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Weight Loss Despite Nutritional Support Predicts Poor Outcomes After Postoperative Chemoradiotherapy for High-Risk Head and Neck Cancer

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Study type: Clinical study

Abstract.

Background

Weight loss is common in patients with locally advanced head and neck squamous cell carcinoma (LA-HNSCC) and is associated with poor prognosis. However, its prognostic significance in patients receiving nutritional support from surgery through postoperative chemoradiotherapy (CRT) remains unclear. We evaluated the impact of treatment-related weight loss on clinical outcomes in this setting.

Methods

This retrospective study included patients with high-risk LA-HNSCC treated with surgery, postoperative CRT, and nutritional intervention. Pre-CRT weight loss was defined as the percentage change in body weight between surgery and CRT initiation and analyzed using a 5% cutoff. Associations with recurrence-free survival (RFS), overall survival (OS), and adverse events were evaluated.

Results

A total of 105 patients were included. Median pre-CRT and overall weight loss were 4.8% and 7.9%, respectively. Patients with recurrence experienced greater pre-CRT weight loss than those without recurrence (6.1% vs. 4.0%, $p = 0.004$). Patients with $\geq 5\%$ pre-CRT weight loss had significantly worse RFS and OS (log-rank $p = 0.001$ and $p < 0.001$). In multivariable analysis, $\geq 5\%$ pre-CRT weight loss remained independently associated with poorer RFS (HR 2.54, 95% CI 1.35–4.80). The incidence of grade ≥ 3 adverse events was comparable between groups (81.8% vs. 86.0%, $p = 0.75$).

Conclusion

Pre-CRT weight loss of $\geq 5\%$ was independently associated with poorer RFS in patients with high-risk LA-HNSCC undergoing surgery followed by postoperative CRT despite nutritional intervention. Pre-CRT weight loss may be a simple and clinically useful prognostic marker in this setting.

Keywords Locally advanced head and neck squamous cell carcinoma (LA-HNSCC) · Pre-CRT weight loss · Postoperative chemoradiotherapy (CRT) · Recurrence-free survival (RFS) · Prognostic nutritional marker

INTRODUCTION

Head and neck squamous cell carcinoma (HNSCC) is a major global health burden, with 891,453 new cases and 458,107 deaths reported in 2020 [1]. Despite advances in antitumor agents, treatment schedules, and multimodal approaches, improvements in survival and quality of life have been modest [2–6]. Overall outcomes remain unsatisfactory, highlighting the need to further refine therapeutic strategies.

Excess body weight contributes to carcinogenesis, tumor progression, invasion, and metastasis in various malignancies through mechanisms including chronic inflammation, hormonal dysregulation, insulin resistance, immune dysfunction, and altered energy metabolism [7–9]. However, weight loss in patients with curatively treated HNSCC predicts poor prognosis and is thought to be mediated by reduced treatment tolerance, progressive sarcopenia, systemic inflammation, and impaired immune function [10, 11].

Unintended weight loss is common during treatment for locally advanced (LA)-HNSCC. LA-HNSCC is typically managed using a multidisciplinary approach combining surgery, radiotherapy, chemoradiotherapy (CRT), and perioperative systemic therapy, imposing substantial physiological stress [12, 13]. Extranodal extension (ENE) and positive surgical margins are well-established high-risk features for which postoperative CRT provides a survival benefit [14, 15]. Consequently, treatment-related weight loss is frequently encountered in patients undergoing surgery followed by postoperative CRT .

Weight loss is associated with poor survival outcomes in patients with LA-HNSCC [16–19]. Studies investigating the impact of weight change in head and neck cancer have been highly heterogeneous in patient populations and treatment modalities, limiting the generalizability of their findings. Consequently, the prognostic significance of weight loss in the specific treatment sequence of surgery followed by postoperative CRT remains unclear.

Nutritional status is as an important prognostic factor in patients with HNSCC, and nutritional interventions have been associated with reduced treatment-related weight loss and improved survival [10, 20, 21]. However, some patients continue to experience substantial weight loss despite receiving nutritional support. Although several studies have examined the prognostic impact of weight loss in HNSCC, the clinical significance of weight change across the full treatment course from surgery to completion of postoperative CRT in patients receiving nutritional intervention remains unclear.

Therefore, this study aimed to evaluate the prognostic impact of weight change in patients with LA-HNSCC treated with surgery followed by postoperative chemoradiotherapy while receiving nutritional support.

Methods

Ethics approval and consent to participate

This retrospective study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of the Japanese Foundation for Cancer Research (Approval No. 2023-GB-076). Study information was disclosed on the institutional website, and patients were provided with the opportunity to opt out.

Study Design and Patients

This retrospective study was conducted at Cancer Institute Hospital, Japanese Foundation for Cancer Research, which maintains Japan's largest cancer registry, between January 2017 and May 2025. Eligible patients had high-risk LA-HNSCC arising of the oropharynx, oral cavity, hypopharynx, or larynx and underwent postoperative CRT. Inclusion criteria age ≥ 18 years, Eastern Cooperative Oncology Group performance status of 0–1, and pathologically confirmed extranodal extension (ENE) and/or positive surgical margins. All patients received postoperative intensity-modulated radiotherapy (66 Gy in 33 fractions) with concurrent weekly cisplatin (40 mg/m²). All patients also received dietitian-led nutritional intervention throughout treatment. Patients who underwent re-operation before CRT or developed distant metastases before or during postoperative treatment were excluded. Body weight was measured before surgery, at CRT initiation, and at CRT completion. Pre-CRT weight loss was defined as the percentage change in body weight between surgery and CRT initiation and analyzed using a 5% cutoff. The analysis included sex, age at diagnosis, ECOG performance status, smoking history, primary tumor site, pre-CRT prognostic nutritional index (PNI), tumor stage (T4 vs. non-T4), nodal burden (<4 vs. ≥ 4 metastatic lymph nodes), ENE, surgical margin status, cumulative cisplatin dose (<200 vs. ≥ 200 mg/m²), gastrostomy status, and time from surgery to CRT initiation as variables. Pre-CRT weight loss was the primary exposure variable.

