

Weight loss and longitudinal weight trajectories during neoadjuvant chemoradiotherapy predict survival after esophagectomy for locally advanced esophageal squamous cell carcinoma

Guiyu Huang

sichuan cancer hospital

Bingrong He

sichuan cancer hospital

Zheng Jia

sichuan cancer hospital

Xin Liu

sichuan cancer hospital

Hanfeng Zhang

sichuan cancer hospital

Xiaoli Tang

sichuan cancer hospital

Rendi Tian

sichuan cancer hospital

Long Zhang

zhanglong@scszluy.org.cn

sichuan cancer hospital

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Abstract

Background

Weight loss frequently occurs during neoadjuvant chemoradiotherapy (NCRT) for locally advanced esophageal squamous cell carcinoma (LA-ESCC). However, whether the prognostic significance of weight loss differs across treatment phases has not been well defined.

Methods

We retrospectively reviewed 377 patients with LA-ESCC who received NCRT followed by curative esophagectomy between 2017 and 2023. Body weight was collected at predefined milestones spanning treatment initiation to the early postoperative period. The associations between phase-specific weight loss and survival outcomes were examined using multivariable Cox regression models. Patterns of longitudinal weight change were characterized using latent class trajectory analysis.

Results

Over a median follow-up of 60.2 months. Weight loss during NCRT emerged as an independent predictor of both poorer OS (hazard ratio[HR] 2.21, 95%CI 1.39–3.51, $P = 0.001$) and PFS(HR 1.87, 95% CI 1.23–2.84, $P = 0.003$). Weight loss during the interval between NCRT completion and before surgery was also associated with inferior OS(HR 2.0, 95%CI 1.18–3.4, $P = 0.01$). In contrast, weight changes before treatment initiation and during the early postoperative period were not associated with survival. Four distinct weight trajectories were identified. Patients with a low gradual decrease trajectory had significantly worse outcomes compared with those whose weight remained stable or increased(HR 2.35, 95% CI 1.4–3.95, $P = 0.001$). Mortality risk increased progressively with greater weight loss during NCRT. The prognostic impact of weight loss was particularly evident among patients treated with paclitaxel–carboplatin and those with a higher baseline performance status.

Conclusions

Among patients with LA-ESCC undergoing trimodality treatment, weight loss during NCRT—but not at other treatment stages—was associated with survival after esophagectomy. Longitudinal weight trajectories provided complementary prognostic information beyond conventional assessments of weight change.

Introduction

Esophageal cancer (EC) remains a major global health challenge, ranking seventh in incidence and sixth in cancer-related mortality worldwide^[1, 2]. Despite advances in multimodality treatment, long-term

outcomes remain unsatisfactory, particularly for patients with locally advanced disease^[3, 4]. For locally advanced esophageal squamous cell carcinoma (LA-ESCC), neoadjuvant chemoradiotherapy (NCRT) followed by surgery is the current standard treatment and has been shown to improve resection rates, locoregional control, and survival compared with surgery alone^[5–9].

Weight loss is a common feature of esophageal cancer and may arise from dysphagia, systemic inflammation, cancer-associated metabolic alterations, and treatment-related toxicities^[10–16]. Accumulating evidence suggests that nutritional deterioration is associated with impaired treatment tolerance and adverse clinical outcomes^[16–18]. Most previous studies, however, have focused on weight loss at a single time point, typically before or after surgery, without accounting for dynamic changes throughout the treatment pathway^[19–21].

For patients undergoing NCRT followed by esophagectomy, weight may change substantially during different phases of treatment. The clinical implications of weight loss during active neoadjuvant therapy may differ from those of weight loss occurring after treatment completion or around surgery. Whether the timing of weight loss influences its prognostic significance remains unclear. Furthermore, little is known about how longitudinal patterns of weight change across the entire treatment course relate to long-term outcomes

We therefore examined weight change from treatment initiation to the early postoperative period in a cohort of patients with LA-ESCC treated with NCRT followed by esophagectomy. Specifically, we evaluated the prognostic relevance of weight loss at different treatment phases and explored whether longitudinal weight trajectories provide additional prognostic information beyond conventional single time-point assessments.

Material and Methods

Study Design and Patients

This retrospective cohort study included consecutive patients with locally advanced esophageal squamous cell carcinoma (LA-ESCC) who underwent neoadjuvant chemoradiotherapy (NCRT) followed by esophagectomy at Sichuan Cancer Hospital between January 2017 and December 2023. The study was approved by the Ethics Committee of Sichuan Cancer Hospital (SCCHEC-02-2023-134) and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived because of the retrospective nature of the study.

Eligible patients were aged 18–80 years, had histologically confirmed ESCC, clinical stage cT1b–2N + or cT3–4a disease according to the 8th edition of the AJCC staging system^[22], completed NCRT followed by curative-intent esophagectomy, and had complete weight records at predefined assessment points (Supplementary Fig. 1). Patients undergoing palliative or salvage surgery, receiving radiotherapy doses

outside 40–45 Gy, presenting with concurrent malignancies, or treated with non-taxane-based chemotherapy regimens were excluded.

Treatment

All patients received two cycles of platinum-based chemotherapy (cisplatin, carboplatin, or nedaplatin) combined with a taxane (paclitaxel or docetaxel). Concurrent radiotherapy was delivered to a total dose of 40–45 Gy in daily fractions of 1.8–2.0 Gy, five days per week. Esophagectomy was performed using either the McKeown or Ivor Lewis approach according to tumour location and surgeon preference.

