# Longitudinal pattern analysis of nutritional supplement prescription during definitive radiotherapy for head and neck cancer: A real-world cohort study using administrative prescription data

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Received October 5, 2026; Accepted November 3, 2026

DOI: 10.3892/mco.2026.2986

**Abstract.** Nutritional supplements serve an important role in the management of patients undergoing radiotherapy for head and neck cancer. However, real-world data on prescribing patterns remain limited. The present study aimed to characterize real-world prescribing patterns of nutritional supplements in patients with head and neck squamous cell carcinoma undergoing definitive radiotherapy. Patients with oropharyngeal, hypopharyngeal or laryngeal squamous cell carcinoma, excluding early-stage glottic cancer, who completed definitive radiotherapy at a dose of 70 Gy in 35 fractions at a single institution between January 2015 and December 2024 were retrospectively analyzed. Prescription data for nutritional supplements were obtained from administrative records, and prescribed calories were quantified longitudinally over the first year following radiotherapy initiation. The prevalence, timing of initiation and temporal patterns of prescription were evaluated. Multivariable logistic regression analysis was performed to identify factors associated with nutritional supplement prescription. A total of 282 patients were included, of whom 191 (67.7%) received nutritional supplement prescriptions. Nutritional supplements were prescribed more frequently in patients with stage III-IVA/B disease than in those with stage I-II disease (78.5 vs. 57.8%) and in those receiving concurrent chemotherapy than in those who did not (75.9 vs. 54.6%). Among patients prescribed nutritional supplements, the median time to initiation was 4.0 weeks. The median total prescribed calories per patient were 31,800 kcal, and the median prescription duration was 5.7 weeks. Although most patients received prescriptions over a short period, 22 patients (11.5%) received prescriptions for 30 weeks or longer. In multivariable analysis, advanced clinical stage was independently associated with nutritional supplement prescription (odds ratio, 2.05; 95% confidence interval, 1.09-3.86; P=0.03). Prescriptions for nutritional supplements increased over time, with prescribed calories peaking during the latter half of radiotherapy. These findings provide a quantitative description of real-world prescribing patterns and may inform timely, risk-adapted nutritional interventions.

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*Key words:* squamous cell carcinoma of head and neck, radiotherapy, enteral nutrition, nutritional support, chemoradiotherapy, longitudinal studies

## Introduction

Head and neck cancer represents a substantial global health burden, with a rising incidence worldwide and a disproportionately higher burden among men and populations in lower-income regions (1). Nutritional compromise is frequently present at diagnosis, reflecting tumor-related dysphagia, reduced oral intake, and systemic catabolism (2). Definitive radiotherapy, delivered either alone or in combination with systemic therapy, typically using conventional fractionation over approximately 7-8 weeks, remains a curative-intent treatment option for many patients with head and neck cancer (3,4). However, radiotherapy to the head and neck region often impairs oral intake due to acute toxicities such as mucositis, odynophagia, dysphagia, xerostomia, and taste alteration (5). These treatment-related effects can lead to weight loss and progressive malnutrition. Fange Gjelstad *et al* (6) reported that 92% of patients were classified as malnourished according to the Patient-Generated Subjective Global Assessment at the end of treatment and 71% at follow-up, while only approximately half of patients with critical weight loss received enteral nutrition therapy.

Nutritional deterioration during treatment has clinically meaningful consequences. In a prospective cohort of 50 patients with locally advanced head and neck cancer treated with definitive chemoradiotherapy, Bahl *et al* (7)

demonstrated that poorer pre-treatment nutritional status, as assessed by the Patient-Generated Subjective Global Assessment, was associated with higher rates of grade 3-4 mucositis and lower complete response rates. Langius *et al* (8) evaluated 533 patients undergoing curative radiotherapy and found that weight loss during and shortly after treatment was independently associated with deterioration across multiple quality-of-life domains; weight loss exceeding 10% remained significantly associated with worse global quality of life and impaired social functioning after adjustment for clinical variables and tube feeding. Several studies have reported that nutritional markers are associated with treatment outcomes in patients with head and neck cancer (9-11).