Outcomes

The study investigated the association between treatment-related body weight changes and clinical outcomes. Clinical outcomes included recurrence-free survival (RFS), overall survival (OS), and grade ≥ 3 adverse events (AEs). RFS was defined as the time from CRT initiation to disease recurrence or death from any cause, whichever occurred first. OS was defined as the time from CRT initiation to death from any cause. Patients without an event were censored at the date of last follow-up. AEs were graded according to the Common Terminology Criteria for Adverse Events, version 5.0.

Statistical analyses

Body weight changes during the pre-CRT period, during CRT, and throughout the entire treatment course were compared between recurrence and non-recurrence groups using the Wilcoxon rank-sum test. Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables were compared using Fisher's exact or chi-square tests, as appropriate. Survival curves were estimated using the Kaplan–Meier method and compared

using the log-rank test. Median follow-up was estimated using the reverse Kaplan–Meier method. Cox proportional hazards models evaluated prognostic factors for RFS and OS, with clinically relevant variables included in multivariable analyses. Pairwise correlations were assessed using Spearman’s rank correlation analysis. Statistical analyses were performed using R version 4.4.3 (R Foundation for Statistical Computing, Vienna, Austria). Statistical tests were two-sided, and statistical significance was defined as $p < 0.05$ was considered statistically significant.

Results

A total of 135 patients with high-risk LA-HNSCC who underwent postoperative chemoradiotherapy were initially identified. Twenty-eight patients who underwent re-operation before adjuvant CRT and two patients who developed distant metastasis before or during postoperative treatment were excluded (Fig. 1). The final cohort included 105 patients with baseline patient characteristics summarized in Table 1. Median body weight change was -4.8% (IQR, -7.4 to -1.0) during the pre-CRT period and -7.9% (IQR, -12.1 to -5.8) across the entire treatment course (Fig. 2A). Patients with recurrence had significantly greater weight loss during the pre-CRT period than those without recurrence (6.1% vs. 4.0% ; $p = 0.004$) (Fig. 2B). No significant differences were observed in weight loss during CRT (4.5% vs. 4.5% ; $p = 0.81$) or across the entire treatment course (9.5% vs. 7.5% ; $p = 0.083$). Baseline characteristics were generally balanced between patients with $<5\%$ and $\geq 5\%$ pre-CRT weight loss (Table 2). The only significant difference was baseline body mass index (BMI), which was higher in the $\geq 5\%$ weight loss group (21.8 vs. 20.4 kg/m², $p = 0.015$). Patients with $\geq 5\%$ pre-CRT weight loss had significantly worse recurrence-free survival (RFS) than those with $<5\%$ weight loss (log-rank $p = 0.001$; Fig. 3A). Similarly, overall survival (OS) was significantly poorer in the $\geq 5\%$ weight loss group than in the $<5\%$ weight loss group (log-rank $p < 0.001$; Fig. 3B). In univariate analyses, $\geq 5\%$ pre-CRT weight loss was significantly associated with worse RFS (HR, 2.72; 95% CI, 1.46–5.07) and OS (HR, 6.10; 95% CI, 2.06–18.06) (Fig. 4A, B). After multivariable adjustment, $\geq 5\%$ pre-CRT weight loss remained an independent predictor of poorer RFS (HR, 2.54; 95% CI, 1.35–4.80). The grade ≥ 3 adverse event incidence did not differ significantly between the two groups (81.8% vs. 86.0% , $p = 0.75$), and no significant differences were observed for individual adverse events (Table 3).

Discussion

Pre-CRT weight loss of $\geq 5\%$ was significantly associated with recurrence-free survival (RFS), and this association remained significant in multivariable analysis. Multivariable analysis for overall survival (OS) was not performed

because only 22 events occurred, raising concerns regarding model overfitting [17, 22]. However, sensitivity analyses including key prognostic variables yielded results consistent with the univariable analysis (Supplement Table 1). Although treatment-related adverse events was comparable between the two groups, patients with $\geq 5\%$ pre-CRT weight loss showed a possible signal increase in radiation dermatitis ($p = 0.061$), warranting further investigation in larger cohorts.

Previous studies evaluating the prognostic impact of weight loss in HNSCC included heterogeneous treatment modalities [16–19]. In contrast, our study analyzed a homogeneous cohort uniformly treated with surgery followed by cisplatin-based postoperative CRT, enabling a more focused assessment of the clinical significance of weight loss. Surgery followed by weekly cisplatin-based postoperative CRT has long been a widely adopted standard treatment for high-risk LA-HNSCC in Japan [15]. However, the treatment landscape is evolving with the introduction of perioperative immune checkpoint inhibitors [3, 4]. Therefore, further studies are needed to determine whether the association between weight loss and clinical outcomes observed in this study remains applicable in the era of perioperative immunotherapy.

Previous studies have demonstrated a progressive decline in body weight from surgery through CRT [17]. Consistent with these findings, continuous weight loss was observed throughout the treatment course in the present study. Although previous studies reported weight loss of approximately 6.8%–9.2% during postoperative CRT alone, data on cumulative weight loss from to through completion of postoperative CRT remain limited [23, 24]. In our cohort, the median overall weight loss across the treatment course was 7.9%.

