International Journal of Clinical Oncology (2020) 25:258–266
https://doi.org/10.1007/s10147-019-01560-5

ORIGINAL ARTICLE

Pretreatment predictive factors for feasibility of oral intake in adjuvant concurrent chemoradiotherapy for patients with locally advanced squamous cell carcinoma of the head and neck

Hidenori Kimura[1] · Satoshi Hamauchi[1] · Sadayuki Kawai[1] · Yusuke Onozawa[1] · Hirofumi Yasui[1] · Aiko Yamashita[2] · Hirofumi Ogawa[3] · Tsuyoshi Onoe[3] · Tomoyuki Kamijo[4] · Yoshiyuki Iida[4] · Tetsuro Onitsuka[4] · Tomoya Yokota[1]

Received: 28 August 2019 / Accepted: 6 October 2019 / Published online: 16 October 2019

Abstract

Background Prophylactic percutaneous endoscopic gastrostomy (PEG) has been widely performed before concurrent chemoradiotherapy (CCRT) for locally advanced squamous cell carcinoma of the head and neck (LASCCHN) because severe oral mucositis and dysphagia induced by CCRT lead to difficulty with oral intake. However, it is controversial whether all patients require prophylactic PEG for adjuvant CCRT. This study evaluated predictive factors for the feasibility of oral intake in adjuvant CCRT for patients with LASCCHN.

Methods This study retrospectively analyzed 117 LASCCHN patients who underwent surgery followed by adjuvant CCRT with cisplatin at Shizuoka Cancer Center between April 2008 and December 2018. To investigate predictive factors for the feasibility of oral intake, tumor factors, treatment factors and social factors were included in multivariate analyses.

Results Of the 117 patients, 25 received total laryngectomy and 92 received other surgery. In multivariate analysis, total laryngectomy [HR (hazard ratio) 0.09, $P=0.001$] and oral cavity of primary tumor location (HR 0.21, $P=0.031$) were significantly associated with the feasibility of oral intake. Difficulty obtaining adequate nutrition via oral intake from initiation of CCRT until 1 year after its completion was significantly rarer in the total laryngectomy group than in the other surgery group (16% vs. 57%, $P<0.001$).

Conclusion Our study suggests that majority of patients who underwent total laryngectomy are able to maintain oral intake during adjuvant chemoradiotherapy.

Keywords Locally advanced squamous cell carcinoma of the head and neck · Adjuvant concurrent chemoradiotherapy · Feasibility of oral intake · Total laryngectomy

Introduction

The standard of care in postoperative therapy for patients with locally advanced squamous cell carcinoma of the head and neck (LASCCHN) is concurrent chemoradiotherapy (CCRT) with high-dose cisplatin (CDDP) [1–6].

Approximately half of patients (34–57%) receiving CCRT experience grade ≥ 3 mucositis induced by CCRT [7], which is often accompanied by dysphagia, dry mouth, and dysgeusia. These adverse events often lead to malnutrition owing to inadequate oral intake, treatment interruption, and a negative impact on treatment outcomes [8–10]. Therefore, nutrition management is important during CCRT for LASCCHN. The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical guidelines recommend enteral nutrition (EN) rather than intravenous nutrition as nutritional

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10147-019-01560-5) contains supplementary material, which is available to authorized users.

✉ Tomoya Yokota
t.yokota@scchr.jp

[1] Division of Gastrointestinal Oncology, Shizuoka Cancer Center, Shizuoka, Japan

[2] Division of Nutrition, Shizuoka Cancer Center, Shizuoka, Japan

[3] Division of Radiation Oncology and Proton Therapy, Shizuoka Cancer Center, Shizuoka, Japan

[4] Division of Head and Neck Surgery, Shizuoka Cancer Center, Shizuoka, Japan

support in patients unable to maintain oral intake [11–13]. Thus, prophylactic percutaneous endoscopic gastrostomy (PEG) has been widely performed before CCRT for LASCCHN [14–17]. However, PEG placement often causes certain complications, such as bleeding or infection [18, 19]. Furthermore, some patients receiving CCRT after total laryngectomy maintain oral intake during and after CCRT and do not necessarily need EN support in clinical practice. Therefore, it is controversial whether all patients require prophylactic PEG for adjuvant CCRT.

The aim of this study is to evaluate predictive factors for the feasibility of oral intake in adjuvant CCRT for patients with LASCCHN.