Data collection and weight assessment

Clinical data were retrieved from electronic medical records, including demographic characteristics, smoking and alcohol history, Karnofsky Performance Status (KPS), Patient-Generated Subjective Global Assessment (PG-SGA), body mass index (BMI), nutritional impact symptoms (NIS), tumour characteristics, treatment regimen, and nutritional support.

Body weight was assessed at five predefined time points: baseline (Time 0, within one month before treatment), initiation of NCRT (Time 1), completion of NCRT (Time 2), within one week before surgery (Time 3), and the early postoperative period (Time 4). Weight-loss percentage (WL%) was calculated relative to the preceding assessment point.

Pre-treatment unintentional weight loss was evaluated according to international nutritional assessment recommendations^[23]. Patients reporting weight loss within the previous month were asked to provide their earlier body weight when available. When exact values could not be recalled, changes in clothing or jewellery fit were used as supportive indicators of clinically relevant weight loss^[23]. Clinically significant weight loss was defined as a reduction of > 5% of body weight^[24, 25].

Follow-up and outcomes

Patients were followed every three months during the first two postoperative years, every six months during years 3–5, and annually thereafter. Survival information was obtained from hospital records, telephone interviews, and registry data.

Overall survival (OS) was defined as the interval from diagnosis to death from any cause or last follow-up. Progression-free survival (PFS) was defined as the interval from diagnosis to disease progression, recurrence, death, or last follow-up.

Statistical analysis

Categorical variables are presented as frequencies and percentages. Survival was estimated using the Kaplan–Meier method and compared with the log-rank test. Associations between weight loss and survival outcomes were evaluated using Cox proportional hazards models and are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). Multivariable models were adjusted for age, sex, BMI, PG-SGA category, treatment regimen, nutritional support, KPS, smoking status, alcohol consumption, tumour location, clinical stage, and time to surgery..

Latent class trajectory modelling (LCTM) was used to identify longitudinal patterns of weight change. Longitudinal trajectories were derived using weight measurements collected across all five predefined assessment points. The optimal model was selected on the basis of model fit (AIC, BIC, and SABIC), posterior class-membership probabilities, entropy, and clinical interpretability^[26]. Associations between trajectory groups and survival outcomes were subsequently examined using Cox regression models. Restricted cubic spline analyses were performed to assess potential dose–response relationships between weight change and survival.

All analyses were conducted using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). All statistical tests were two-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

Patient characteristics

Among 518 consecutively screened patients, 377 met the eligibility criteria and were included in the analysis. The median age was 62 years, and 311 patients (82.5%) were male. Most patients had good baseline performance status, with 86.5% having a KPS score of 90–100. According to the PG-SGA, 62.1% were classified as being at moderate or high nutritional risk. Baseline demographic, clinical, and treatment characteristics are presented in Table 1.

Table 1
Baseline Characteristics of Patients with
Locally Advanced Esophageal Squamous Cell
Carcinoma

Variables, n (%)	Total (n = 377) n(%)
Age	
<65	237 (62.9)
≥ 65	140 (37.1)
Gender	
Female	66 (17.5)
Male	311 (82.5)
ΔWL%(time0-1)	
No	297 (78.8)
Yes	80 (21.2)
ΔWL%(time1-2)	
No	321 (85.1)
Yes	56 (14.9)
ΔWL%(time2-3)	
No	330 (87.5)
Yes	47 (12.5)
ΔWL%(time3-4)	
No	334 (88.6)
Yes	43 (11.4)
Malnutrition	
No	59 (15.6)
Mild	84 (22.3)
Moderate	164 (43.5)
Severe	70 (18.6)
BMI	
Low weight	24 (6.4)
Normal weight	227 (60.2)

Variables, n (%)	Total (n = 377) n(%)
Overweight	111 (29.4)
Obesity	15 (4.0)
Therapeutic regimen	
TP	134 (35.5)
TC	213 (56.5)
Tax + NDP	30 (8.0)
Nutritional support	
No	168 (44.6)
Yes	209 (55.4)
NIS	
0	67 (17.8)
1	94 (24.9)
≥ 2	216 (57.3)
KPS	
90–100	326 (86.5)
70–80	51 (13.5)
Smoking	
No	136 (36.1)
Yes	241 (63.9)
Drinking	
No	141 (37.4)
Yes	236 (62.6)
Tumor location	
Upper 1/3	48 (12.7)
Middle 1/3	152 (40.3)
Lower 1/3	177 (46.9)
Clinical stage	
Ⅱ	20 (5.3)

Variables, n (%)	Total (n = 377) n(%)
☒	273 (72.4)
☒	84 (22.3)
TTS	
≤ 42	343(91)
>42	32(9)

Patterns of weight change during treatment

Body weight declined progressively from baseline to completion of NCRT, showed partial recovery before surgery, and decreased again during the early postoperative period (Supplementary Fig. 2A). The prevalence and magnitude of weight loss differed across treatment phases. Before treatment initiation (Time 0–1), 80 patients (21.2%) experienced weight loss, with a mean change of – 2% (SD 4%). During NCRT (Time 1–2), weight loss occurred in 56 patients (14.9%), with a mean change of – 1% (SD 6%). Between completion of NCRT and surgery (Time 2–3), 47 patients (12.5%) lost weight, whereas 43 patients (11.4%) experienced weight loss during the perioperative period (Time 3–4)(Supplemental Fig. 2B).