From a clinical implementation perspective, international guidelines emphasize early screening and stepwise nutritional intervention. The European Society for Clinical Nutrition and Metabolism practical guideline on clinical nutrition in cancer recommends regular screening for nutritional risk, assessment of nutritional intake and nutritional status, and individualized nutritional counseling, with escalation to oral nutritional supplements and enteral nutrition when needed (12). The American Society for Parenteral and Enteral Nutrition evidence-based guideline for adult head and neck cancer nutrition care synthesizes evidence across the care continuum and recommends early enteral nutrition when oral intake is inadequate, supported by interdisciplinary care models and regular input from dietitians and speech pathology (13). Previous studies have primarily focused on the effectiveness and timing of nutritional interventions, whereas longitudinal data on nutritional supplement prescriptions in routine clinical practice remain limited (14-16). Quantifying prescribed calories over time may help characterize changes in nutritional support demand during and after radiotherapy and identify periods when additional nutritional assessment may be needed.

We conducted a retrospective cohort study to characterize nutritional supplement prescribing patterns among patients with head and neck cancer undergoing definitive radiotherapy, focusing on prescription prevalence, timing of initiation, longitudinal changes in prescribed calories, and clinical factors associated with nutritional supplement prescription.

## Materials and methods

*Study design, patient selection and clinical variables*. This study was approved by the Research Ethics Committee of the Faculty of Medicine of the University of Tokyo (No. 3372-8) and was conducted in accordance with the Declaration of Helsinki. We retrospectively screened the institutional radiotherapy database and identified patients with head and neck squamous cell carcinoma who underwent definitive intensity-modulated radiotherapy delivered with the TomoTherapy system (Accuray Inc., Sunnyvale, CA, USA) at The University of Tokyo Hospital between January 2015 and December 2024. During the study period, TomoTherapy was routinely used for definitive intensity-modulated radiotherapy for head and neck cancer at our institution. Radiotherapy planning and delivery, including patient immobilization and target volume delineation, were performed according to our institutional protocols (17-20). Clinical staging was performed according to the eighth edition of the staging system of the American Joint Committee on Cancer. The inclusion criteria were as follows: (1) primary tumor located in the oropharynx, hypopharynx, or larynx; (2) histologically confirmed squamous cell carcinoma; (3) completion of definitive radiotherapy with a prescribed dose of 70 Gy in 35 fractions; and (4) patients treated in the initial (primary) treatment setting. The exclusion criteria were as follows: (1) early-stage glottic cancer, which generally does not require elective nodal irradiation and is treated with radiation doses and techniques different from those used in the present cohort (21); (2) presence of distant metastasis at the time of diagnosis; and (3) insufficient clinical data for analysis. Clinical variables included age, sex, ECOG performance status, clinical stage, concurrent chemotherapy, upfront neck dissection, and prophylactic PEG placement. Performance status was analyzed according to the predefined categorization used in the clinical database.

*Study objectives*. Data on nutritional supplement prescriptions, including oral and enteral formulations, were extracted from our institution's administrative prescription records. Seven nutritional supplement formulations from different manufacturers were prescribed during the study period, and their prescription data were harmonized into a unified dataset (Table SI). Prescribed quantities, recorded in milliliters or grams depending on the formulation, were converted into calories (kcal) using product-specific energy densities (kcal/ml or kcal/g), which were available for all formulations. No changes in formulation composition occurred during the study period. The study aimed to characterize real-world patterns of nutritional supplement prescription during the first year after radiotherapy initiation, including prescription prevalence, timing of the first prescription, and temporal changes in prescribed calories. For each patient, the interval from radiotherapy initiation to the first nutritional supplement prescription was calculated. Continuous variables are presented as medians and interquartile ranges (IQRs). For the weekly analysis, the total caloric content of each prescription was assigned to the date on which the prescription was issued. Because the frequency of supplement prescription varied, prescribed calories were not distributed across the intended duration of use. Weekly prescribed calories were calculated by summing the calories from all prescriptions issued during each week relative to radiotherapy initiation across the entire cohort. Therefore, these values represent the total calories prescribed during each week rather than the calories actually consumed during that week. Weekly totals were calculated from radiotherapy initiation through 1 year to visualize temporal prescribing patterns.