Materials and methods

Patients

This study retrospectively analyzed LASCCHN patients who had undergone surgery followed by adjuvant CCRT with CDDP at Shizuoka Cancer Center between April 2008 and December 2018. Inclusion criteria were as follows: histologically proven squamous cell carcinoma located in the oral cavity, oropharynx, hypopharynx, or larynx; age 20–80 years; Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0–2; dysphagia score (DS) ≤ 2 on the Ogilvie scale [20, 21] without nutritional support before CCRT initiation; total radiotherapy (RT) tumor dose of 50–70 Gray (Gy); pathological stage III, IVA, or IVB (UICC eighth edition); no distant metastasis identified by computed tomography (CT); no prior RT or chemotherapy; and adequate organ function. Exclusion criteria were as follows: double cancers except for carcinoma in situ or intramucosal tumor; patients who depended on EN or intravenous nutrition when starting CCRT; and patients also exhibiting active infection. All clinical data were retrospectively obtained from medical records. This study was carried out in accordance with the recommendations of the institutional review committee of Shizuoka Cancer Center (Shizuoka, Japan). The study was approved by the institutional review committee of Shizuoka Cancer Center (institutional ID: 30-J125-30-1-3) and met the standards set forth in the Declaration of Helsinki. Written informed consent was obtained from all patients. If it was difficult to get, authors provided the information of this study and patients' right on the website or in a notice board at the hospital.

Adjuvant chemoradiotherapy

The decision to choose adjuvant therapy for each patient was made during a multidisciplinary tumor board discussion, depending on the presence of extracapsular extension, microscopically involved surgical margins, the extent of lymph node disease, age, PS, organ function, and patient preference, among others.

The RT was performed by either three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated radiotherapy (IMRT) [22] up to a dose of 50–70 Gy. RT was administered in 25–35 fractions with 2.0 Gy given once a day. The radiation dose was decided in accordance with the International Commission on Radiation Units and Measurements. Volume definition and dose calculation were CT-based. There were no planned treatment interruptions, except for weekends.

Concurrent chemotherapy with CDDP was administered tri-weekly at 80–100 mg/m^2 on days 1, 22, and 43. Some patients received weekly cisplatin at 40 mg/m^2 on days 1, 8, 15, 22, 29, 36, and 43, or tri-weekly split-dose cisplatin at 20 mg/m^2 on 4 consecutive days.

Prophylactic PEG

The determination to perform prophylactic PEG before CCRT depended on each physician's discretion, considering pre-treatment PS, DS, and patient preference. PEG placement was carried out by the direct method (Direct Ideal PEG Kit; Olympus Corp., Tokyo, Japan) under endoscopic support. All patients received local anesthesia, analgesia, and sedation with midazolam. Prophylactic antibiotics were given for 3 days.

Evaluation of adverse events related to CCRT and nutritional support

Adverse events related to CCRT were assessed using the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. The cumulative incidence of aspiration pneumonia from the initiation of CCRT until 1 year after its completion was also evaluated. Aspiration pneumonia was defined as a clinical condition that met all of the criteria presented in a previous paper [23]. The rates of patients with difficulty obtaining adequate nutrition via oral intake from the initiation of CCRT until 1 year after its completion and nutrition-support-free survival were evaluated. Feasibility of oral intake was defined as ability to orally consume adequate amounts of water and calories without any nutritional support.

Statistical analysis

The candidates for predictive factors for feasibility of oral intake were as follows: age; sex; primary tumor location; ECOG PS; total laryngectomy or other surgery; pre-treatment DS; pre-treatment body mass index (BMI) (kg/m^2); pre-treatment serum albumin (Alb) (g/

ml); total dose of CDDP; method of CDDP administration (tri-weekly, weekly, or split dose); method of RT (3D-CRT or IMRT); irradiation field (bilateral-neck RT or ipsilateral-neck RT); total dose of RT; mean RT dose to the constrictor muscles; and mean RT dose to the oral cavity. Regarding mean RT dose to the pharyngeal constrictor muscles and that to the oral cavity, the cut-off values were decided on basis of a receiver operating characteristic (ROC) curve. All variables in univariate analysis were included for the multivariate analysis. Hazard ratios (HR) and 95% confidence intervals (95% CI) were calculated using the Cox proportional hazards model to identify predictive factors for the feasibility of oral intake. The nutrition-support-free survival rate and cumulative incidence of aspiration pneumonia were calculated using the Kaplan–Meier method, and significance was evaluated using the log-rank test. The nutrition-support-free survival rate was calculated from the first day of CCRT until the onset of difficulty obtaining adequate nutrition via oral intake and was censored at the last follow-up visit or death from any cause. We used the Mann–Whitney *U* test for comparisons of continuous variables and Fisher's exact test for comparisons of categorical variables between the groups. $P < 0.05$ was considered statistically significant. All statistical analyses were conducted using EZR (version 1.37; Saitama Medical Center, Jichi Medical University, Saitama, Japan) [24].

