Predictors of the need for prophylactic percutaneous endoscopic gastrostomy in head and neck cancer patients treated with concurrent chemoradiotherapy

Satoshi Kano, M.D., Ph.D.[1], Nayuta Tsushima, M.D.[1], Takayoshi Suzuki, M.D., Ph.D.[1], Seijiro Hamada, M.D.[1], Taizo Yokokawa, M.D.[1], Hiroshi Idogawa, M.D.[1], Koichi Yasuda, M.D., Ph.D.[2], Hideki Minatogawa, M.D.[2], Yasuhiro Dekura, M.D.[2], Hidefumi Aoyama, M.D., Ph.D.[2], Akihiro Homma, M.D., Ph.D.[1]

[1] Department of Otolaryngology-Head and Neck Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan.

[2] Department of Radiation Oncology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan.

Corresponding author: Satoshi Kano, Department of Otolaryngology-Head and Neck Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Kita 15, Nishi 7, Kita-ku, Sapporo 060-8638, Japan, Tel: +81-11-706-5958, Fax: +81-11-717-7566, E-mail: skano@med.hokudai.ac.jp

Abstract

Background. We investigated whether prophylactic percutaneous endoscopic gastrostomy (PEG) is used effectively for patients treated with definitive concurrent chemoradiotherapy (CCRT) and the predictors of the need for PEG.

Methods. Three hundred and twenty-six patients with laryngeal, oropharyngeal or hypopharyngeal cancers were retrospectively reviewed.

Results. The PEG tube use group had more favorable results than the total parenteral nutrition and nasogastric tube groups in terms of rate of serum albumin loss, incidence of severe fever and aspiration pneumonia, CCRT completion rate and hospitalization period. However, it was inferior to oral intake. Analysis of the relative risk of requiring enteral or parenteral nutrition revealed that performance status (PS) 2, primary site (supraglottis, oropharynx, or hypopharynx), N3 disease, and cisplatin were predictors of the need for nutritional support.

Conclusions. Prophylactic PEG is effective for patients treated with definitive CCRT and is especially required for patients with PS2 or oropharyngeal cancer.

Keywords: PEG, head and neck cancer, chemoradiotherapy

INTRODUCTION

Concurrent chemoradiotherapy (CCRT) is one of the standard treatments for advanced pharyngeal and laryngeal cancers and has the advantage in organ preservation. However, CCRT for head and neck cancers frequently causes severe mucositis, intolerable pain, prolonged nausea, and permanent xerostomia, which can result in dysphagia. Moreover, swallowing dysfunction causes malnutrition, aspiration pneumonia, and makes it difficult to continue scheduled treatment. In such cases, we had previously administered enteral nutrition with a nasogastric (NG) tube or total parenteral nutrition (TPN) intravenously. However, NG tubes caused patients constant nasal and pharyngeal discomfort, and TPN increased the risk of bacteremia and sepsis. Therefore, we currently recommend prophylactic percutaneous endoscopic gastrostomy (PEG) for patients treated with CCRT. PEG is expected to maintain nutritional status, prevent aspiration pneumonia, allow completion of scheduled treatments, and shorten the hospitalization period. Many authors have previously reported the effectiveness of prophylactic PEG in patients treated with CCRT; however, these studies are somewhat problematic in that the primary site and treatment methods varied and the number of cases was small. [1-5] On the other hand, some researchers have reported that reactive PEG is better than prophylactic PEG. [6] Additionally, some patients undergoing prophylactic PEG did not use it during CCRT. Therefore, we retrospectively investigated

whether PEG is used effectively for patients treated with definitive CCRT and the predictors of the need for prophylactic PEG.

MATERIALS AND METHODS

Patients

This is a retrospective study using the medical records of patients with head and neck cancers treated at Hokkaido University Hospital between January 2008 and December 2017. The inclusion criteria for this study were as follows: (1) previously untreated laryngeal, oropharyngeal or hypopharyngeal cancer, (2) histologically proven squamous cell carcinoma (SCC), and (3) definitive CCRT.