Weight loss at different treatment phases and survival

After a median follow-up of 60.2 months (95% CI 56.4–62.4), the 5-year OS and PFS rates were 67.5% and 60.7%, respectively (Supplementary Fig. 3). In univariate analyses, weight loss during the NCRT (Time 1–2) was associated with poorer OS (HR 2.17, 95% CI 1.41–3.34, $P < 0.001$) and PFS (HR 1.89, 95% CI 1.28–2.79, $P = 0.001$). Weight loss occurring between completion of NCRT and surgery (Time 2–3) was also associated with worse OS (HR 1.67, 95% CI 1.02–2.73, $P = 0.04$)(Fig. 1). After multivariable adjustment, weight loss during NCRT remained independently associated with both OS (HR 2.21, 95% CI 1.39–3.51, $P = 0.001$) and PFS (HR 1.87, 95% CI 1.23–2.84, $P = 0.003$). Weight loss during the interval between NCRT completion and surgery was likewise associated with inferior OS (HR 2.00, 95% CI 1.18–3.40, $P = 0.01$) (Fig. 1, Supplemental Table 1, Supplemental Table 2). Kaplan–Meier analyses yielded consistent results. Patients who lost weight during NCRT had significantly lower 5-year OS (48.9% vs. 70.8%, $P < 0.001$) and PFS(46.4% vs. 63.1%, $P < 0.001$) than those without weight loss. Weight loss between completion of NCRT and surgery was also associated with lower 5-year OS (53.8% vs. 69.5%, $P = 0.028$)(Fig. 2). In contrast, weight loss before treatment initiation or during the perioperative period was not associated with survival (Supplementary Fig. 4).

Subgroup analyses

Significant interactions were observed for chemotherapy regimen and baseline KPS score (both P for interaction < 0.05) (Fig. 3). Among patients treated with paclitaxel–carboplatin, weight loss was associated with increased risks of death (HR 3.1, 95% CI 1.74–5.52, $P < 0.001$) and disease progression (HR 1.93, 95% CI 1.13–3.29, $P = 0.015$). Similarly, among patients with KPS scores of 90–100, weight loss was associated with worse OS (HR 2.15, 95% CI 1.3–3.55, $P = 0.003$) and PFS (HR 1.69, 95% CI 1.06–2.71, $P = 0.028$). No significant interactions were identified according to age, sex, nutritional impact symptoms, tumour location, clinical stage, or time to surgery.

Weight-change trajectories and survival

Latent class trajectory modeling identified four distinct patterns of weight change across the treatment course: low gradual increase trajectory ($n = 204$), increase followed by decrease trajectory ($n = 5$), decrease followed by increase trajectory ($n = 16$), and low gradual decrease trajectory ($n = 152$) (Fig. 4; Supplemental Table 3). Although two trajectory classes contained relatively few patients, they were retained because they met predefined model-selection criteria and represented clinically distinct patterns of weight change. Baseline characteristics differed across trajectory groups, particularly with respect to sex distribution, baseline nutritional status, and body mass index (Supplemental Table 4).

Compared with the low gradual increase trajectory, the low gradual decrease trajectory was associated with worse OS (HR = 1.71, 95% CI 1.17–2.51, $P = 0.006$) and PFS (HR = 1.44, 95% CI 1.03–2.00, $P = 0.03$) in unadjusted analyses. After full adjustment, the association remained significant for OS (HR = 2.35, 95% CI 1.4–3.95, $P = 0.001$), whereas the association with PFS was attenuated (HR = 1.54, 95% CI 0.98–2.4, $P = 0.06$) (Table 2). Kaplan–Meier analyses further demonstrated lower 5-year OS (59.7% vs 73.3%, $P = 0.005$) and PFS (57% vs 63.9%, $P = 0.03$) among patients in the low gradual decrease trajectory group (Supplemental Fig. 5). No significant survival differences were observed for the remaining trajectory groups.

Table 2
Multivariable Cox Regression Analyses of Overall Survival and Progression-Free Survival According to Weight Trajectory Groups

Weight index trajectories	Died (N)	Weight Trajectory Groups					
		Model 1		Model 2		Model 3	
		HR (95% CI)	P	HRs (95% CIs)	P	HRs (95% CIs)	P
overall survival							
low gradual increase trajectory	50/204	Reference		Reference		Reference	
low gradual increase trajectory	2/5	1.64 (0.4 ~ 6.76)	0.49	1.56 (0.38 ~ 6.45)	0.54	1.83 (0.4 ~ 8.31)	0.44
decrease followed by increase trajectory	5/16	1.32 (0.53 ~ 3.32)	0.55	1.22 (0.48 ~ 3.07)	0.67	1.67 (0.63 ~ 4.38)	0.31
low gradual decrease trajectory	56/152	1.71 (1.17 ~ 2.51)	0.006	1.63 (1.1 ~ 2.41)	0.02	2.35 (1.4 ~ 3.95)	0.001
progression-free survival							
low gradual increase trajectory	73/204	Reference		Reference		Reference	
low gradual increase trajectory	3/5	1.49 (0.46 ~ 4.87)	0.51	1.48 (0.45 ~ 4.84)	.519	1.45 (0.43 ~ 4.96)	0.55
decrease followed by increase trajectory	7/16	1.3 (0.59 ~ 2.84)	0.51	1.2 (0.55 ~ 2.62)	.656	1.4 (0.6 ~ 3.26)	0.43
low gradual decrease trajectory	68/152	1.44 (1.03 ~ 2)	0.03	1.43 (1.01 ~ 2.01)	.041	1.54 (0.98 ~ 2.4)	0.06

Dose–response relationship between weight change and survival

Restricted cubic spline analyses showed a linear inverse association between weight change during NCRT and both OS and PFS. Greater weight loss was associated with progressively higher risks of death and disease progression, with no evidence of nonlinearity in either unadjusted or fully adjusted models (all P for nonlinearity > 0.30) (Supplementary Fig. 6).