Results

Patients' characteristics

Of 134 patients who received adjuvant CCRT, 2 patients with dysphagia score ≥ 3, 9 patients who depended on enteral nutrition or intravenous nutrition when starting CCRT, 4 patients who received Cetuximab or Carboplatin, and 2 patients with RT dose < 50 Gy were excluded (Supplement Fig. 1). Finally, a total of 117 patients were analyzed in this study (Table 1). Twenty-five patients received total laryngectomy, while 92 received other surgery. Forty-nine patients (42%) received IMRT and 34 patients (29%) underwent ipsilateral-neck RT. The median overall treatment time of RT was 44 days (range 32–56). The median total doses of RT and CDDP were 66 Gy and 240 mg/m^2, respectively. Although RT was interrupted in four patients (3.4%), all patients completed the planned RT. More than half of the patients received the planned dose of chemotherapy without dose reduction.

Predictive factors for feasibility of oral intake

Predictive factors for feasibility of oral intake are presented in Table 2. On basis of the ROC curve, mean RT dose of 30 Gy to the oral cavity was determined as a cut-off value with a sensitivity of 83.9%, the specificity of 49.2%, and area under the curve (AUC) of 0.793. Similarly, mean RT dose of 37 Gy to pharyngeal constrictor muscles was determined

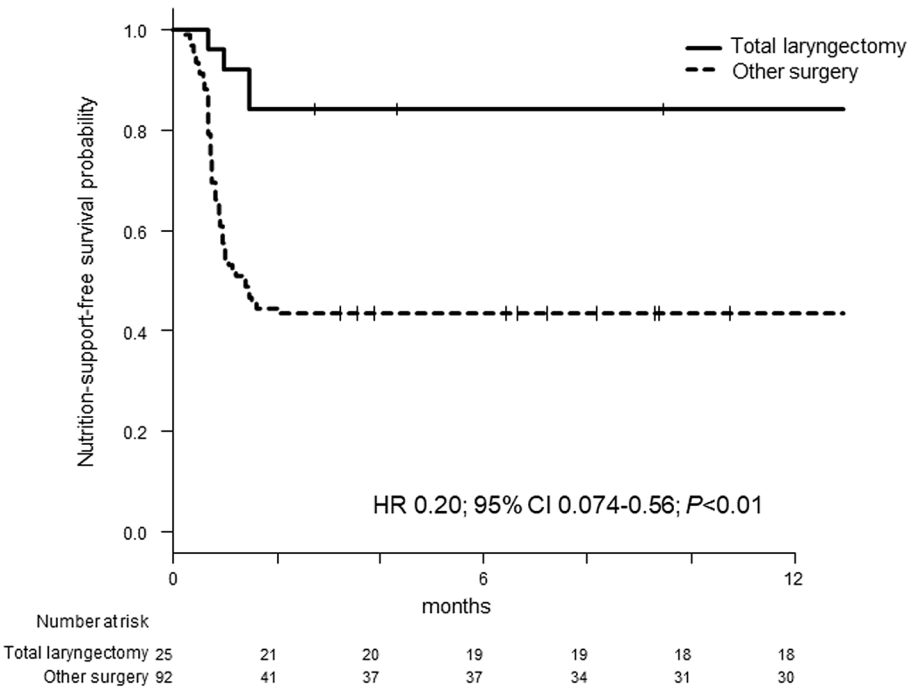

Fig. 1 Kaplan–Meier plot showing nutrition-free survival in the total laryngectomy group ($n = 25$) and the other surgery group ($n = 92$)

Table 1 Patients' characteristics

Number of patients	117
Age, years; median (range)	62 (23–76)
Sex, male *n* (%)	99 (85)
Surgery	
Total laryngectomy	25 (21)
Other surgery	92 (79)
ECOG performance status *n* (%)	
0–1	113 (97)
2	4 (3.4)
Primary surgery or surgery for local recurrence *n* (%)	
Primary surgery	80 (68)
Surgery for local recurrence	37 (32)
Primary tumor location *n* (%)	
Hypopharynx	16 (14)
Oropharynx	19 (16)
Larynx	14 (12)
Oral cavity	68 (58)
T category *n* (%)	
T1	24 (21)
T2	33 (28)
T3	15 (13)
T4	42 (36)
Tx	3 (2.6)
N category *n* (%)	
N0	30 (26)
N1	7 (6.0)
N2	75 (64)
N3	5 (4.3)
Pathological stage (primary surgery: $n=80$) *n* (%)	
III	3 (4)
IV	77 (96)
The reason of adjuvant chemoradiotherapy *n* (%)	
ECE	84 (72)
Microscopically involved surgical margins	6 (5.1)
ECE and microscopically involved surgical margins	11 (9.4)
Other reasons	16 (14)
The method of CDDP administration *n* (%)	
Tri-weekly	102 (87)
Weekly	7 (6.0)
Split	8 (6.8)
Total dose of RT (Gy); median (range)	60 (50–70)
Mean RT dose to the oral cavity (Gy); median (range)	35 (0–66)
Mean RT dose to the pharyngeal constrictor muscles (Gy); median (range)	46 (10–66)
Overall treatment time of RT (day); median (range)	44 (32–56)
The method of RT *n* (%)	
3D-CRT	68 (58)
IMRT	49 (42)
Irradiation field *n* (%)	
Bilateral-neck	83 (71)
Ipsilateral-neck	34 (29)
Pre-treatment DS *n* (%)	
0	44 (38)
1	51 (44)
2	22 (19)
Pre-treatment BMI (kg/m2); median (range)	21.5 (15.0–33.4)
Pre-treatment Alb (g/ml); median (range)	4.1 (3.2–5.0)