Treatment

Radiation was administered in five x 2 Gy single daily fractions per week for a total dose of 66-70Gy. In general, the prophylactic field was irradiated with a total of 44 Gy and the primary site and metastatic lymph nodes were irradiated with a total of 70 Gy. The concomitant chemotherapy consisted of various regimens. The dose, schedule and route of cisplatin injections (CDDP) were as follows: 30–40 mg/m^2 was administered intravenously once a week (5–6 cycles), 80-100 mg/m^2 was administered intravenously once every three

weeks (3 cycles) and the superselective intra-arterial infusion of high-dose CDDP (100-120 mg/m^2) was given once a week (4–6 cycles). On the other hand, carboplatin (CBDCA) was administered intravenously at a dose of 1.5 x the area under the curve (AUC) once a week and cetuximab (Cmab) was administered intravenously at a loading dose of 400 mg/m^2 in the first week, followed by 250 mg/m^2 once a week. All patients were hospitalized during CCRT.

Some patients received induction chemotherapy (IC) prior to CCRT when the primary tumors were thought to be too large to be cured by CCRT alone, or distant metastases were likely to develop as lymph node metastases were evaluated as N2c or 3. The regimens of IC were tri-weekly TPF (docetaxel 75 mg/m^2 on day 1, CDDP 75 mg/m^2 on day 1 and 5FU of 750 mg/m^2 on day 1-5), tri-weekly PF (CDDP 100 mg/m^2 on day 1 and 5FU of 1000 mg/m^2 on day 1-5) and weekly PCE (paclitaxel 80 mg/m^2 on day 1, CBDCA AUC1.5 on day 1 and cetuximab at an initial dose of 400 mg/m^2, followed by 250 mg/m^2 on day1).

In principle, we recommended prophylactic PEG to patients with laryngeal, oropharyngeal or hypopharyngeal cancer who were set to undergo CCRT; however, some patients did not receive PEG due to the physician's preference, patient's refusal or due to its impossibility for anatomical reasons such as history of gastric surgery or intestinal tract on the stomach. Prophylactic PEG was usually performed prior to or in the early phase of CCRT. The timing of the initiation of PEG tube use and the content and amount of enteral nutrition

were determined individually based on the patients' needs and medical staff evaluation. If some patients without PEG tube became malnourished, a NG tube was inserted or TPN was administered thorough the central vein.

Data collection

We retrospectively collected the patients' clinical data including age, sex, performance status (PS), body mass index (BMI), primary site, TNM classification according to the UICC 7th edition, treatment details, nutritional intake method, nutritional condition (body weight and serum albumin level), adverse events (fever and aspiration pneumonia) and hospitalization period (from the end of CCRT to discharge). The threshold of BMI was defined as 25, which is the boundary value between normal body weight and obesity in adults. Laryngeal cancer was analyzed separately for the glottis/subglottis and supraglottis according to the differences in radiation dose to the pharyngeal space. Rate of body weight loss and rate of serum albumin loss were calculated from the respective values prior to CCRT and the lowest value during CCRT. Adverse events related to fever were classified according to the Common Terminology Criteria for Adverse Events ver. 5.0. Diagnosis of aspiration pneumonia was based on the symptoms during feeding, endoscopic findings and computed tomography or X-ray images. The completion of CCRT was defined as the full administration of the

scheduled dose of radiation without a break of over seven days, and the chemotherapy was administered as follows; intravenous injection of over 200 mg/m^2 cisplatin, intra-arterial injection of over 400 mg/m^2 cisplatin, over six courses of carboplatin or over seven courses of cetuximab.