Discussion

The principal finding of this study is that the prognostic significance of weight loss was not uniform throughout treatment. Rather, its association with survival depended on when weight loss occurred and how body weight changed over time. In this cohort of patients with locally advanced esophageal squamous cell carcinoma undergoing neoadjuvant chemoradiotherapy followed by esophagectomy, weight loss during NCRT and during the interval between completion of NCRT and surgery was associated with poorer long-term outcomes, whereas weight changes before treatment initiation and during the early postoperative period were not. We also found that longitudinal weight trajectories provided additional prognostic information beyond individual weight measurements. Patients with a gradual and sustained decline in body weight experienced the poorest survival outcomes.

Previous studies have consistently linked malnutrition and weight loss to adverse outcomes in esophageal cancer^[16–18]. However, most investigations have relied on preoperative or postoperative assessments and have treated weight loss as a static variable^[19–21]. Our findings suggest that the timing of weight loss is clinically relevant. Among the treatment phases examined, weight loss during NCRT showed the strongest and most consistent association with both OS and PFS. This observation may reflect the combined effects of treatment-related toxicities, impaired oral intake, systemic inflammation, and cancer-associated metabolic disturbances during active treatment^[19, 27–31]. The additional prognostic value of weight loss occurring between completion of NCRT and surgery further suggests that failure to regain or stabilise body weight before surgery may identify patients with limited physiological reserve^[25, 30, 32, 33].

An important finding of this study is that longitudinal patterns of weight change carried prognostic information beyond single assessments. Patients in the low gradual decrease trajectory had significantly poorer survival than those with stable or increasing weight. By contrast, trajectories characterised by partial recovery or fluctuating weight were not associated with worse outcomes. These findings indicate that persistent weight decline across the treatment course may be more informative than isolated episodes of weight loss. From a clinical perspective, repeated weight measurements are inexpensive, universally available, and readily incorporated into routine care, making trajectory-based assessment a potentially practical approach to perioperative risk stratification.

The observed dose–response relationship further supports the clinical significance of weight change during treatment. Rather than identifying a threshold effect, our analyses demonstrated a progressive increase in risk with increasing weight loss. This finding is consistent with the concept that nutritional deterioration exists along a continuum and suggests that clinically relevant risk may develop before conventional weight-loss cut-offs are reached^[34].

We also observed stronger associations between weight loss and survival among patients receiving paclitaxel–carboplatin and among those with high baseline performance status. Although these subgroup findings should be interpreted cautiously, they suggest that the prognostic implications of

weight loss may differ according to treatment intensity and underlying physiological reserve^[35]. Further studies are warranted to determine whether these observations can be replicated in independent cohorts.

Several limitations should be acknowledged. First, this was a retrospective study conducted at a single institution, which may limit the generalisability of the findings. Second, some body-weight measurements obtained outside the hospital relied on patient self-report and may be subject to measurement error. Third, postoperative weight assessment was limited to the early recovery period and did not capture longer-term nutritional trajectories after surgery. Finally, as with all observational studies, residual confounding cannot be excluded despite multivariable adjustment.

In conclusion, among patients with LA-ESCC treated with NCRT followed by esophagectomy, the prognostic significance of weight loss depended on both its timing and its longitudinal pattern. Weight loss during NCRT and before surgery was associated with poorer survival, while a sustained trajectory of weight decline identified patients at particularly high risk. These findings support the value of serial weight assessment throughout multimodality treatment and highlight the potential role of weight trajectories in perioperative risk evaluation.

Several limitations merit consideration. The retrospective, single-institution design may limit external validity. A proportion of weight measurements obtained outside the hospital were self-reported, introducing potential measurement variability. In addition, postoperative weight data were confined to the early recovery period and do not capture longer-term trends. Prospective, multicenter studies with standardized assessments and extended follow-up are needed to confirm these findings and to clarify whether intervention during high-risk intervals translates into improved surgical and oncologic outcomes.

In conclusion, in patients with locally advanced esophageal squamous cell carcinoma undergoing neoadjuvant chemoradiotherapy followed by esophagectomy, the prognostic significance of weight loss depends on its timing and longitudinal pattern. Weight decline during neoadjuvant therapy and in the preoperative interval independently identifies patients at increased risk of adverse outcomes. Serial assessment of weight trajectory may offer a practical tool for perioperative risk stratification and may help guide supportive strategies prior to surgery.

Declarations

Ethics approval and consent to participate

This retrospective study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Sichuan Cancer Hospital (KY-2025-232-01). The requirement for informed consent was waived by the Ethics Committee due to the retrospective nature of the study and the use of anonymized clinical data.