ECOG Eastern Cooperative Oncology Group, *CDDP* cisplatin, *ECE* extracapsular extension, *RT* radiotherapy, *3D-CRT* three-dimensional conformal radiotherapy, *IMRT* intensity-modulated radiotherapy, *DS* dysphagia score on the Ogilvie scale, *BMI* body mass index, *Alb* serum albumin

as a cut-off value with a sensitivity of 76.8%, specificity of 37.7%, and area under the curve (AUC) of 0.522. In univariate analysis, total laryngectomy, ipsilateral-neck RT, pre-treatment DS, male sex, mean RT dose to the oral cavity < 30 Gy, and BMI ≥ 18.5 were significantly associated with the feasibility of oral intake. In multivariate analysis, total laryngectomy (HR 0.09, 95% CI 0.020–0.37, $P=0.001$) and oral cavity of primary tumor location (HR 0.21, 95% CI 0.051–0.87, $P=0.031$) were significantly associated with the feasibility of oral intake. Of these factors, in accordance with HR, total laryngectomy was identified as one of the strongest independent predictive factors for the feasibility of oral intake.

Nutritional support, opioid use, and PEG-related adverse events

Because total laryngectomy was identified as one of the strongest independent predictive factors for the feasibility of oral intake in accordance with HR, we compared the nutritional support and adverse events between the total laryngectomy group and the other surgery group.

Nutritional support in both groups is summarized in Table 3. The rate of patients with difficulty obtaining adequate nutrition via oral intake was significantly lower in the total laryngectomy group than in the other surgery group (16% vs. 57%, $P<0.001$). In fact, although prophylactic PEG was performed in 10 patients in the total laryngectomy, only 3 patients used PEG. The main reason for this difficulty in both groups was mucositis. The rate of patients using opioids was significantly lower (9% vs. 55%, $P=0.04$) and the median maximum dose of opioids per day tended to be lower in the total laryngectomy group than in the other surgery group (0 mg/day vs. 15 mg/day, $P=0.07$). Consistent with the findings on the feasibility of oral intake, the rate of usage

Table 2 The assessment of predictive factors for the feasibility of oral intake

Candidates for predictive factors	Number of patients with difficulty obtaining adequate nutrition via oral intake	Univariate analysis		*P* value	Multivariate analysis		*P* value
		HR	95% CI		HR	95% CI	
Surgery							
Total laryngectomy	4	0.2	0.074–0.56	0.002	0.09	0.020–0.37	0.001
Other surgery	52	Ref			Ref		
Method of RT							
IMRT	19	0.58	0.34–1.02	0.058	0.45	0.19–1.1	0.081
3D-CRT	37	Ref			Ref		
Irradiation field							
Bilateral-neck	45	Ref			Ref		
Ipsilateral-neck	11	0.51	0.27–0.995	0.048	0.45	0.21–1.001	0.0503
Pre-treatment DS							
0	13	Ref			Ref		
1	27	2.2	1.1–4.2	0.023	1.5	0.68–3.3	0.31
2	16	3.8	1.8–7.9	< 0.001	1.9	0.65–5.4	0.24
ECOG performance status							
0–1	54	0.91	0.22–3.7	0.9	0.79	0.15–4.1	0.78
2	2	Ref			Ref		
Sex							
Male	44	0.51	0.27–0.97	0.039	1.1	0.49–2.3	0.88
Female	12	Ref			Ref		
Primary tumor location							
Hypopharynx	5	Ref			Ref		
Oropharynx	11	2.1	0.73–6.1	0.17	0.35	0.081–1.5	0.15
Larynx	3	0.6	0.14–2.5	0.49	0.54	0.11–2.6	0.44
Oral cavity	37	2	0.80–5.2	0.14	0.21	0.051–0.87	0.031
Method of CDDP dose							
Tri-weekly	51	1.6	0.49–5.0	0.45	1.2	0.34–4.4	0.76
Weekly	2	0.76	0.13–4.5	0.78	0.94	0.14–6.4	0.95
Split	3	Ref			Ref		
Age (years)							
≥ 65	18	Ref			Ref		
< 65	38	1.5	0.83–2.6	0.18	1.02	0.51–2.1	0.96
Total dose of RT (Gy)							
≥ 66	27	Ref			Ref		
< 66	29	1.03	0.61–1.7	0.92	1.1	0.49–2.3	0.89
Mean RT dose to the oral cavity (Gy)							
≥ 30	47	Ref			Ref		
< 30	9	0.29	0.14–0.60	< 0.001	0.40	0.15–1.03	0.059
Mean RT dose to the pharyngeal constrictor muscles (Gy)							
≥ 37	43	Ref			Ref		
< 37	13	0.61	0.33–1.1	0.12	0.59	0.27–1.3	0.19
Pre-treatment Alb (g/ml)							
≥ 3.8	44	1.3	0.69–2.5	0.42	1.7	0.80–3.7	0.16
< 3.8	12	Ref			Ref		
Pre-treatment BMI (kg/m^2)							
≥ 18.5	45	0.41	0.21–0.79	0.008	0.43	0.18–1.02	0.057
< 18.5	11	Ref			Ref		

