week of RT. Further analysis revealed that weight loss ≥ 5% during RT was associated with significantly inferior ten-year DFS, OS, and DMFS for NPC. Additionally, older age and chemotherapy were predictive of greater weight loss for NPC.

Numerous studies have demonstrated that weight loss is correlated with poor prognosis among individuals diagnosed with head and neck cancer [20, 21], especially among NPC patients [10, 11]. Results from the present study aligned closely with prior studies. There are several potential reasons for these findings. First, critical weight loss may result in loosening of posture fixation, inaccurate radiation field, and significant dosimetric change during IMRT [22]. Second, weight loss potentially causes reduction in treatment tolerance and radiotherapy breaks, thus influencing therapeutic efficacy [23, 24]. Third, weight loss is often used as a tool for assessment of newly developed malnutrition, which contributes to weakness in immunity defense mechanism, such as phagocyte function, anatomic barriers, cellular and humoral immunity. Therefore, increasing infection susceptibility and reduced response to malignancy [25, 26].

Previous studies reported that weight loss ≥ 5% during RT was associated with poor survival [12, 23]. Our results showed that RWL ≤ -5% was associated with poor DFS, OS, and DMFS, aligning with prior studies. However, Du et al. [11] assessed weight loss during the entire treatment procedure and observed weight loss ≥ 10% was an indicator for likelihood of metastasis and survival. One reason underlying this inconsistency cutoff value of RWL may partly be due to potential selection bias in the study population. Collectively, the impact of weight loss on prognosis of NPC can be determined in the present study. Previous literatures [27, 28] reported approximately 90% local control rates for NPC in the IMRT era. Due to recent advances in RT technology, no observed associated differences in LRRFS between patients in high and low RWL groups were found in the present study. These finding are reasonable as excellent

locoregional control is expected for IMRT, therefore actual impact of weight loss on LRRFS would be limited.

Numerous factors may influence weight loss among cancer patients. We observed that patients treated with chemotherapy suffered more weight loss, similar with findings by Qiu et al. [9] and Du et al. [11]. Although encouraging results attained by multimodal therapy for NPC, acute toxicities are more likely to occur during aggressive chemoradiotherapy [9], including severe oral mucositis, nausea, and vomiting. Additionally, we observed that patients aged > 60 years had a greater likelihood of suffering higher weight loss. We speculate that elderly patients' reduced organ reserve, multiple comorbidities, and poor treatment tolerance explain the reason for greater weight loss. Other risk factors including radiation technique, segmentation model, and prescribed dose are partly relevant to oral mucositis and weight loss. Because this research adopts the unified radiation technique, segmentation model, and prescribed dose, we did not include the above factors for analysis at last.

Since weight loss is common among NPC patients, it is necessary to assess weight change over RT time. This is due to potentially providing a more complete understanding on the relationship between bodyweight and survival among NPC patients. However, prior researches primarily evaluated weight loss at a single time point, usually pre- or post-treatment. For this reason, limited knowledge exists about the dynamic change of weight loss during RT. Our results indicated that bodyweight remained generally unchanged in the first two weeks of RT, and then began to drop relatively stable the next three weeks, though fastest in the sixth week of RT. The following reasons may explain the observed results. First, the oral mucous membrane reaction of patients is mild and diet is less affected in the first two weeks of RT. With the increasing number of RT, weight loss is gradually accelerated due to oral mucositis, aggravated swallowing pain, and decreased treatment tolerance [4].

There are some limitations should be noted. First, we lacked detailed information on dietary habit and food intake, as well as data on nutritional status was unavailable for further analysis of weight loss. However, during the study period, no standard criteria for nutritional support in patients undergoing RT has been established. Second, the data used in this study derived from only one institution in an endemic area, where a large proportion of physicians have expertise in diagnosing and treating of NPC. Future studies that incorporate external validation is needed.

Conclusions

In conclusion, our findings revealed weight loss decreased fastest during the sixth week of RT. The optimal threshold for RWL adversely impacting NPC prognosis was − 5%. More efforts are needed to be given towards limiting weight loss during RT under 5% in clinical practice as a result of the detrimental impact of RWL on survival outcomes. In addition, use of chemotherapy and old age were attributed to the development of high weight loss. These findings would be helpful in selecting optimal time for nutritional intervention and RT replanning.

Abbreviations

NPC: Nasopharyngeal carcinoma; RT: Radiotherapy; IMRT: RWL: Rate of weight loss; Intensity-modulated radiation therapy; MRI: Magnetic resonance imaging; CT: Computed tomography; ECT: Whole body bone scan; PET-CT: 18F-fluorodeoxyglucose positron emission tomography and CT; EBV: Epstein-Barr virus; PTV: Planning target volume; GTVnx: Nasopharyngeal gross tumor volume; GTVnd: GTV of the metastatic lymph nodes; CTV1: High-risk clinical target volume; CTV2: Low-risk clinical target volume; IC: Induction chemotherapy; CCRT: Concurrent chemoradiotherapy; LDH: Lactate dehydrogenase; hs-CRP: High sensitivity C-reactive protein; WPre-RT: Bodyweight before RT; DFS: Disease-free survival; DMFS: Distant metastasis free survival; LRRFS: Locoregional relapse free survival; OS: Overall survival; RPAs: Recursive partitioning analyses;

Declarations

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Availability of data and materials

The datasets analysed during the current study are available in the Research Data Deposit (RDD) public platform www.researchdata.org.cn, with the approval RDD number of RDDA2019001296. If someone need to access the data, he/she should obtain our consent, and have to explain the source of the data in their study.