Consent for publication

Not applicable. This manuscript does not contain any individual person's identifiable information.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy and institutional regulations. The datasets are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Guiyu Huang and Long Zhang conceived and designed the study. Bingrong He, Zheng Jia, and Xin Liu collected and analyzed the data. Long Zhang performed the statistical analysis. Guiyu Huang drafted the manuscript. Hanfeng Zhang, Rendu Tian and Xiaoli Tang, critically revised the manuscript. All authors read and approved the final manuscript.

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Tables

TABLE 1. Baseline Characteristics of Patients with Locally Advanced Esophageal Squamous Cell Carcinoma

Variables n (%)	Total (n = 377) n(%)
Age	
<65	237 (62.9)
≥65	140 (37.1)
Gender	
Female	66 (17.5)
Male	311 (82.5)
ΔWL% time0-1	
No	297 (78.8)
Yes	80 (21.2)
ΔWL% time1-2	
No	321 (85.1)
Yes	56 (14.9)
ΔWL% time2-3	
No	330 (87.5)
Yes	47 (12.5)
ΔWL% time3-4	
No	334 (88.6)
Yes	43 (11.4)
Malnutrition	
No	59 (15.6)
Mild	84 (22.3)
Moderate	164 (43.5)
Severe	70 (18.6)
BMI	
Low weight	24 (6.4)
Normal weight	227 (60.2)
Overweight	111 (29.4)
Obesity	15 (4.0)

Therapeutic regimen	
TP	134 (35.5)
TC	213 (56.5)
Tax+NDP	30 (8.0)
Nutritional support	
No	168 (44.6)
Yes	209 (55.4)
NIS	
0	67 (17.8)
1	94 (24.9)
≥2	216 (57.3)
KPS	
90-100	326 (86.5)
70-80	51 (13.5)
Smoking	
No	136 (36.1)
Yes	241 (63.9)
Drinking	
No	141 (37.4)
Yes	236 (62.6)
Tumor location	
Upper 1/3	48 (12.7)
Middle 1/3	152 (40.3)
Lower 1/3	177 (46.9)
Clinical stage	
Ⅰ	20 (5.3)
Ⅱ	273 (72.4)
Ⅲ	84 (22.3)
TTS	

≤42	343(91)
≥42	32(9)

Abbreviations: BMI, body mass index; KPS, Karnofsky performance status; NCRT, neoadjuvant chemoradiotherapy; Time0-1, Within one month before the initiation of NCRT; Time1-2, the entire course of NCRT; Time2-3, from the end of NCRT to before surgery ;Time3-4, from before surgery to after surgery; TC, taxane combined with carboplatin; TP, taxane combined with cisplatin; Tax, paclitaxel; DNP, nedaplatin;TTS, the time to surgery interval.

TABLE 2 . Multivariable Cox Regression Analyses of Overall Survival and Progression-Free Survival According to Weight Trajectory Groups

Weight index trajectories	Died (N)	Model 1		Model 2		Model 3	
		HR	P	HRs	P	HRs	P
		(95% CI)		(95% CIs)		(95% CIs)	
overall survival							
low gradual increase trajectory	50/204	Reference		Reference		Reference	
low gradual increase trajectory	2/5	1.64 (0.4~6.76)	0.49	1.56 (0.38~6.45)	0.54	1.83 (0.4~8.31)	0.44
decrease followed by increase trajectory	5/16	1.32 (0.53~3.32)	0.55	1.22 (0.48~3.07)	0.67	1.67 (0.63~4.38)	0.31
low gradual decrease trajectory	56/152	1.71 (1.17~2.51)	0.006	1.63 (1.1~2.41)	0.02	2.35 (1.4~3.95)	0.001
progression-free survival							
low gradual increase trajectory	73/204	Reference		Reference		Reference	
low gradual increase trajectory	3/5	1.49 (0.46~4.87)	0.51	1.48 (0.45~4.84)	.519	1.45 (0.43~4.96)	0.55
decrease followed by increase trajectory	7/16	1.3 (0.59~2.84)	0.51	1.2 (0.55~2.62)	.656	1.4 (0.6~3.26)	0.43
low gradual decrease trajectory	68/152	1.44 (1.03~2)	0.03	1.43 (1.01~2.01)	.041	1.54 (0.98~2.4)	0.06