HR hazard ratio, *95% CI* 95% confidence interval, *ref.* reference, *RT* radiotherapy, *3D-CRT* three-dimensional conformal radiotherapy, *IMRT* intensity-modulated radiotherapy, *DS* dysphagia score on the Ogilvie scale, *ECOG* Eastern Cooperative Oncology Group, *CDDP* cisplatin, *BMI* body mass index, *Alb* serum albumin

Table 3 Summary of nutritional support

	Total laryngectomy ($n=25$)	Other surgery ($n=92$)	P value
Patients with difficulty obtaining adequate nutrition via oral intake; n (%)	4 (16)	52 (57)	< 0.001
Reasons for difficulty obtaining adequate nutrition via oral intake; n (%)			0.59
Mucositis	2 (8)	33 (36)	
Dysphagia	0 (0)	5 (5.4)	
Dysgeusia	1 (4)	6 (6.5)	
Anorexia	1 (4)	7 (7.6)	
Other reason	0 (0)	1 (1.1)	
Method of nutritional support; n (%)			0.18
Enteral nutrition	2 (8)	44 (48)	
Central venous nutrition	0 (0)	1 (1.1)	
Peripheral venous nutrition	2 (8)	7 (7.6)	
Usage of opioids; n (%)	9 (36)	55 (60)	0.04
Maximum dose of opioids (mg/day); median (range)	0 (0–50)	15 (0–70)	0.07

PEG percutaneous endoscopic gastrostomy

of enteral nutrition was statistically significantly lower in the total laryngectomy group than in the other surgery group (8% vs. 48%, $P=0.001$). Furthermore, the 1-year nutrition-support-free survival rate was significantly higher in the total laryngectomy group than in the other surgery group (84%, 95% CI 62.8–93.7% vs. 44%, 95% CI 33.2–53.3%, $P<0.001$, Fig. 1). Adverse events related to PEG occurred in 5/76 patients (6.5%), including two cases of major wound infection (2.6%), 1 of major bleeding (1.3%), and 2 of minor bleeding (2.6%).

Adverse events related to CCRT

The incidences of grade ≥ 3 mucositis and dysphagia were significantly lower in the total laryngectomy group than in the other group (12% vs. 51%, $P<0.001$, 12% vs. 51%, $P<0.001$, respectively). There were no significant differences with regard to the incidences of neutropenia, anemia, creatinine increase, dry mouth, and radiation dermatitis (Table 4). One-year cumulative incidences of aspiration pneumonia were 0% in the total laryngectomy group and 13.5% in the other surgery group ($P=0.06$) (Fig. 2). No deaths occurred within 30 days after treatment.

Discussion

Postoperative CCRT is the standard treatment for patients with LASCCHN. However, it is associated with severe mucositis, dry mouth, and dysphagia, resulting in difficulty obtaining adequate nutrition via oral intake. Therefore, nutritional support is required during CRT. As methods of nutritional support, intravenous nutrition, nasogastric tube, and PEG are available. Among these, long-term intravenous nutrition has a higher risk of infectious morbidity than EN, which is not recommended in the A.S.P.E.N. clinical