Several mechanisms, including reduced treatment tolerance, systemic inflammation, and impaired immune function, have been proposed to explain the association between weight loss and poor outcomes [10, 11]. In this study, comparable radiotherapy completion rates and cumulative cisplatin doses between groups suggested that reduced treatment tolerance does not fully explain our findings. The PNI, a composite marker of nutritional and immune status is a prognostic factor in patients with HNSCC [25–27]. Although systemic inflammation and impaired immune function may contribute to poor outcomes, showed minimal correlation with PNI (Supplement Table 2). Pre-CRT weight loss also remained prognostic after adjustment for PNI, showing that it captures prognostic information beyond conventional nutritional and immunological indices. Patients with $\geq 5\%$ weight loss had a higher

baseline BMI. However, BMI was not associated with recurrence, indicating that the findings were unlikely to be driven by differences in baseline body size.

Despite structured nutritional intervention, weight loss from surgery to postoperative CRT was associated with poorer clinical outcomes. Given the retrospective nature of this study, whether weight loss directly contributes to worse prognosis or merely reflects a higher risk of recurrence remains unclear. Nevertheless, persistent weight loss despite nutritional support emerged as a clinically relevant prognostic marker. Further studies are needed to clarify the causes of postoperative weight loss and determine whether intensified nutritional management can improve prognosis.

This study had several limitations. First, its retrospective single-center design may have introduced selection bias. However, all patients received a uniform treatment strategy consisting of surgery followed by weekly cisplatin-based postoperative chemoradiotherapy, reducing treatment heterogeneity. Second, the sample size was relatively small. Nevertheless, the association between pre-CRT weight loss and survival outcomes remained consistent across multiple analytical approaches, including sensitivity analyses adjusted for key prognostic factors. Finally, because the study population consisted predominantly of Japanese patients treated at a high-volume cancer center, the generalizability of these findings to other populations remains uncertain.

Conclusion

In conclusion, pre-CRT weight loss of $\geq 5\%$ was independently associated with poorer recurrence-free survival in patients with high-risk LA-HNSCC undergoing surgery followed by postoperative chemoradiotherapy, despite standardized nutritional intervention. These findings suggest that pre-CRT weight loss may be a simple and clinically useful prognostic marker in this setting. Further prospective studies are needed to validate these findings.

Author contributions

Study conception: Y.I, J.Y, S.E, E.T, Y.S; Writing the manuscript: Y.I, J.Y, S.E, N.F E.T; Data acquisition: Y.I, J.Y, N.F; Literature review: J.Y, N.F, E.T; Imaging evaluation: J.Y, N.F, K.N, A.O, A.K, Y.S, H.M, S.T, Y.M; Manuscript Supervision: A.O, A.K, Y.S, H.M, S.T, Y.M; Final approval : All authors.

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Data availability statement

The data supporting the findings of this study are not publicly available owing to patient confidentiality but can be obtained from the corresponding author upon reasonable request.

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Conflict of Interest:

J.Y: Honoraria for lectures from Kyowa Kirin. **N.F:** Research funding to the author's institution from Eisai; honoraria for lectures and presentations, including speaker bureaus, from Ono Pharmaceutical, MSD, Merck Biopharma, Lilly, Eisai, Novartis, Thermo Fisher Scientific, Daiichi Sankyo, and AstraZeneca. **Y.M:** Research funding to the author's institution from MSD, Daiichi Sankyo, UCB Japan; honoraria for lectures and presentations, including speaker bureaus, from Takeda Pharmaceutical, Ono Pharmaceutical, MSD, Eisai, Bristol-Myers Squibb, Merck biopharma, Janssen and Astellas Pharma. **S.T:** Research funding to the author's institution from Daiichi Sankyo, Sanofi, Eisai, and Bayer; honoraria for lectures and presentations, including speaker bureaus, from Daiichi Sankyo, Eisai, Bayer, Taiho Pharmaceutical, MSD, Chugai Pharma, Bristol-Myers Squibb Japan, Ono Pharmaceutical, and Lilly Japan; consulting from Bayer.