*Statistical analysis*. Differences in nutritional supplement prescription between patient subgroups were assessed using Pearson's chi-square test without continuity correction. For primary site, an overall comparison across the three groups was performed. Univariate and multivariable logistic regression analyses were performed to identify factors associated with nutritional supplement prescription. Receipt of any nutritional supplement prescription within 1 year of radiotherapy initiation was the dependent variable; age, sex, performance status, upfront neck dissection, stage, chemotherapy, and

Table I. Baseline patient characteristics and nutritional supplement prescription in 282 patients.

| Variables | All patients | Patients prescribed nutritional supplements | Patients not prescribed nutritional supplements | P-value |
|---|---|---|---|---|
| Median age, years (range) | 68 (40-89) | - | - | - |
| Sex, n (%) | | | | 0.024 |
| Male | 241 | 157 (65.1) | 84 (34.9) | |
| Female | 41 | 34 (82.9) | 7 (17.1) | |
| ECOG-PS, n (%) | | | | 0.690 |
| 0 | 235 | 158 (67.2) | 77 (32.8) | |
| 1 | 47 | 33 (70.2) | 14 (29.8) | |
| Primary disease, n (%) | | | | 0.369 |
| Hypopharynx | 121 | 81 (66.9) | 40 (33.1) | |
| Oropharynx | 104 | 75 (72.1) | 29 (27.9) | |
| Larynx | 57 | 35 (61.4) | 22 (38.6) | |
| Clinical stage, n (%) | | | | <0.001 |
| I-II | 147 | 85 (57.8) | 62 (42.2) | |
| III-IVA/B | 135 | 106 (78.5) | 29 (21.5) | |
| Chemotherapy, n (%) | | | | <0.001 |
| No | 108 | 59 (54.6) | 49 (45.4) | |
| Yes | 174 | 132 (75.9) | 42 (24.1) | |
| Upfront neck dissection, n (%) | | | | 0.567 |
| No | 258 | 176 (68.2) | 82 (31.8) | |
| Yes | 24 | 15 (62.5) | 9 (37.5) | |
| Prophylactic PEG placement, n (%) | | | | 0.003 |
| No | 166 | 101 (60.8) | 65 (39.2) | |
| Yes | 116 | 90 (77.6) | 26 (22.4) | |

Percentages were calculated within each category. P-values were calculated using Pearson's $\chi^2$ test without continuity correction to compare the proportions of patients prescribed nutritional supplements across categories of each variable. ECOG-PS, Eastern Cooperative Oncology Group performance status; PEG, percutaneous endoscopic gastrostomy.

PEG placement were included as covariates. All patients had complete data for the variables included in the model; therefore, no imputation was required. All covariates were entered as categorical variables, so assessment of linearity in the logit was not applicable. Model calibration was not assessed because the analysis aimed to examine associated factors rather than to develop an individual prediction model. Odds ratios and 95% confidence intervals were calculated. A two-sided P-value <0.05 was considered statistically significant.

## Results

A total of 282 patients with head and neck cancer who underwent radiotherapy were included in the analysis (Table I). Among them, 191 patients received nutritional supplement prescriptions, corresponding to an overall prescription prevalence of 67.7%. By primary tumor site, patients with oropharyngeal cancer showed the highest prescription prevalence at 72.1% (75/104), followed by hypopharyngeal cancer at 66.9% (81/121) and laryngeal cancer at 61.4% (35/57). According to clinical stage, the prescription prevalence was higher in patients with stage III-IVA/B disease than in those with stage I-II disease, 78.5% (106/135) vs. 57.8% (85/147) (P<0.001). Patients who received concurrent chemotherapy had a higher rate of nutritional supplement prescription than those who did not, 75.9% (132/174) vs. 54.6% (59/108) (P<0.001).