Table 4 Adverse events related to CCRT

	Total laryngectomy ($n=25$)		Other surgery ($n=92$)		P value
Adverse events	Any grade; n (%)	≥ Grade 3; n (%)	Any grade; n (%)	≥ Grade 3; n (%)	
Neutropenia	23 (92)	7 (28)	86 (94)	14 (15)	0.15
Thrombocytopenia	19 (76)	0 (0)	42 (46)	0 (0)	N/A
Anemia	22 (88)	0 (0)	66 (72)	0 (0)	N/A
Creatinine increase	9 (36)	0 (0)	16 (17)	0 (0)	N/A
Mucositis	25 (100)	3 (12)	90 (98)	47 (51)	< 0.001
Dry mouth	22 (88)	0 (0)	87 (95)	1 (1.1)	1.00
Radiation dermatitis	24 (96)	1 (4)	91 (99)	0 (0)	0.21
Dysphagia	25 (100)	3 (12)	92 (100)	47 (51)	< 0.001
Others	1 (4)	0 (0)	4 (4.3)	2 (2.2)	N/A

CCRT concurrent chemoradiotherapy, *N/A* not available

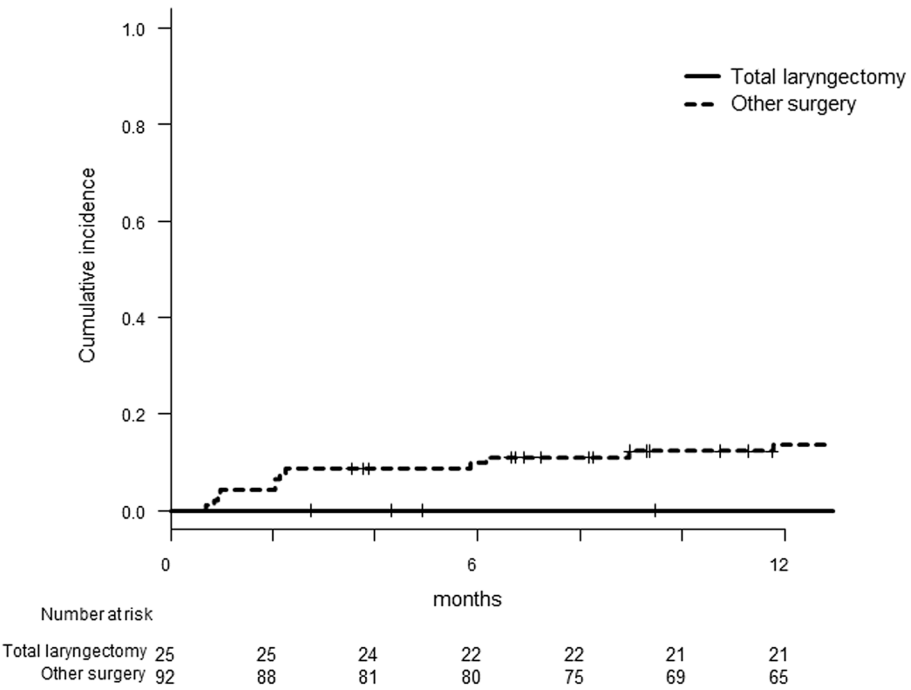

Fig. 2 Kaplan–Meier plot showing cumulative incidences of aspiration pneumonia in the total laryngectomy group ($n=25$) and the other surgery group ($n=92$)

guidelines [11–13]. Continuous nasogastric tube insertion could increase the risk of dysphagia and aspiration pneumonia, which is not suitable for long-term use during CRT. Thus, the need for prophylactic PEG has been widely recognized in the treatment with CCRT [14–17]. However, PEG-related adverse events sometimes lead to not just minor but also major complications. In a previous study, there were four major complications (3.3%) in 121 patients receiving PEG, including two cases of bleeding and two of wound infection [18]. Our patients treated by postoperative CCRT also experienced major PEG-related complications. Therefore, it is critical to avoid complications caused by prophylactic PEG as much as possible. Our hypothesis is that primary surgical procedures may play a major role in the ability of oral intake in the adjuvant CCRT.

Our multivariate analysis identified total laryngectomy as one of the strongest independent predictive factors for the feasibility of oral intake. In accordance with this finding, the rate of patients with difficulty obtaining adequate nutrition via oral intake was significantly lower in the total laryngectomy group than in the other surgery group for LASCCHN in adjuvant CCRT. Furthermore, the incidences of grade ≥ 3 mucositis and dysphagia were significantly lower in the total laryngectomy group than in the other group. These results suggest that surgical procedures with laryngectomy specifically influence the ability to perform oral intake in postoperative CCRT and that prophylactic PEG may not be required for patients who have undergone laryngectomy.