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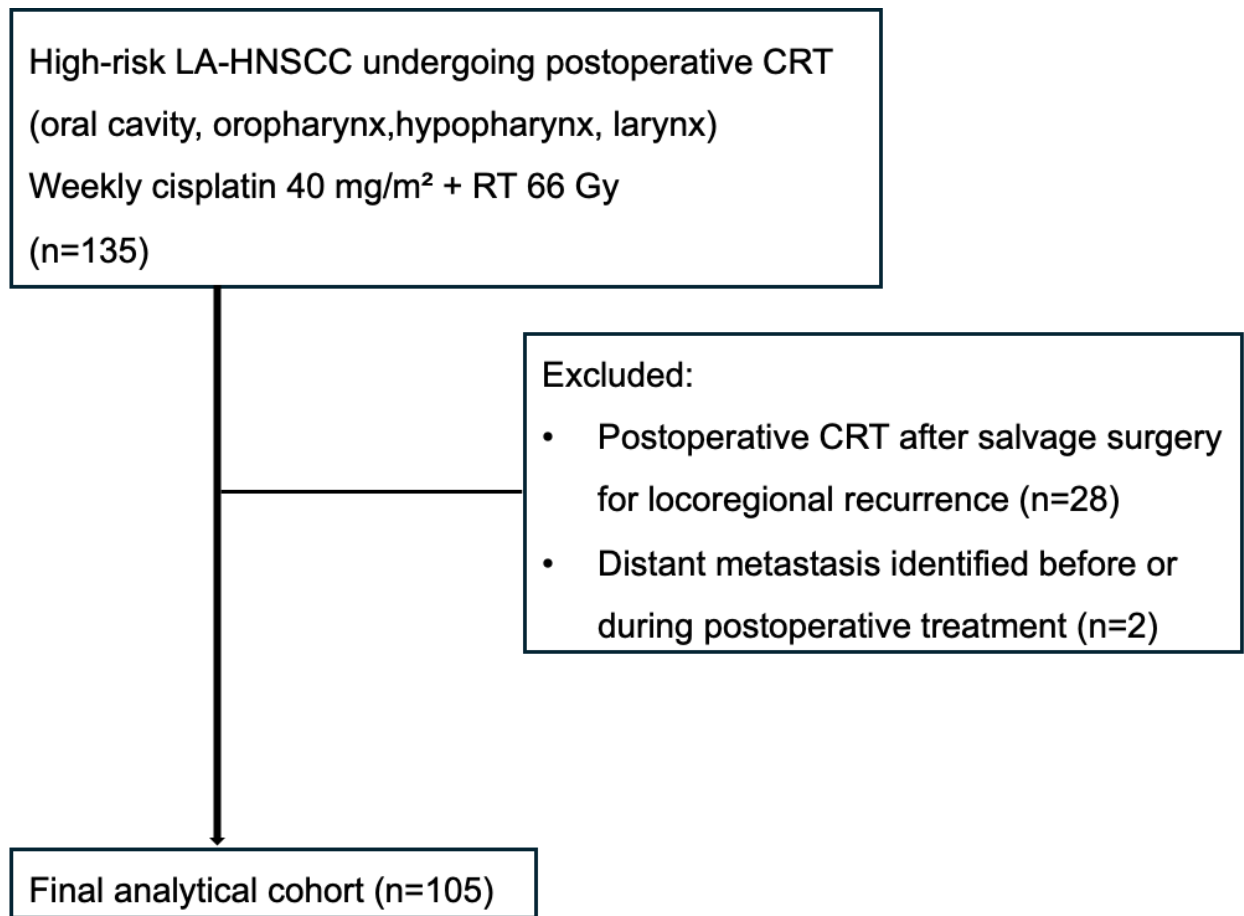


Fig. 1 Patient selection flowchart.

A total of 135 patients with high-risk locally advanced head and neck squamous cell carcinoma (LA-HNSCC) who underwent postoperative chemoradiotherapy (CRT) were initially identified. Patients were excluded if they received postoperative CRT following salvage surgery for locoregional recurrence (n = 28) and developed distant metastasis before or during postoperative treatment (n = 2). The final analytical cohort included 105 patients.