Among the 191 patients who received nutritional supplement prescriptions, the median time from radiotherapy initiation to the first prescription was 4.0 weeks (IQR, 2.9-6.3 weeks). The cumulative incidence of nutritional supplement prescription was 19.9% [95% confidence interval (CI), 15.7-25.0%] at 3 weeks, 43.6% (95% CI, 38.1-49.6%) at 5 weeks, and 54.6% (95% CI, 48.9-60.5%) at 7 weeks (Fig. 1A). Weekly total prescribed nutritional supplement calories increased during treatment, peaking around weeks 6-8, and gradually declined thereafter (Fig. 1B). The median total prescribed calories per patient were 31,800 kcal (IQR, 12,862.5-68,312.5), and the median duration of prescription was 5.7 weeks (IQR, 2.1-14.1 weeks). Although most patients received prescriptions over a limited period, 22 of 191 patients (11.5%) had prescriptions spanning 30 weeks or longer. Among these 22 patients, 12 (54.5%) had stage III-IV disease, 14 (63.6%) received concurrent chemotherapy, and 14 (63.6%) underwent prophylactic PEG placement.

Table II provides descriptive summaries of nutritional supplement prescribing patterns across patient subgroups.

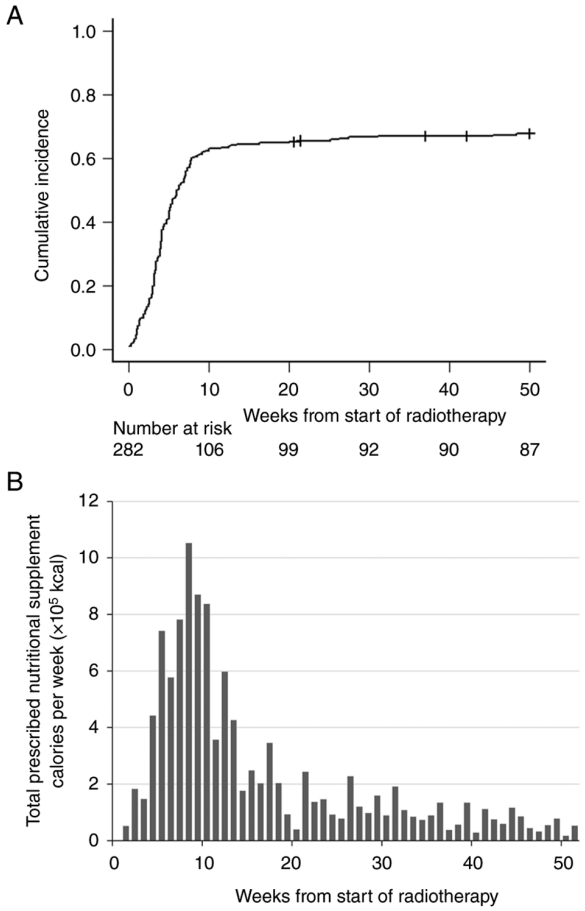



Figure 1. Longitudinal trajectories of nutritional supplement prescription during definitive radiotherapy. (A) Cumulative incidence of nutritional supplement initiation following the start of radiotherapy. Tick marks indicate censored observations. (B) Weekly prescribed nutritional supplement calories for the entire cohort following the start of radiotherapy, with the y-axis representing total prescribed nutritional supplement calories per week (x$10^5$ kcal). A value of 10 on the y-axis corresponds to 1,000,000 kcal prescribed across the cohort during that week.

The median time of initiation was 4.1 weeks (IQR, 3.0-6.3) in hypopharyngeal cancer, 3.6 weeks (IQR, 2.4-5.4) in oropharyngeal cancer, and 5.0 weeks (IQR, 3.3-7.0) in laryngeal cancer. The median total prescribed calories were 24,200 kcal (IQR, 11,375-49,500), 50,400 kcal (IQR, 14,688-127,488), and 24,750 kcal (IQR, 8,438-38,250), respectively.