Figures

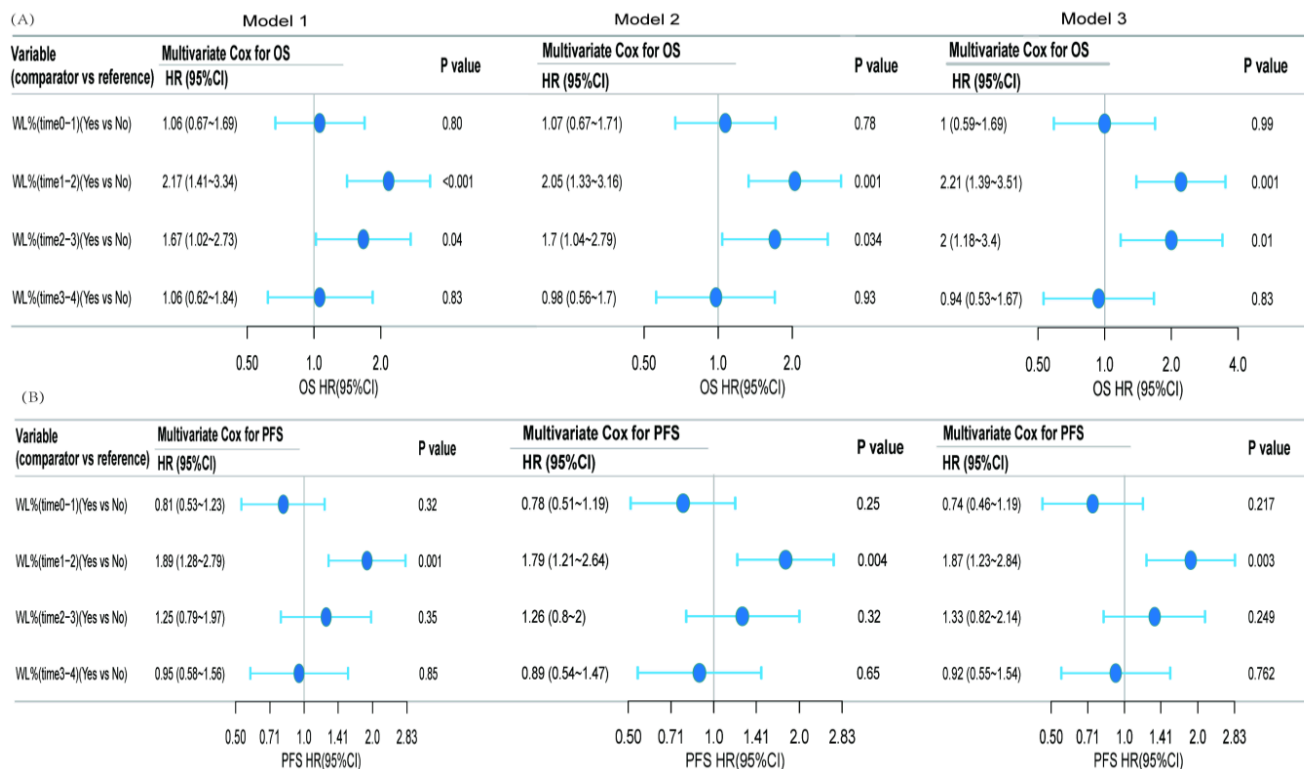


Figure 1

Association Between Weight Change and Survival Outcomes.

Association between weight change and overall survival (OS) and progression-free survival (PFS). Model 1 was unadjusted. Model 2 was adjusted for age and sex. Model 3 was adjusted for age, sex, body mass index (BMI), malnutrition, therapeutic regimen, nutritional support, Karnofsky performance status (KPS), smoking status, alcohol consumption, tumor location, clinical stage, and time-to-surgery interval (TTS).

Abbreviations: BMI, body mass index; KPS, Karnofsky performance status; OS, overall survival; PFS, progression-free survival; TTS, time-to-surgery interval.