Statistical analysis

Chi-square test and Student's *t* test were performed for comparisons between two groups. In comparison among more than three groups, residual analysis was performed following Chi-square test, and one-way ANOVA with Bartlett's test and Holm's post hoc test was used. PEG tube dependence was calculated using the Kaplan-Meier method, which defined the final day of CCRT as the start date of measurement, PEG removal as an event and patient death as censoring. Binomial logistic regression analysis was used to analyze the relative risk factors for the need for enteral or parenteral nutrition for patients treated with CCRT. A 2-tailed p value <0.05 was considered statistically significant. Statistical analyses were performed using BellCurve for Excel (Social Survey Research Information Co., Ltd., Japan). This study was approved by Hokkaido University Hospital Ethical Committee and informed consent was obtained in the form of opt-out on the website.

RESULTS

Patient characteristics

A total of 326 patients met the inclusion criteria. Of those patients, 181 (56%) underwent prophylactic PEG, while 145 (44%) did not. Table 1 shows the characteristics of patients stratified by PEG tube placement. Patient characteristics with statistically significant differences between the two groups were BMI, primary site and clinical stage. In particular, the number of patients with glottic or subglottic cancer with PEG tube was low (8%), while the number of with oropharyngeal cancer was high (71%).

PEG tube usage and complications

Of the patients with PEG tube, 129 patients (71%) actually used it, while 50 patients (28%) could maintain oral intake without use of the PEG tube and two patients (1%) were administered TPN due to serious nausea and pseudomembranous colitis. The median time to start PEG tube use was 21 days after the start of CCRT (range, 0-61 days). On the other hand, of the patients without PEG tube, 100 patients (69%) could maintain oral intake without other nutritional support, while 24 patients (17%) needed TPN administration and 21 patients (14%) needed nutrition via NG tube (Table 2).

Of the patients with PEG tube, 11 patients (6%) had PEG-related complications, including nine with peristomal infections and two with peristomal ulcers. One patient required PEG tube removal due to peristomal infection.

Nutritional condition

Maintaining nutritional condition during treatment is clinically important for the completion of scheduled CCRT without interruption. To evaluate the nutritional condition of patients, we calculated the rate of body weight loss and that of serum albumin loss. First, we compared the values between the groups with or without PEG tube placement. The results showed that there was no significant difference between them (Figure 1A and 2A). Second, we focused on the actual nutritional intake methods and compared values among the following four groups; PEG tube use, NG tube, TPN and oral intake alone. The results showed that there were no significant differences in the rate of body weight loss (Figure 1B), whereas there were statistically significant differences in the rate of serum albumin loss ($p = 0.003$, Figure 2B). The median rate of serum albumin loss was -16.3, -25.0, -26.7 and -28.6% in the group with oral intake alone, PEG tube use, TPN and NG tube, respectively.

Adverse events

To clarify whether PEG could prevent aspiration pneumonia during CCRT, we examined fever and aspiration pneumonia as adverse events associated with CCRT. No significant differences were observed in fever or aspiration pneumonia between patients with and without PEG tube placement. However, a comparison among the four groups divided according to actual nutritional intake method, the incidence of grade 3 fever was significantly higher in the group with TPN and the incidence of aspiration pneumonia was significantly higher in that with NG tube and TPN (Table 3 and supplemental table 1).

CCRT completion rate

The CCRT completion rate was 78% among all patients. Among the total patients, 13 patients failed to complete radiotherapy and 67 patients failed to complete chemotherapy. Of the 67 patients who could not complete chemotherapy, 25 patients underwent IC prior to CCRT. A comparison between patients with and without PEG tube placement showed no significant difference in the CCRT completion rate. However, a comparison among the four groups divided according to actual nutritional intake method, the completion rate was significantly lower in the groups with NG tube and TPN (Table 4 and supplemental table 2).

Hospitalization period after the end of CCRT

Of 326 patients, nine patients continued their hospitalization and underwent additional treatment, such as salvage surgery, adjuvant chemotherapy or treatment for other disease. Furthermore, three patients were transferred to different hospitals, hence we could not obtain the date of discharge. Therefore, we excluded these 12 patients from this analysis, and examined the hospitalization period after the end of CCRT in the remaining 314 patients. The median duration was 19 days, the average was 25 days and the range was 1-327 days. Six patients needed a hospitalization for more than 100 days after CCRT.