Univariate and multivariable logistic regression analyses of factors associated with nutritional supplement prescription are presented in Table III. In the multivariable logistic regression analysis, clinical stage was significantly associated with nutritional supplement prescription. Patients with advanced-stage disease (stage III-IV) had higher odds of being prescribed nutritional supplements compared with those with early-stage disease [odds ratio (OR), 2.05; 95% confidence interval (CI), 1.09-3.86; P=0.03]. Concurrent chemotherapy was not significantly associated with nutritional supplement prescription (OR, 1.85; 95% CI, 0.88-3.89; P=0.10).

## Discussion

In this retrospective cohort study, we characterized real-world patterns of nutritional supplement prescriptions among patients with head and neck squamous cell carcinoma treated with definitive radiotherapy. Overall, 67.7% of patients received at least one prescription within the first year after radiotherapy initiation. Prescription rates were higher among patients with stage III-IVA/B disease than among those with stage I-II disease, and among those receiving concurrent chemotherapy than among those who did not. However, the association with concurrent chemotherapy was not statistically significant in the multivariable analysis, whereas clinical stage remained independently associated with prescription receipt. Given the relationship between clinical stage and chemotherapy administration, residual confounding cannot be excluded. Prescriptions increased predominantly during the latter half of treatment and were more frequent in clinically higher-risk subgroups. Among patients who received nutritional supplement prescriptions, 22 (11.5%) had prescriptions spanning at least 30 weeks. Previous studies have reported that some patients require long-term tube feeding after head and neck radiotherapy because of persistent swallowing dysfunction (22,23). Therefore, prolonged prescriptions in our cohort may partly reflect continued nutritional support for patients with persistent dysphagia, although the underlying reasons could not be confirmed. These findings underscore the importance of continued nutritional assessment and follow-up after radiotherapy.

A growing body of evidence has addressed nutritional support during chemoradiotherapy for head and neck cancer. Huang *et al* (14) reported, in a prospective randomized trial of locally advanced nasopharyngeal carcinoma treated with chemoradiotherapy, that prophylactic oral nutritional supplementation was associated with fewer treatment interruptions, including lower rates of radiotherapy interruption (0% vs. 7.14%) and concurrent chemotherapy interruption (10.34% vs. 28.57%). Jiang *et al* (15) also reported, in a randomized trial of postoperative head and neck squamous cell carcinoma patients receiving chemoradiotherapy, that initiating oral nutritional supplement two weeks before treatment was associated with less weight loss than conventional, as-needed dietitian-guided supplementation. However, the effect of simply increasing prescribed intake may depend on whether supplementation is integrated into structured nutritional management. In a prospective randomized trial of patients receiving radiotherapy for head and neck cancer, Ravasco *et al* (24) reported that oral nutritional supplements increased energy intake during treatment, but the benefit was less likely to be sustained without appropriate nutritional management. Pei *et al* (25) reported that a multidisciplinary supportive-care program, which delivered coordinated nutritional, psychological, and rehabilitation support, reduced radiotherapy interruptions compared with usual care (11.1% vs. 25.0%) and was associated with better end-of-treatment outcomes across quality of life, psychological distress measures, and nutritional risk/status metrics. In a systematic review and meta-analysis, non-invasive nutritional interventions in head and neck cancer patients undergoing chemoradiotherapy (11 randomized controlled trials, n=1000) were associated with improvements in body weight, serum albumin, and Patient-Generated Subjective Global Assessment scores (26). However, considerable variability remains across studies regarding intervention thresholds and screening approaches, underscoring the need for standardized,

Table II. Nutritional supplement prescribing patterns in 191 patients prescribed nutritional supplements.