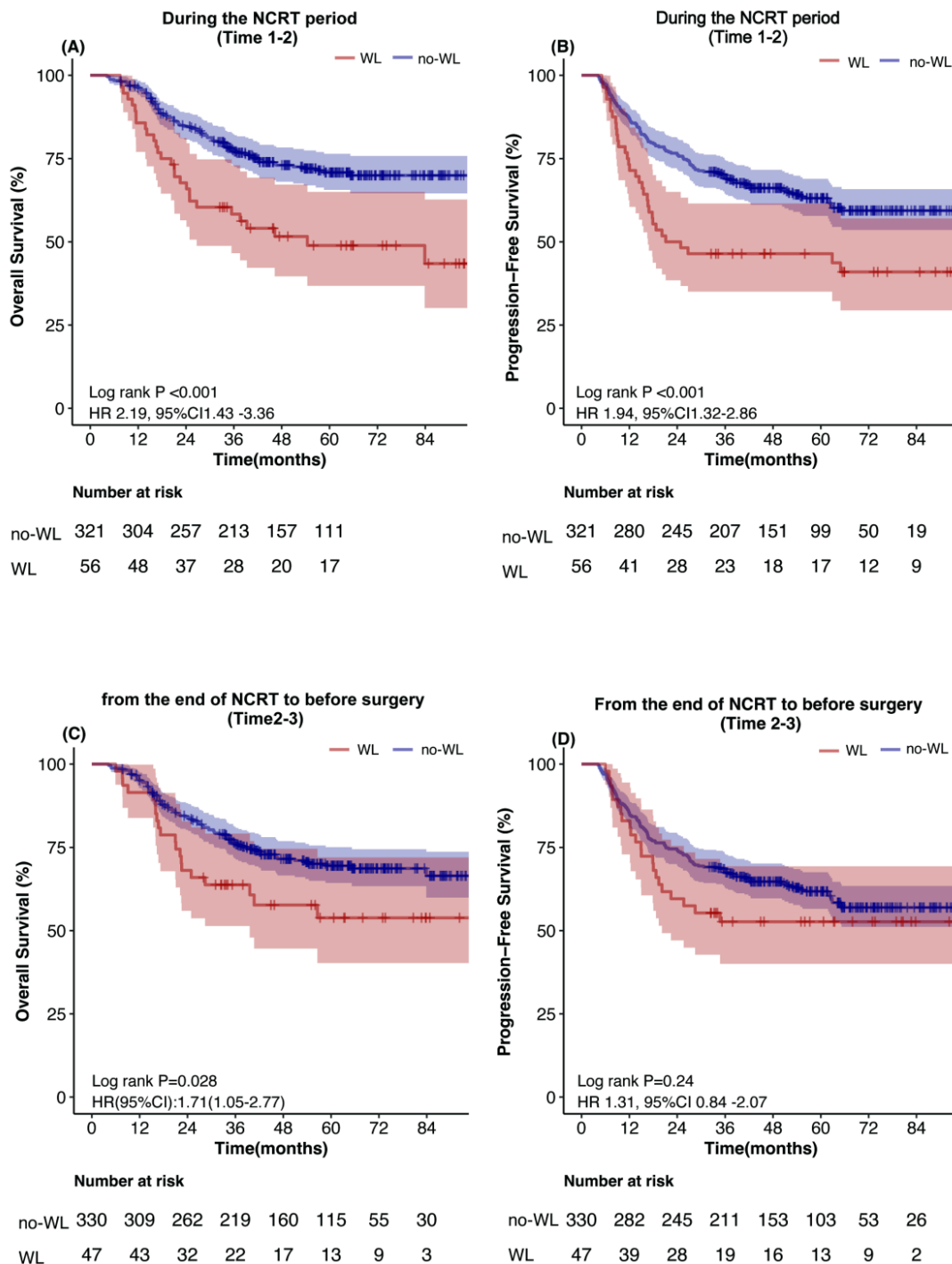


Figure 2

Kaplan–Meier Survival Curves According to Weight Loss Status at Different Treatment Stages in Patients With Locally Advanced Esophageal Squamous Cell Carcinoma.

(A) OS according to weight loss status during the neoadjuvant chemoradiotherapy (NCRT) phase (Time 1–2); (B) PFS according to weight loss status during the NCRT phase (Time 1–2); (C) OS according to

weight loss status during the interval between completion of NCRT and before surgery (Time 2–3); and (D) PFS according to weight loss status during the interval between completion of NCRT and before surgery (Time 2–3).

Abbreviations: LA-ESCC, locally advanced esophageal squamous cell carcinoma; NCRT, neoadjuvant chemoradiotherapy; no-WL, no weight loss; OS, overall survival; PFS, progression-free survival; WL, weight loss.

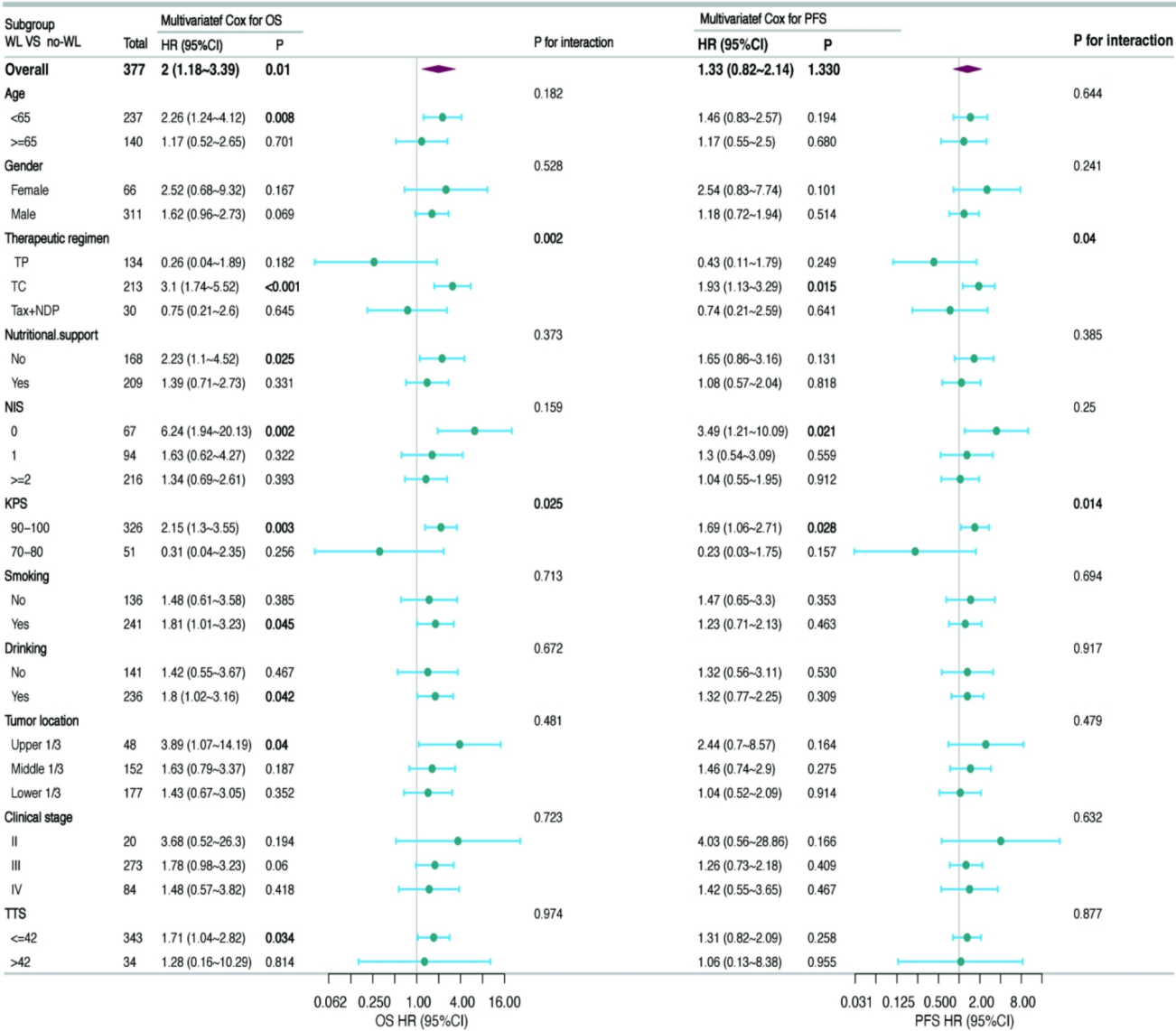


Figure 3

Multivariable Cox Hazard Ratios for Weight Loss Versus No Weight Loss Across Prespecified Subgroups.