A comparison between patients with or without PEG tube placement revealed no significant difference in the hospitalization period after the end of CCRT. However, a comparison among the four groups divided according to actual nutritional intake method showed the hospitalization period was longer in order of oral intake alone, PEG tube use, TPN and NG tube ($p < 0.001$, Figure 3). The median of period was 15, 24, 27 and 36 days for the group with oral intake alone, PEG tube use, TPN and NG tube, respectively.

PEG tube dependence after CCRT

Of 181 patients with PEG tube, two patients could not use the PEG tube due to serious nausea and pseudomembranous colitis, and the PEG tube was removed in one patient due to peristomal infection. Therefore, we excluded these three patients from this analysis, and

examined PEG tube dependence after CCRT in the remaining 178 patients. Seventy-two patients (40%) had their tubes removed before discharge from the hospital. Analysis using the Kaplan-Meier method, PEG tube dependence was found to be 17.7, 13.2 and 9.0% at 6, 12, and 36 months after CCRT, respectively (Figure 4).

Relative risk of requiring enteral or parenteral nutrition in patients treated with CCRT

In this study, 28% of patients with PEG tube never used it during CCRT, while 31% of patients without PEG tube needed it due to dysphagia (Table 2). Therefore, we analyzed the relative risk of requiring enteral or parenteral nutrition in patients treated with CCRT. Multivariate analysis was performed using binominal logistic regression analysis which defined the use of PEG tube, NG tube and TPN as events for estimating the relative risk. The threshold of age was the median of all cases in this study. The results showed significant differences in terms of PS, primary site, N classification and chemotherapy regimen (Table 5). In particular, the odds ratios for PS2 and oropharyngeal cancer were extremely high (56.09 and 52.89, respectively).

DISCUSSION

In this study, a comparison among the groups divided according to the actual nutritional intake method revealed that, the PEG tube use group had more favorable results than did the NG tube and TPN group in terms of the rate of serum albumin loss, the incidence of severe fever and aspiration pneumonia, the completion rate and the hospitalization period after the end of CCRT. These results showed that prophylactic PEG tube was beneficial for patients who had difficulty with oral intake during CCRT. Prophylactic PEG tube allows patients to begin their nutritional support faster than reactive NG tube or TPN. Patients could reduce the risk of aspiration because they do not have to force themselves to eat, and they could maintain their serum albumin level by nutrition through PEG tube. In addition, the decrease of inflammations due to infection is also considered to suppress the serum albumin loss. The maintenance of nutritional status and the prevention of aspiration pneumonia because of the presence of the PEG tube are thought to lead to an improvement in the CCRT completion rate. Furthermore, because the PEG tube can be managed at home, the period until discharge is shorter than for other parenteral nutrition methods. In this study, 60% of patients were discharged with PEG tubes still in place. Reducing the length of hospitalization will not only lead to greater mental comfort for the patients themselves, but also reduce medical costs from a social perspective. However, the PEG tube was inferior to oral intake. The reason for this could be the timing of the start of PEG tube use and the content of the nutritional supplements.

Our institution has no unified rule about the timing of the start of PEG tube use and the nutritional content, and they were determined by the patient and medical staff. Patients generally do not want to use a PEG tube as they want to eat as much as possible by mouth; therefore, the timing of the start of PEG tube use is often delayed. Takahashi et al. have reported that intensive nutrition support in addition to prophylactic PEG is important for patients with oropharyngeal cancer treated with CCRT. [7] In addition to receiving prophylactic PEG, we should also consider more a better planned and more aggressive use of PEG tube for patients treated with CCRT.