| Variables | Median time to initiation, weeks (IQR) | Median duration, weeks (IQR) | Median cumulative prescribed calories, kcal (IQR) |
|---|---|---|---|
| Age | | | |
| <68 years | 4.1 (3.1-6.9) | 4.9 (1.4-11.6) | 27,100 (11,375-68,000) |
| ≥68 years | 4.0 (2.5-6.0) | 6.9 (2.3-15.9) | 33,188 (14,063-67,219) |
| Sex | | | |
| Male | 4.1 (2.9-6.6) | 5.1 (1.9-13.7) | 31,800 (12,975-59,250) |
| Female | 3.5 (2.5-5.0) | 8.1 (4.0-17.2) | 31,875 (11,812-86,093) |
| ECOG PS | | | |
| ECOG 0 | 4.1 (3.0-6.3) | 5.1 (2.0-13.4) | 30,375 (11,812-67,406) |
| ECOG 1 | 3.3 (1.0-5.9) | 6.9 (3.0-23.0) | 33,000 (16,875-77,750) |
| Primary disease | | | |
| Hypopharynx | 4.1 (3.0-6.3) | 5.1 (2.0-12.3) | 24,200 (11,375-49,500) |
| Oropharynx | 3.6 (2.4-5.4) | 6.7 (2.4-21.4) | 50,400 (14,688-127,488) |
| Larynx | 5.0 (3.3-7.0) | 4.0 (2.1-12.1) | 24,750 (8,438-38,250) |
| Clinical stage | | | |
| I-II | 3.9 (2.9-5.3) | 5.3 (2.1-12.3) | 25,500 (11,250-54,750) |
| III-IVA/B | 4.1 (3.0-7.1) | 5.8 (2.1-15.9) | 34,850 (13,219-77,438) |
| Chemotherapy | | | |
| No | 3.9 (2.4-5.1) | 5.1 (1.5-15.5) | 23,625 (7,937-39,637) |
| Yes | 4.1 (3.0-7.0) | 5.9 (2.3-13.8) | 38,437 (16,143-93,050) |
| Upfront neck dissection | | | |
| No | 4.0 (2.8-6.3) | 6.0 (2.1-14.3) | 31,275 (12,918-71,337) |
| Yes | 4.3 (3.7-6.5) | 5.1 (2.4-9.5) | 32,250 (13,650-52,000) |
| Prophylactic PEG | | | |
| No | 4.1 (2.4-6.0) | 4.6 (1.1-10.3) | 19,125 (7,875-36,750) |
| Yes | 4.0 (3.0-6.8) | 7.4 (3.9-17.2) | 51,187 (25,281-113,562) |

ECOG-PS, Eastern Cooperative Oncology Group performance status; PEG, percutaneous endoscopic gastrostomy.

Table III. Univariate and multivariate logistic regression analyses of factors associated with nutritional supplement prescription.

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| Variables | Odds ratio (95% CI) | P-value | Odds ratio (95% CI) | P-value |
| Age (≥68 vs. <68 years) | 1.03 (0.63-1.70) | 0.905 | 1.53 (0.85-2.75) | 0.157 |
| Sex (female vs. male) | 2.60 (1.10-6.11) | 0.029 | 2.26 (0.94-5.44) | 0.069 |
| ECOG performance status (≥1 vs. 0) | 1.15 (0.58-2.27) | 0.690 | 0.98 (0.47-2.04) | 0.959 |
| Clinical stage (III-IVA/B vs. I-II) | 2.67 (1.58-4.51) | <0.001 | 2.05 (1.09-3.86) | 0.026 |
| Chemotherapy (yes vs. no) | 2.61 (1.56-4.36) | <0.001 | 1.85 (0.88-3.89) | 0.102 |
| Upfront neck dissection (yes vs. no) | 0.78 (0.33-1.85) | 0.567 | 0.55 (0.21-1.43) | 0.222 |
| Prophylactic PEG placement (yes vs. no) | 2.23 (1.30-3.81) | 0.003 | 1.33 (0.66-2.69) | 0.420 |

ECOG-PS, Eastern Cooperative Oncology Group performance status; PEG, percutaneous endoscopic gastrostomy.

operational criteria (27). Laskar *et al* (16) reported no significant difference in weight loss at 6 months between prophylactic and reactive nasogastric tube feeding strategies in a phase III randomized trial. In our cohort, the median time to nutritional supplement prescription was 4.0 weeks after radiotherapy initiation, indicating that prescriptions were commonly initiated during treatment. However, prescription timing alone cannot distinguish between prophylactic and reactive nutritional strategies, and our findings cannot be directly compared with studies evaluating feeding tube placement. Our study

instead provides longitudinal data on the timing, volume, and duration of nutritional supplement prescriptions in routine clinical practice.