Figure 2A

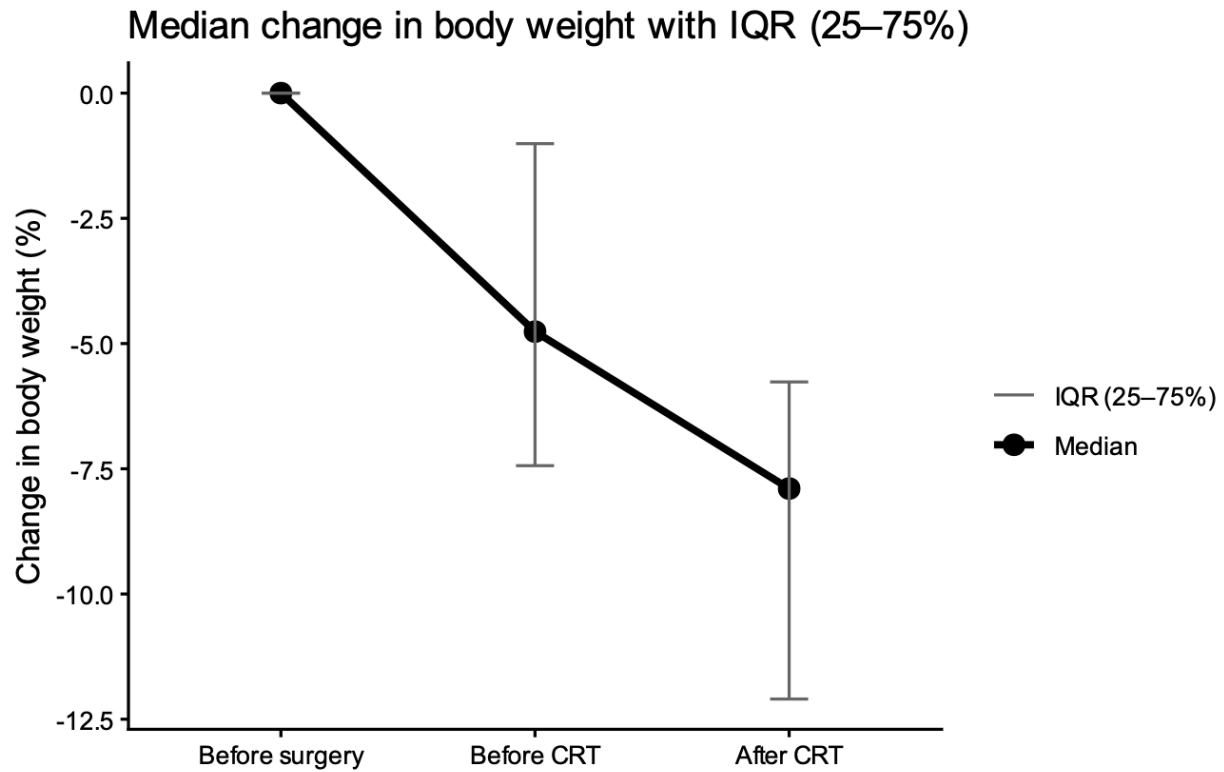


Figure 2B

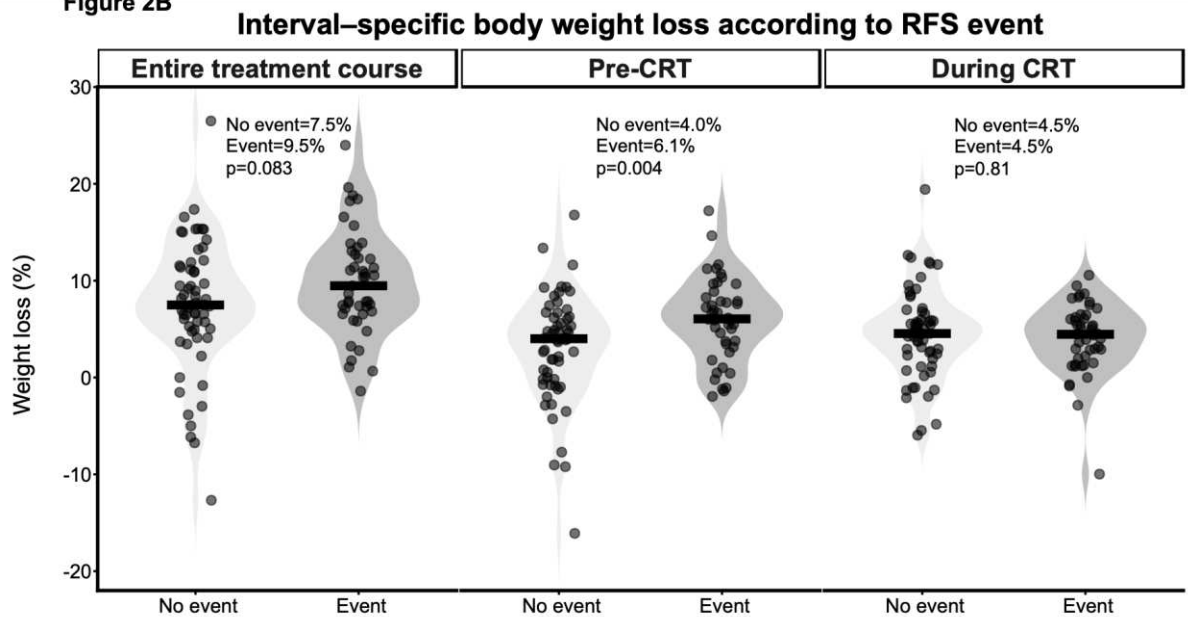


Fig. 2 Body weight changes during the treatment course and according to recurrence status.

(A) Median percentage change in body weight from before surgery to chemoradiotherapy (CRT) initiation and from

surgery to CRT completion. Error bars represent the interquartile range (IQR).

(B) Percentage body weight loss during the entire treatment course, the pre-CRT period, and during CRT, stratified by recurrence-free survival (RFS) status. Horizontal bars indicate median values. P values were calculated using the Wilcoxon rank-sum test.