On the other hand, we failed to find any significant differences between patients with or without the prophylactic PEG tube placement in terms of nutritional condition, adverse events, CCRT completion rate, and hospitalization period. We consider that the reason for this is the differences in patient characteristics between the two groups. Patients with PEG tube significantly tended to have low BMI, oropharyngeal cancer and advanced cancer (Table 1). In other words, prophylactic PEG was frequently performed for patients expected to have difficulty in oral intake during CCRT. Two previous prospective randomized trials showed that the quality of life after treatment was significantly better and the weight loss was significantly less in the prophylactic PEG group. [3,4] However, these reports were based on a small number of enrolled patients, included various treatment

modalities and nonstandard chemotherapy. A prospective randomized trial involving a large number of cases treated with a standard and uniform modality is required to demonstrate the utility of prophylactic PEG tube in definitive CCRT.

Several studies have reported that long-term dysphagia may be associated with the use of PEG tubes. [8-10] The authors hypothesized that PEG tubes may cause more pronounced atrophy of the muscles responsible for swallowing because of the prolonged absence of oral intake. These studies were retrospective; however, Axelsson et al. examined the effect of prophylactic PEG tubes on post-treatment swallowing function using a randomized controlled study. [11] The results showed that there were no significant differences in swallowing function between the prophylactic PEG tube group and the control group after 12 months, 24 months, and 8 years. In this study, the proportion of patients with their PEG tube still in place was 17.7, 13.2 and 9.0% at 6, 12, and 36 months after CCRT. Burney et al. examined the long-term outcome of PEG tube use in 565 patients with head and neck cancer, and reported that 20% of patients needed PEG tubes for a year or more. [12] Regarding the difference in the PEG tube dependency ratio between Japanese and Western patients, we have previously reported that Japanese patients resume oral intake earlier than do Western patients. [13] Furthermore, we speculated that the cricopharyngeal muscle

condition in the Japanese population might differ from that in the Western population based on the fact that Zenker diverticulum is rare in Japan. [14]

In this study, about 30% of patients with PEG tube never used it during CCRT, while about 30% of patients without PEG tube needed it due to dysphagia. In addition, the rate of PEG-related complications in our study was 6%, which was equivalent to other study (4–10%). [5,12,15] Therefore, unnecessary prophylactic PEG needs to be reduced in terms of its complication and medical costs. Therefore, we investigated the predictors for the need of prophylactic PEG in patients treated with definitive CCRT. Several authors have previously reported about the predictors for requiring enteral feeding in head and neck cancer patients. Mekhail et al. examined 158 patients with head and neck cancer and reported that a hypopharyngeal primary site, female, T4 primary tumor, and treatment with CRT were predictive of a need for feeding tube placement. [9] Sachdev et al. analyzed 100 patients with head and neck cancer and concluded that older age was the most significant risk factor for needing enteral feeding in patients with locally advanced head and neck cancer. [16] van der Linden et al. reviewed 240 patients with head and neck cancer and reported that nodal disease presence and bilateral neck irradiation were significantly related to enteral nutrition. [17] These three studies included not only the patients treated with definitive CRT but also those treated with postoperative CRT or radiotherapy alone. On the other hand, Strom et al.

investigated 128 oropharyngeal cancer patients treated with definitive CRT and concluded that the risk factors for requiring PEG tube placement included accelerated irradiation fractionation, a T classification of three or higher, a cumulative CDDP dose of 200 mg/m^2 or higher, and a BMI of less than 25. [18] Our study had a larger number of cases than the previous reports analyzing the predictors for the need of prophylactic PEG for patients undergoing definitive CCRT. We found that PS2, primary site (supraglottis, oropharynx, or hypopharynx), N3, and CDDP were risk factors for requiring nutritional support. Among them, the odds ratios for PS2 and oropharyngeal cancer were extremely high. Patients with PS2 already have poor general condition before treatment due to their tumor and comorbidity, therefore they would be prone to dysphagia by CCRT. In supraglottic, oropharyngeal and hypopharyngeal cancer, the wide field of irradiation to the pharynx is thought to cause severe mucositis. Among them, the full-dose definitive irradiation applied to the oropharyngeal region is considered to have the most adverse effect on oral intake. Similarly, in patients with N3 lymph node metastasis, the extensive full-dose definitive irradiation to the affected neck side is thought to cause dysphagia. In terms of concomitant chemotherapy, CDDP could cause more severe mucositis and nausea than other drugs. These results are especially useful as a guide when recommending prophylactic PEG to patients undergoing definitive CCRT. We could find the predictors for the need of prophylactic PEG in patients treated with