Several factors may explain why oral intake was feasible in patients after laryngectomy. First, the sensory functions of the larynx and hypopharynx decrease due to removal of the superior laryngeal nerve after total laryngectomy. Indeed, the rate of patients who needed opioids and the dose of opioids were lower in the total laryngectomy group than in the other surgery group. Second, the risk of aspiration is extremely low in the total laryngectomy group since the airway is completely separated from the gastrointestinal tract through total laryngectomy [25–28]. Indeed, our results revealed that no aspiration pneumonia occurred in the total laryngectomy group. Because of the difference in sensory functions of the larynx and hypopharynx and that in the risk of aspiration, oral intake could be more feasible in patients receiving total laryngectomy followed by CCRT than in those receiving other surgery followed by CCRT. Therefore, prophylactic PEG for adjuvant CCRT may not necessarily be required in patients who have undergone total laryngectomy.

Our multivariate analysis also revealed that ipsilateral-neck RT and mean RT dose to the oral cavity < 30 Gy tended to be associated with the feasibility of oral intake. As for the irradiation field, previous studies reported that the incidences of oral mucositis and dysphagia were significantly lower in ipsilateral-neck RT than in bilateral-neck RT for LASCCHN [29, 30], which may reflect the difference in the feasibility of oral intake. A previous study also reported that risk of oral mucositis increased as RT dose to the oral cavity increased [31]. This supports our results. Although oral cavity of primary tumor location was significantly associated with feasibility of oral intake, this mechanism for feasibility of oral intake is unknown and

cannot be explained as a hypothesis, such as that of total laryngectomy. In addition, no previous studies reported association between oral cavity of primary tumor location and feasibility of oral intake during and after adjuvant CCRT. Therefore, this result should be interpreted carefully at this moment.

Our study has several limitations. First, this is a retrospective study at a single medical center with a small number of patients. Further multicenter cohort study is thus needed to confirm our findings. Second, there were the unbalance in patients' baseline characteristics between the total laryngectomy group and the other surgery group. However, to solve the issue on the heterogeneity of the populations as much as possible, multivariate analysis was firstly performed to exclude confounding with each predictive factor. Importantly, our multivariate analysis identified total laryngectomy as a strongest and independent predictive factor for the feasibility of oral intake. Third, we used DS on the Ogilvie scale for inclusion criteria and analysis of predictive factors for the feasibility of oral intake. Although Ogilvie scale is simple and widely used for assessment of dysphasia in the area of esophageal cancer [32, 33], Functional Outcome Swallowing Scale (FOSS) and Food Intake LEVEL Scale (FILS) may be more standardized and sophisticated in the area of head and neck. Despite these limitations, our study suggests the low need for prophylactic PEG before adjuvant CCRT for patients with LASCCHN after total laryngectomy.

In conclusion, our study suggests that the majority of patients who underwent total laryngectomy are able to maintain oral intake and may not need nutritional support. Therefore, prophylactic PEG for adjuvant CCRT may not necessarily be required for LASCCHN patients who have undergone total laryngectomy. These information from our study is of great significance in terms not just of clinical convenience, avoidance of PEG-related adverse events, but also of cost reduction.

Funding Not applicable.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Cooper J, Pajak T, Forastiere A et al (2004) Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. N Engl J Med 350:1937–1944
2. Bernier J, Domenge C, Ozsahin M et al (2004) Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. N Engl J Med 350:1945–1952
3. Bernier J, Cooper JS, Pajak TF et al (2005) Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (# 9501). Head Neck 27:843–850
4. Winquist E, Oliver T, Gilbert R (2007) Postoperative chemoradiotherapy for advanced squamous cell carcinoma of the head and neck: a systematic review with meta-analysis. Head Neck 29:38–46
5. Bachaud JM, Cohen Jonathan E, Alzieu C et al (1996) Combined postoperative radiotherapy and weekly cisplatin infusion for locally advanced head and neck carcinoma: final report of a randomized trial. Int J Radiat Oncol Biol Phys 36:999–1004
6. Rampino M, Ricardi U, Munoz F et al (2011) Concomitant adjuvant chemoradiotherapy with weekly low-dose cisplatin for high-risk squamous cell carcinoma of the head and neck: a phase II prospective trial. Clin Oncol (R Coll Radiol) 23:134–140
7. Trotti A, Bellm LA, Epstein JB et al (2003) Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. Radiother Oncol 66:253–262
8. Barton MB, Keane TJ, Gadalla T et al (1992) The effect of treatment time and treatment interruption on tumour control following radical radiotherapy of laryngeal cancer. Radiother Oncol 23:137–143
9. Fowler JF, Lindstrom MJ (1992) Loss of local control with prolongation in radiotherapy. Int J Radiat Oncol Biol Phys 23:457–467
10. Herrmann T, Jakubek A, Trott KR (1994) The importance of the timing of a gap in radiotherapy of squamous cell carcinomas of the head and neck. Strahlenther Onkol 170:545–549
11. August D, Huhmann M (2009) A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. JPEN J Parenter Enteral Nutr 33:472–500
12. Bankhead R, Boullata J, Brantley S et al (2009) Enteral nutrition practice recommendations. JPEN J Parenter Enteral Nutr 33:122–167
13. McClave S, Martindale R, Vanek V et al (2009) Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: society of critical care medicine (sccm) and american society for parenteral and enteral nutrition (A.S.P.E.N.). JPEN J Parenter Enteral Nutr 33:277–316
14. Silander E, Nyman J, Bove M et al (2012) Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer: a randomized study. Head Neck 34:1–9
15. Chen A, Li B-Q, Lau D et al (2010) Evaluating the role of prophylactic gastrostomy tube placement prior to definitive chemoradiotherapy for head and neck cancer. Int J Radiat Oncol Biol Phys 78:1026–1032
16. Nguyen N, North D, Smith H et al (2006) Safety and effectiveness of prophylactic gastrostomy tubes for head and neck cancer patients undergoing chemoradiation. Surg Oncol 15:199–203
17. Lee JH, Machtay M, Unger LD et al (1998) Prophylactic gastrostomy tubes in patients undergoing intensive irradiation for cancer of the head and neck. Arch Otolaryngol Head Neck Surg 124:871–875