Forest plot showing adjusted hazard ratios and 95% confidence intervals for the association between weight loss and survival outcomes across clinically relevant subgroups.

Abbreviations: DNP, nedaplatin; no-WL, no weight loss; OS, overall survival; PFS, progression-free survival; Tax, paclitaxel; TC, taxane plus carboplatin; TP, taxane plus cisplatin; TTS, time-to-surgery interval; WL, weight loss.

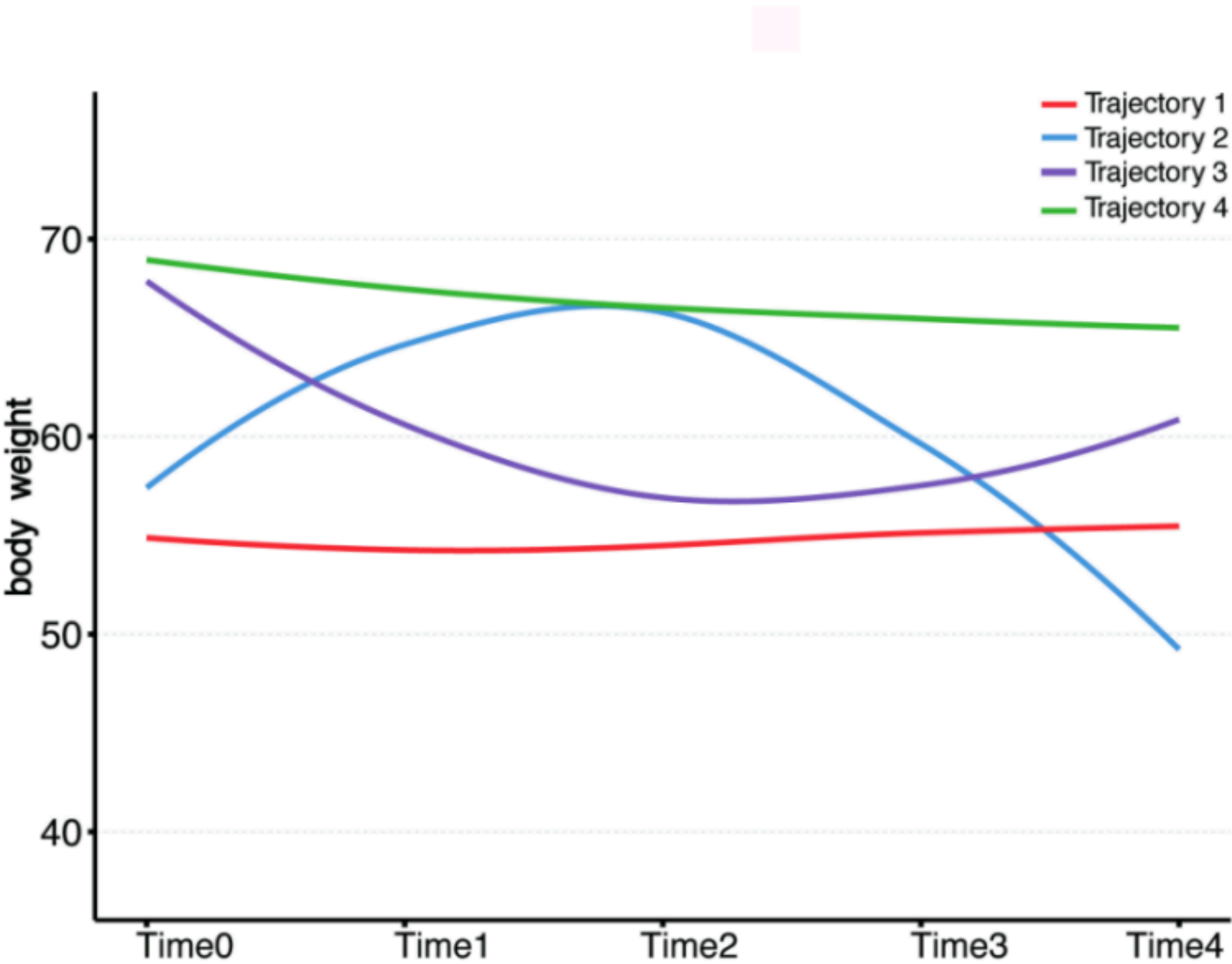


Figure 4

Distinct Trajectories of Body Weight From Baseline to the Early Postoperative Period.

Trajectory 1, low gradual increase trajectory; Trajectory 2, increase followed by decrease trajectory; Trajectory 3, decrease followed by increase trajectory; and Trajectory 4, low gradual decrease trajectory.

Time 0, baseline; Time 1, initiation of NCRT; Time 2, completion of NCRT; Time 3, within 1 week before surgery; and Time 4, early postoperative period.

Abbreviations: NCRT, neoadjuvant chemoradiotherapy.

Supplementary Files

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