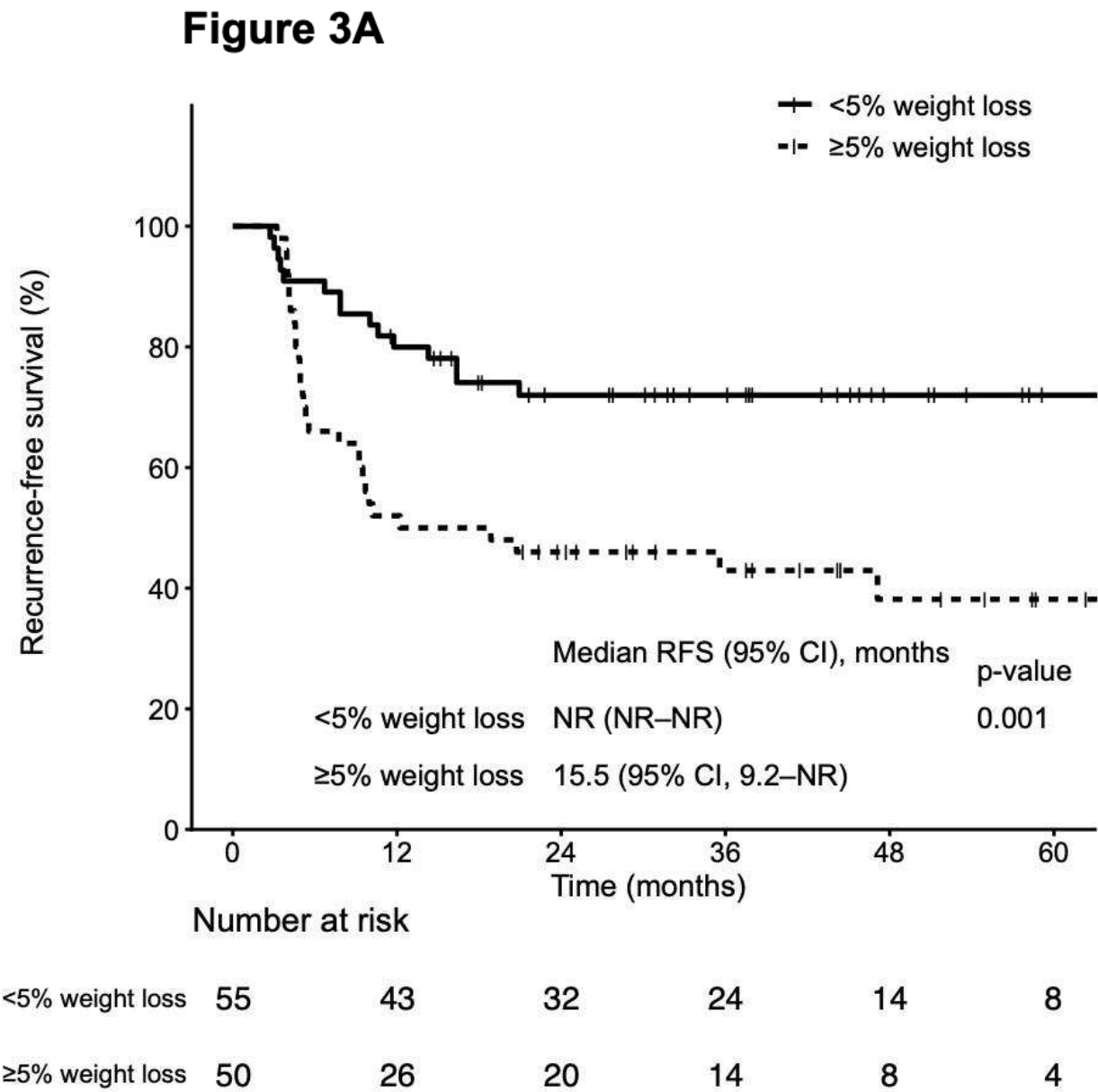


Figure 3B

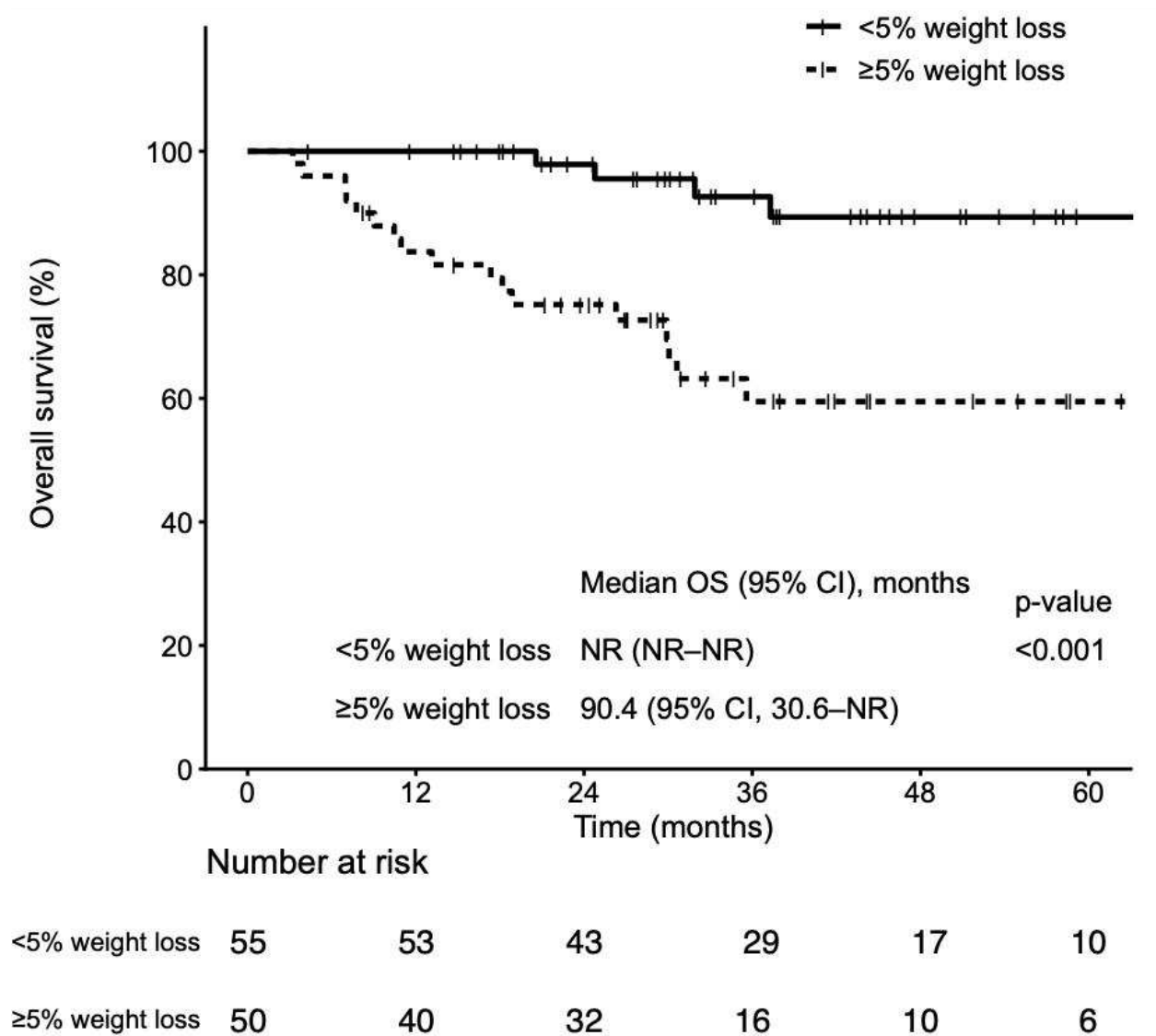


Fig. 3 Kaplan–Meier analysis of recurrence-free survival and overall survival according to pre-CRT weight loss.

(A) Recurrence-free survival (RFS) stratified by pre-CRT weight loss (<5% vs. ≥5%). Patients with ≥5% weight loss before postoperative chemoradiotherapy initiation exhibited significantly poorer RFS than those with <5% weight loss.

(B) Overall survival (OS) stratified by pre-CRT weight loss (<5% vs. ≥5%). Patients with ≥5% pre-CRT weight loss showed significantly worse OS than those with <5% weight loss.