18. Grant DG, Bradley PT, Pothier DD et al (2009) Complications following gastrostomy tube insertion in patients with head and neck cancer: a prospective multi-institution study, systematic review and meta-analysis. Clin Otolaryngol 34:103–112
19. Corry J, Poon W, McPhee N et al (2009) Prospective study of percutaneous endoscopic gastrostomy tubes versus nasogastric tubes for enteral feeding in patients with head and neck cancer undergoing (chemo)radiation. Head Neck 31:867–876
20. Atkinson M, Ferguson R, Ogilvie AL (1979) Management of malignant dysphagia by intubation at endoscopy. J R Soc Med 72:894–897
21. Ogilvie AL, Dronfied MW, Ferguson R et al (1982) Palliative intubation of oesophagogastric neoplasms at fibreoptic endoscopy. Gut 23:1060–1067
22. Rothschild S, Studer G, Seifert B et al (2007) PET/CT staging followed by Intensity-Modulated Radiotherapy (IMRT) improves treatment outcome of locally advanced pharyngeal carcinoma: a matched-pair comparison. Radiat Oncol 2:22
23. Kawai S, Yokota T, Onozawa Y et al (2017) Risk factors for aspiration pneumonia after definitive chemoradiotherapy or bio-radiotherapy for locally advanced head and neck cancer: a monocentric case control study. BMC Cancer 17:59
24. Kanda Y (2013) Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant 48:452–458
25. Topf M, Magaña L, Salmon K et al (2018) Safety and efficacy of functional laryngectomy for end-stage dysphagia. Laryngoscope 128:597–602
26. Hutcheson KA, Alvarez CP, Barringer DA et al (2012) Outcomes of elective total laryngectomy for laryngopharyngeal dysfunction in disease-free head and neck cancer survivors. Otolaryngol Head Neck Surg 146:585–590
27. Theunissen EAR, Timmermans A, Zuur C et al (2012) Total laryngectomy for a dysfunctional larynx after (chemo)radiotherapy. Arch Otolaryngol Head Neck Surg 138:548–555
28. Lazarus C, Logemann J, Shi G et al (2002) Does laryngectomy improve swallowing after chemoradiotherapy? A case study. Arch Otolaryngol Head Neck Surg 128:54–57
29. Kim Y, Cho KH, Moon SH et al (2017) Comparison of the clinical outcomes of patients with squamous cell carcinoma of the tonsil receiving postoperative ipsilateral versus bilateral neck radiotherapy: a propensity score matching analysis (KROG 11-07). Cancer Res Treat 49:1097–1105
30. Le NS, Janik S, Simmel H et al (2019) Bilateral vs ipsilateral adjuvant radiotherapy in patients with cancer of unknown primary of the head and neck: an analysis of the clinical outcome and radiation-induced side effects. Head Neck 41:1785–1794
31. Mazzola R, Ricchetti F, Fersino S et al (2016) Predictors of mucositis in oropharyngeal and oral cavity cancer in patients treated with volumetric modulated radiation treatment: a dose-volume analysis. Head Neck 38(Suppl 1):E815–E819
32. Ikeda E, Kojima T, Kaneko K et al (2011) Efficacy of concurrent chemoradiotherapy as a palliative treatment in stage IVB esophageal cancer patients with dysphagia. Jpn J Clin Oncol 41:964–972
33. Mezes P, Krokidis ME, Katsanos K et al (2014) Palliation of esophageal cancer with a double-layered covered nitinol stent: long-term outcomes and predictors of stent migration and patient survival. Cardiovasc Intervent Radiol 37:1444–1449