definitive CCRT; however, our report is only a retrospective study. Therefore, a prospective study should be performed to verify our findings.

CONCLUSIONS

Our study showed that the PEG tube use group had more favorable results than did the NG tube and TPN group in terms of the rate of serum albumin loss, the incidence of severe fever and aspiration pneumonia, the CCRT completion rate, and the hospitalization period. Additionally, we identified predictors for the need of prophylactic PEG in patients treated with definitive CCRT. Prophylactic PEG is useful; however, we need to select patients who need prophylactic PEG tube placement more carefully and PEG tubes should be used in more effective timing and with more effective nutritional supplements.

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FIGURE CAPTIONS

Figure 1. The rate of body weight loss during concurrent chemoradiotherapy. (A) A comparison between patients with or without PEG tube placement. The median is -8.9% in the group with PEG and -8.6% in the group without PEG. (B) A comparison among the four groups divided according to actual nutritional intake method. The median is -8.9, -8.4, -9.7 and -8.5% in the group with PEG tube use, NG tube, TPN and oral intake alone, respectively.

Figure 2. The rate of serum albumin loss during concurrent chemoradiotherapy. (A) A comparison between patients with or without PEG tube placement. The median is -22.2% in the group with PEG and -18.8% in the group without PEG. (B) A comparison among the four groups divided according to actual nutritional intake method. The median is -25.0, -28,6, -26.7 and -16.3% in the group with PEG tube use, NG tube, TPN and oral intake alone, respectively.

Figure 3. Hospitalization period after the end of CCRT. (A) A comparison between patients with or without PEG tube placement. The median is 20 days in the group with PEG and 19 days in the group without PEG. (B) A comparison among the four groups divided according to actual nutritional intake method.

The median is 24, 36, 27 and 15 days in the group with PEG tube use, NG tube, TPN and oral intake alone, respectively.

Figure 4. PEG tube dependence after CCRT. A Kaplan-Meier curve was drawn by defining PEG removal as an event and patient death as censoring. The PEG tube dependence rate was 17.7, 13.2 and 9.0% at 6, 12, and 36 months after CCRT, respectively.

Table 1. Characteristics of patients stratified by PEG tube placement

	Number of patients (%)				
	All	PEG +		PEG –		*p* value
Age						0.252
Median (Range)	64 (40-80)	63	(40-80)	64	(40-80)	
Sex						0.254
Male	292	159	(54)	133	(46)	
Female	34	22	(65)	12	(35)	
PS						0.089
0-1	317	179	(56)	138	(44)	
2	9	2	(22)	7	(78)	
BMI						0.004
< 25	243	146	(60)	97	(40)	
≥ 25	83	35	(42)	48	(58)	
Primary site						< 0.001
Glottis/Subglottis	24	2	(8)	22	(92)	
Supraglottis	31	16	(52)	15	(48)	
Oropharynx	139	98	(71)	41	(29)	
Hypopharynx	132	65	(49)	67	(51)	
T classification						0.127
1	19	10	(53)	9	(47)	
2	144	70	(49)	74	(51)	
3	79	50	(63)	29	(37)	
4	84	51	(61)	33	(39)	
N classification						0.063
0	85	37	(44)	48	(56)	
1	30	18	(60)	12	(40)	
2	195	115	(59)	80	(41)	
3	16	11	(69)	5	(31)	
Stage						0.004
I	1	1	(100)	0	(0)	
II	51	17	(33)	34	(67)	
III	44	24	(55)	20	(45)	
IV	230	139	(60)	91	(40)	
IC						0.345
+	73	37	(51)	36	(49)	