This study has several limitations. First, its retrospective, single-institution design and restriction to selected primary sites treated with definitive intensity-modulated radiotherapy using the TomoTherapy system may limit generalizability. Second, prescription records do not establish actual intake or administration route, and prescribed calories may not reflect actual consumption. During radiotherapy for head and neck cancer, treatment-related adverse effects, including taste disturbances and oral or pharyngeal mucositis, frequently reduce oral intake, making it difficult to meet nutritional requirements through regular meals alone (28). Oral nutritional supplements may be used in such cases, whereas tube feeding may become necessary when adequate nutritional intake cannot be maintained despite oral supplementation. However, because the administration route could not be identified from prescription records, we were unable to evaluate whether or when patients transitioned from oral supplementation to tube feeding, limiting our ability to interpret changes in prescribing patterns in relation to clinical nutritional needs. Third, institutional practices, including prophylactic percutaneous endoscopic gastrostomy placement in patients receiving concurrent chemoradiotherapy, may have influenced prescribing patterns. Fourth, data on nutritional screening, nutritional status assessments, and dietitian consultations were unavailable, precluding evaluation of adherence to guideline recommendations regarding regular nutritional assessment and weekly dietitian consultations during radiotherapy. Finally, the absence of longitudinal clinical outcome data, including weight changes, treatment interruptions, and hospitalizations, precluded assessment of the adequacy or clinical effectiveness of nutritional support. The findings should therefore be interpreted as descriptive and hypothesis-generating. Nevertheless, linking radiotherapy and prescription datasets enabled weekly quantification of prescribed calories throughout the first year after radiotherapy initiation.

In conclusion, this study aimed to characterize real-world prescribing patterns of nutritional supplements rather than to determine the optimal timing of nutritional intervention. Nutritional supplement prescribing increased predominantly during the latter half of definitive radiotherapy for head and neck cancer and was more frequent among patients with advanced-stage disease. Although the median time to prescription initiation was 4.0 weeks, this finding does not establish when nutritional assessment or intervention should be initiated. Our study provides quantitative information on the timing, duration, and caloric content of nutritional supplement prescriptions in routine clinical practice, including their variation over the treatment course and subsequent follow-up.

## Acknowledgements

Not applicable.

## Funding

No funding was received.

## Availability of data and materials

The data generated in the present study are not publicly available due to patient privacy and institutional ethical restrictions but may be requested from the corresponding author.

## Authors' contributions

AK conceptualized the study, developed the methodology, curated the dataset, performed the statistical analyses and drafted the manuscript. KN, MM and SS contributed to the acquisition and verification of radiotherapy and prescription data, and assisted in interpreting the results. YI, KY, KK and YS contributed to the collection and review of clinical information, and provided clinical input on the interpretation of the findings. HY supervised the project, contributed to the study design, and provided guidance on the analyses and interpretation. AK and HY confirm the authenticity of all the raw data. All authors critically reviewed and revised the manuscript for important intellectual content, and agreed to be accountable for all aspects of the work. All authors have read and approved the final version of the manuscript.

## Ethics approval and consent to participate

The present retrospective study was approved by the Research Ethics Committee of the Faculty of Medicine of the University of Tokyo (approval no. 3372-8; Tokyo, Japan). In accordance with the approved institutional procedures, patients were notified that their clinical information and examination results could be used for research and were given the opportunity to opt out. All study procedures complied with the ethical standards of the institutional research committee and the Declaration of Helsinki.

## Patient consent for publication

Not applicable.

## Competing interests

The authors declare that they have no competing interests.

## Use of artificial intelligence tools

During the preparation of this work, artificial intelligence tools were used to improve the readability and language of the manuscript, and subsequently, the authors revised and edited the content produced by the artificial intelligence tools as necessary, taking full responsibility for the ultimate content of the present manuscript.

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