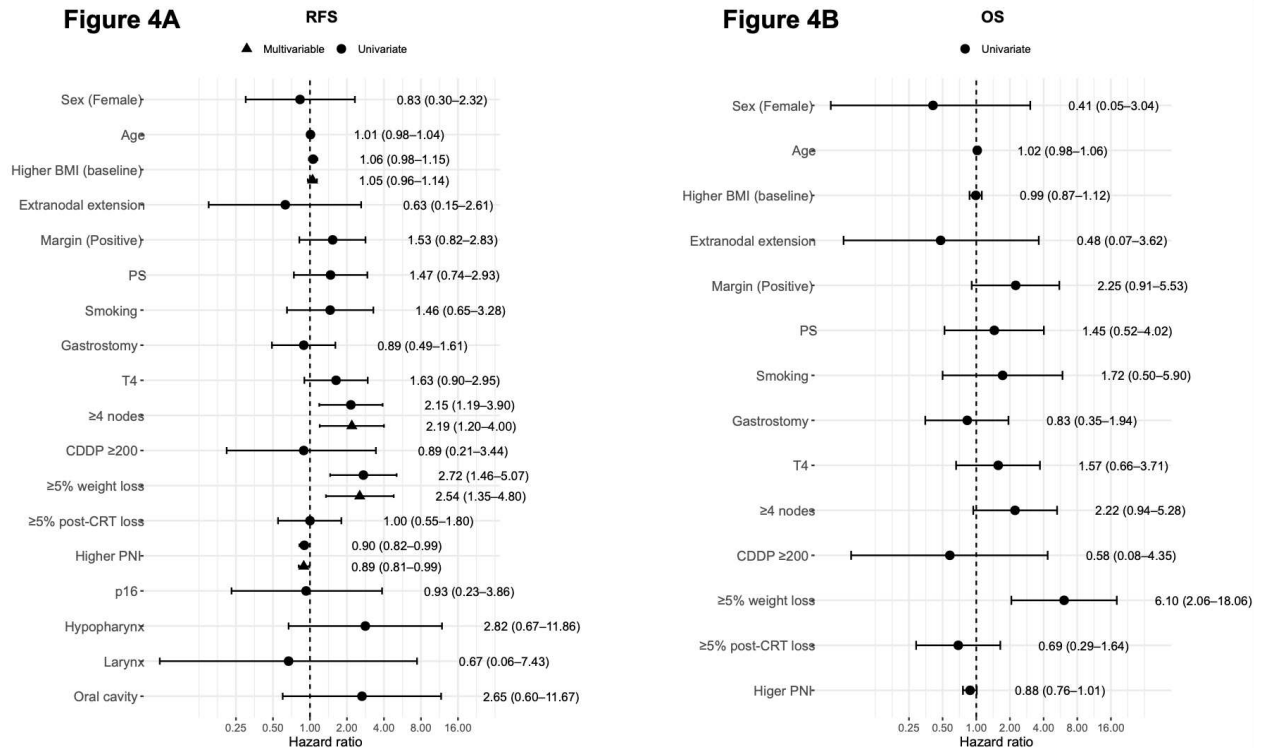


Fig. 4 Univariate and multivariable Cox proportional hazards analyses of factors associated with recurrence-free survival and overall survival.

(A) Forest plot showing hazard ratios (HRs) and 95% confidence intervals (CIs) for recurrence-free survival (RFS). Circles indicate univariate analysis results, and triangles indicate multivariable model results. Pre-CRT weight loss $\geq 5\%$ and involvement of ≥ 4 lymph nodes were independently associated with poorer RFS, whereas higher prognostic nutritional index (PNI) was independently associated with improved RFS.

(B) Forest plot showing hazard ratios (HRs) and 95% confidence intervals (CIs) for overall survival (OS) based on univariate Cox regression analyses. Pre-CRT weight loss $\geq 5\%$ was significantly associated with worse OS. Horizontal lines represent 95% confidence intervals, and the vertical dashed line indicates a hazard ratio of 1.0.

Age (median [IQR])	64 (56–71)
Follow-up period (months)	38.0 (32.3–44.4)
Sex - Male	93 (88.6%)
- Female	12 (11.4%)
BMI (baseline)	21.1 (19.4–24.1)

Performance status - 0	84 (80.0%)
- 1	21 (20.0%)
Primary tumor site - Oropharynx	10 (9.5%)
- Hypopharynx	54 (51.4%)
- Larynx	8 (7.6%)
- Oral cavity	33 (31.4%)
p16 - positive	5 (4.8%)
- negative	100 (95.2%)
Extranodal extension - Negative	4 (3.8%)
- Positive	101 (96.2%)
Surgical margin - Present	14 (13.3%)
- Absent	89 (84.8%)
- Unknown	2 (1.9%)
Smoking history	84 (80.0%)
Gastrostomy	48 (45.7%)
T stage - T1–3	56 (53.3%)
- T4	49 (46.7%)

Lymph node metastases - 0–3 nodes	63 (60.0%)
- ≥ 4 nodes	42 (40.0%)
Radiation completion - completion	101 (96.2%)
- not completion	4 (3.8%)
Cisplatin dose - $<200\text{mg/m}^2$	5 (4.8%)
- $\geq 200\text{mg/m}^2$	100 (95.2%)
PNI before CRT	41.0 (38.0–43.0)

Table 1 Baseline characteristics of the study population

Baseline demographic, clinical, and treatment characteristics of patients with high-risk locally advanced head and neck squamous cell carcinoma (LA-HNSCC) undergoing surgery followed by postoperative chemoradiotherapy (CRT). Data are presented as median (interquartile range [IQR]).