–	253	144	(57)	109	(43)	
Regimens of chemotherapy						0.243
CDDP iv	244	132	(54)	112	(46)	
CDDP ia	52	35	(67)	17	(33)	
CBDCA	12	6	(50)	6	(50)	
Cmab	18	8	(44)	10	(56)	

PEG: percutaneous endoscopic gastrostomy, PS: performance status, BMI: body mass index, IC: induction chemotherapy, CDDP iv: intravenous injection of cisplatin, CDDP ia: intraarterial injection of cisplatin, CBDCA: carboplatin, Cmab: cetuximab

Table 2. Nutritional intake methods

		Number of patients (%)
PEG +	PEG tube use	129 (71)
	Oral intake alone	50 (28)
	TPN use	2 (1)
PEG –	Oral intake alone	100 (69)
	TPN use	24 (17)
	NG tube use	21 (14)

PEG: percutaneous endoscopic gastrostomy, TPN: total parenteral nutrition, NG tube: nasogastric tube

Table 3. Adverse events of chemoradiotherapy

	Number of patients (%)											
	PEG +		PEG –		PEG tube use		NG tube		TPN		Oral intake alone	
Fever			$p = 0.611$								$p < 0.001$	
G0	97	(53)	82	(57)	58	(45)	5	(24)	6	(23)	110	(73)
G1	45	(25)	38	(26)	38	(29)	10	(48)	7	(27)	28	(19)
G2	32	(18)	18	(12)	26	(20)	4	(19)	9	(35)	11	(7)
G3	7	(4)	7	(5)	7	(5)	2	(9)	4	(15)	1	(1)
Aspiration pneumonia			$p = 0.479$								$p < 0.001$	
–	163	(90)	127	(87)	112	(87)	12	(57)	20	(77)	146	(97)
+	18	(10)	18	(13)	17	(13)	9	(43)	6	(23)	4	(3)

PEG: percutaneous endoscopic gastrostomy, NG tube: nasogastric tube, TPN: total parenteral nutrition

Table 4. Completion rate of chemoradiotherapy

	Number of patients (%)											
	PEG +		PEG –		PEG tube use		NG tube		TPN		Oral intake alone	
Completion			$p = 0.225$								$p = 0.013$	
Yes	145	(80)	108	(74)	102	(79)	13	(62)	15	(58)	123	(82)
No	36	(20)	37	(26)	27	(21)	8	(38)	11	(42)	27	(18)

PEG: percutaneous endoscopic gastrostomy, NG tube: nasogastric tube, TPN: total parenteral nutrition

Table 5. Relative risk of requiring the enteral or parenteral nutrition

	OR	(95% CI)	*p*-value
Age			
< 64	1		
≥ 64	1.42	(0.85-2.39)	0.178
Sex			
Male	1		
Female	1.81	(0.76-4.31)	0.177
PS			
0-1	1		
2	56.09	(3.27-962.10)	0.005
BMI			
≥ 25	1		
< 25	1.10	(0.62-1.96)	0.733
Primary site			
Glottis/Subglottis	1		
Supraglottis	14.21	(1.55-130.12)	0.018
Oropharynx	52.89	(6.09-458.59)	< 0.001
Hypopharynx	17.26	(2.02-147.61)	0.009
T classification			
1-2	1		
3-4	1.55	(0.92-2.60)	0.098
N classification			
0	1		
1	1.71	(0.63-4.63)	0.289
2	1.27	(0.65-2.47)	0.466
3	4.32	(1.07-17.49)	0.039
IC			
–	1		
+	0.77	(0.40-1.49)	0.446
Regimens of chemotherapy			
CBDCA	1		
CDDP iv	9.99	(1.88-52.94)	0.006
CDDP ia	13.07	(2.23-76.61)	0.004
Cmab	4.91	(0.71-33.68)	0.104