Authors' contributions

Data collection and writing original draft was performed by JYN, XTL, and MDM. Formal analysis, reviewing and editing was done by YJJ and JC. JYN and XTL participated in project administration and study design. Study design was conceived and designed by XLP and HWZ. Prior to submission of this manuscript, all authors have reviewed and approved.

Ethics approval and consent to participate

This study was conducted in compliance with institutional policy to protect patients' private information, and was approved by the Institutional Review Board of Sun Yat-sen University Cancer Center. As the

current study was a retrospective assessment of routine data, the ethics committee of our Cancer Center waived the need for individual informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

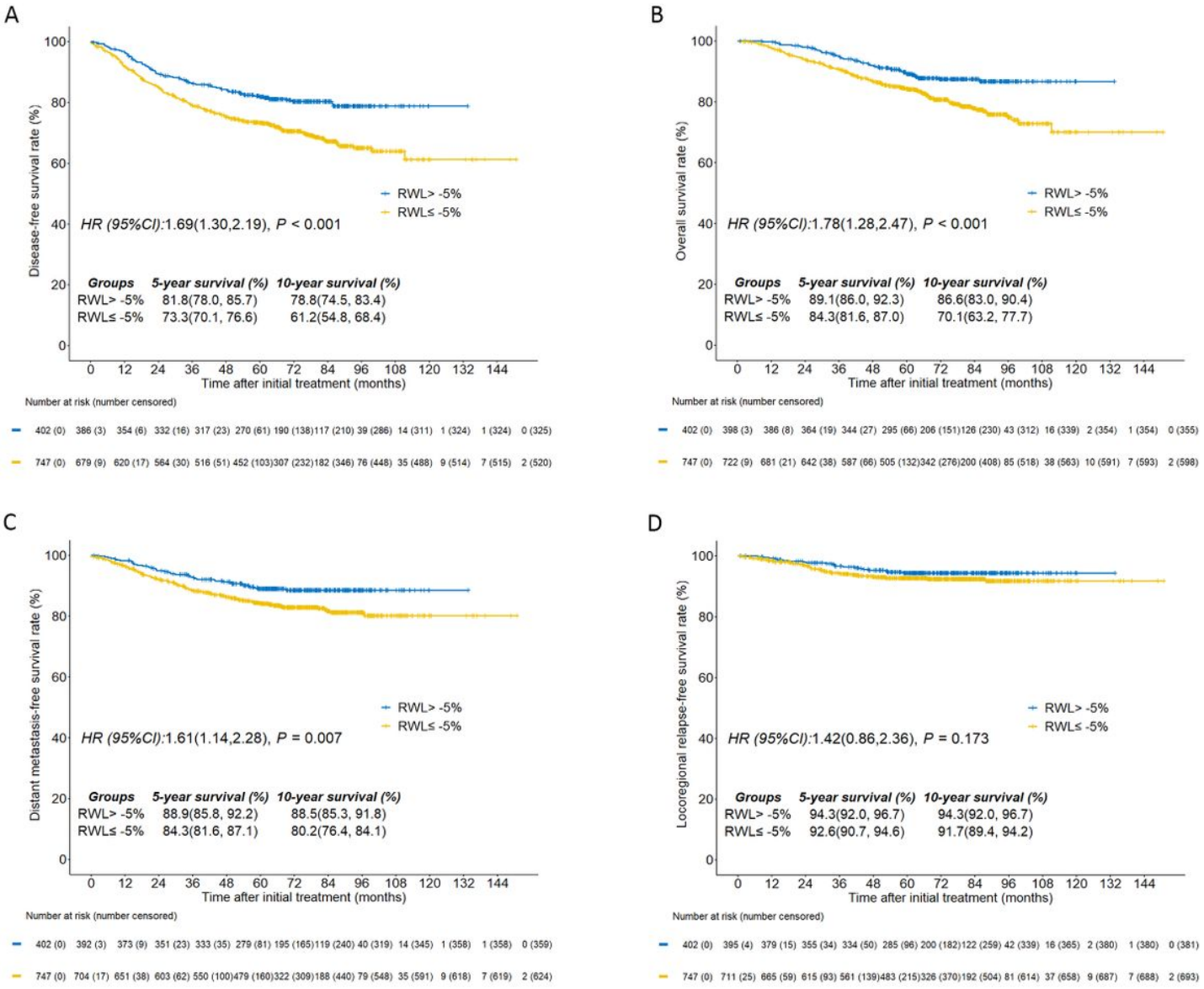

Figure 1

Comparison between the RWL >-5% group and the RWL ≤-5% group for disease-free survival (A), overall survival (B), distant metastasis-free survival (C), and locoregional relapse-free survival (D). RWL, rate of weight loss.