Variable	$<5\%$ weight loss (n=55)	$\geq 5\%$ weight loss (n=50)	p value
Age, median (IQR)	65 (53–72)	63.5 (56–68)	0.81
Follow-up period (months)	38.0 (31.8–46.7)	38.0 (29.3–44.4)	—
Sex - Male	50 (91%)	43 (86%)	0.43
- Female	5 (9%)	7 (14%)	
BMI (baseline)	20.4 (18.5–23.4)	21.8 (20.2–25.1)	0.015
Performance status - 0	46 (84%)	38 (76%)	0.33

- 1	9 (16%)	12 (24%)	
Primary tumor site - Oropharynx	5 (9%)	5 (10%)	0.15
- Hypopharynx	29 (53%)	25 (50%)	
- Larynx	7 (13%)	1 (2%)	
- Oral cavity	14 (25%)	19 (38%)	
p16 - positive	2 (4%)	3 (6%)	0.57
- negative	53 (96%)	47 (94%)	
Extranodal extension - Negative	2 (4%)	2 (4%)	0.92
- Positive	53 (96%)	48 (96%)	
Surgical margin - Present	7 (13%)	7 (14%)	0.31
- Absent	48 (87%)	41 (82%)	
- Unknown	0 (0%)	2 (4%)	
Smoking history	44 (80%)	40 (80%)	1.00
Gastrostomy	23 (42%)	25 (50%)	0.40
T stage - T1–3	27 (49%)	29 (58%)	0.36
- T4	28 (51%)	21 (42%)	

Lymph node metastases - 0–3 nodes	35 (64%)	28 (56%)	0.43
- ≥4 nodes	20 (36%)	22 (44%)	
Radiation completion - completion	53 (96%)	48 (96%)	0.92
- not completion	2 (4%)	2 (4%)	
Cisplatin dose - <200 mg/m ²	3 (5%)	2 (4%)	0.73
- ≥200 mg/m ²	52 (95%)	48 (96%)	
PNI before CRT, median (IQR)	40.0 (38.0–43.0)	40.5 (38.0–43.0)	0.94

Table 2 Baseline characteristics according to pre-CRT weight loss

Baseline demographic, clinical, and treatment characteristics stratified by pre-CRT weight loss (<5% vs. ≥5%). Continuous variables are presented as median (interquartile range [IQR]) and categorical variables as number (%). P values were calculated using the Wilcoxon rank-sum, Fisher's exact, or chi-square tests, as appropriate.

Adverse event	<5% weight loss	≥5% weight loss	P value
Any Grade ≥3 AE	45/55 (81.8%)	43/50 (86.0%)	0.75
Anemia	1/55 (1.8%)	4/50 (8.0%)	0.19
Leukocytopenia	34/55 (61.8%)	27/50 (54.0%)	0.54
Neutropenia	12/55 (21.8%)	16/50 (32.0%)	0.34
Thrombocytopenia	2/55 (3.6%)	0/50 (0.0%)	0.50
Hypocalcemia	2/55 (3.6%)	3/50 (6.0%)	0.67

Hyperkalemia	0/55 (0.0%)	1/50 (2.0%)	0.48
Hypokalemia	2/55 (3.6%)	2/50 (4.0%)	1.00
Mucositis	9/55 (16.4%)	9/50 (18.0%)	1.00
Radiation dermatitis	4/55 (7.3%)	11/50 (22.0%)	0.061
Anorexia	16/55 (29.1%)	22/50 (44.0%)	0.17
Nausea	6/55 (10.9%)	5/50 (10.0%)	1.000
Dysphagia	4/55 (7.3%)	8/50 (16.0%)	0.27
Constipation	0/55 (0.0%)	1/50 (2.0%)	0.48
Infection	7/55 (12.7%)	11/50 (22.0%)	0.32
Fatigue	1/55 (1.8%)	0/50 (0.0%)	1.00
Vomiting	3/55 (5.5%)	0/50 (0.0%)	0.25
Lung infection	1/55 (1.8%)	1/50 (2.0%)	1.00
Tracheitis	1/55 (1.8%)	0/50 (0.0%)	1.00
Ileus	0/55 (0.0%)	1/50 (2.0%)	0.48
Sick sinus syndrome	0/55 (0.0%)	1/50 (2.0%)	0.48
Thromboembolic event	1/55 (1.8%)	0/50 (0.0%)	1.00

Table 3 Comparison of grade ≥ 3 adverse events according to pre-CRT weight loss

Data are presented as number of patients (%). Hematologic adverse events were defined as grade ≥ 3 and non-hematologic adverse events as grade ≥ 2 according to the Common Terminology Criteria for Adverse Events (CTCAE). Patients were stratified according to pre-CRT weight loss ($<5\%$ vs. $\geq 5\%$).

Sensitivity model	Variable	HR	95% CI	P value
Model 1	Pre-CRT weight loss $\geq 5\%$	6.01	2.03–17.80	0.001
	≥ 4 nodes	2.15	0.91–5.11	0.083
Model 2	Pre-CRT weight loss $\geq 5\%$	6.53	2.20–19.42	0.001
	PNI during CRT	0.86	0.74–0.99	0.043
Model 3	Pre-CRT weight loss $\geq 5\%$	7.12	2.33–21.74	0.001
	Baseline BMI	0.92	0.79–1.06	0.25

Supplementary Table 1 Sensitivity analyses evaluating the association between pre-CRT weight loss and overall survival

Multivariable Cox proportional hazards models were constructed to assess the robustness of the association between pre-CRT weight loss and overall survival (OS).

Variable	Pre-CRT weight loss $\geq 5\%$	BMI	PNI	≥ 4 nodes
Pre-CRT weight loss $\geq 5\%$	1	0.24	0.008	0.078
BMI	0.24	1	0.10	-0.049
PNI	0.008	0.102	1	-0.061
N4 group	0.078	-0.049	-0.061	1

Supplementary Table 2 Correlation matrix of variables included in the sensitivity analyses

Pairwise correlation coefficients were calculated among pre-CRT weight loss, baseline body mass index (BMI), prognostic nutritional index (PNI), and nodal burden (≥ 4 metastatic lymph nodes) to evaluate potential collinearity among candidate prognostic factors.