OR: odds ratio, CI: confidence interval, PS: performance status, BMI: body mass index,

IC: induction chemotherapy, CBDCA: carboplatin, CDDP iv: intravenous injection of cisplatin, CDDP ia: intraarterial injection of cisplatin, Cmab: cetuximab

Figure 1

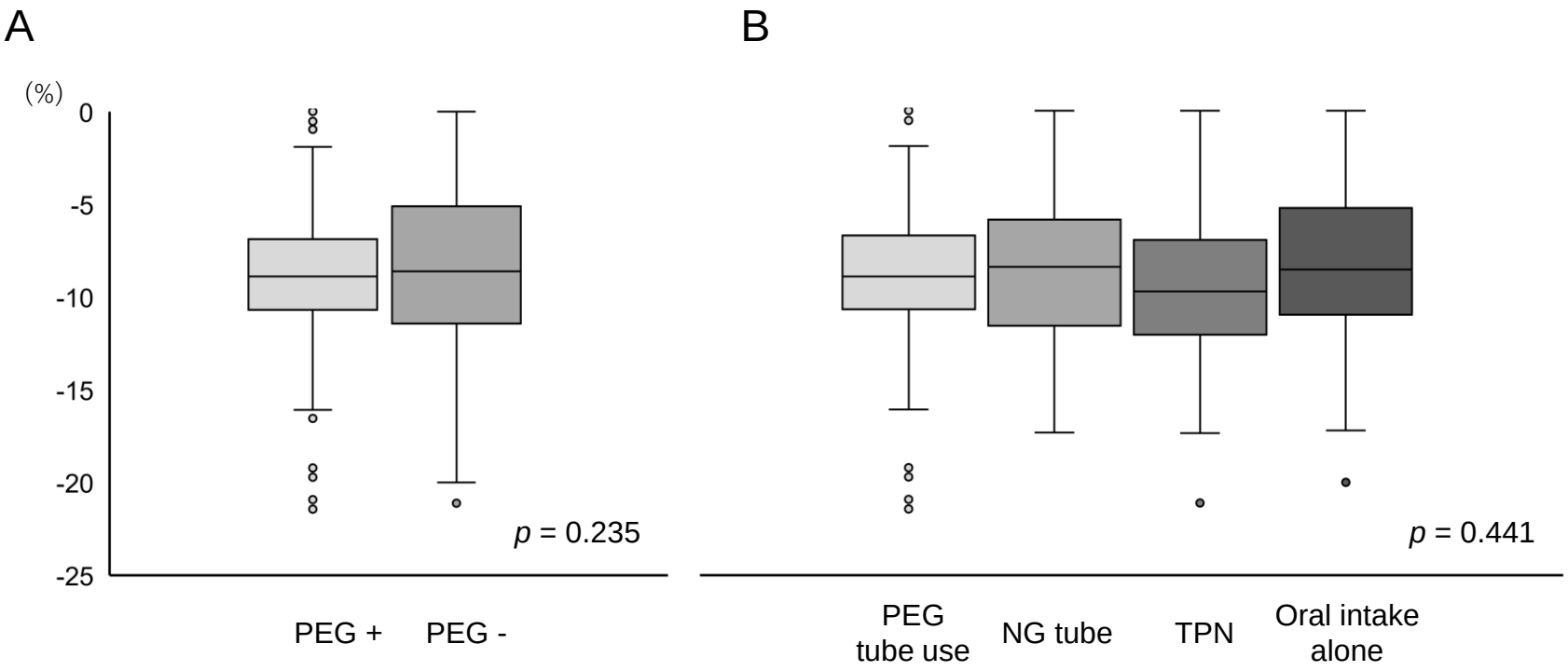
A
(%)
0
-5
-10
-15
-20
-25
p = 0.235
PEG +
PEG -
B
p = 0.441
PEG tube use
NG tube
TPN
Oral intake alone

Figure 2

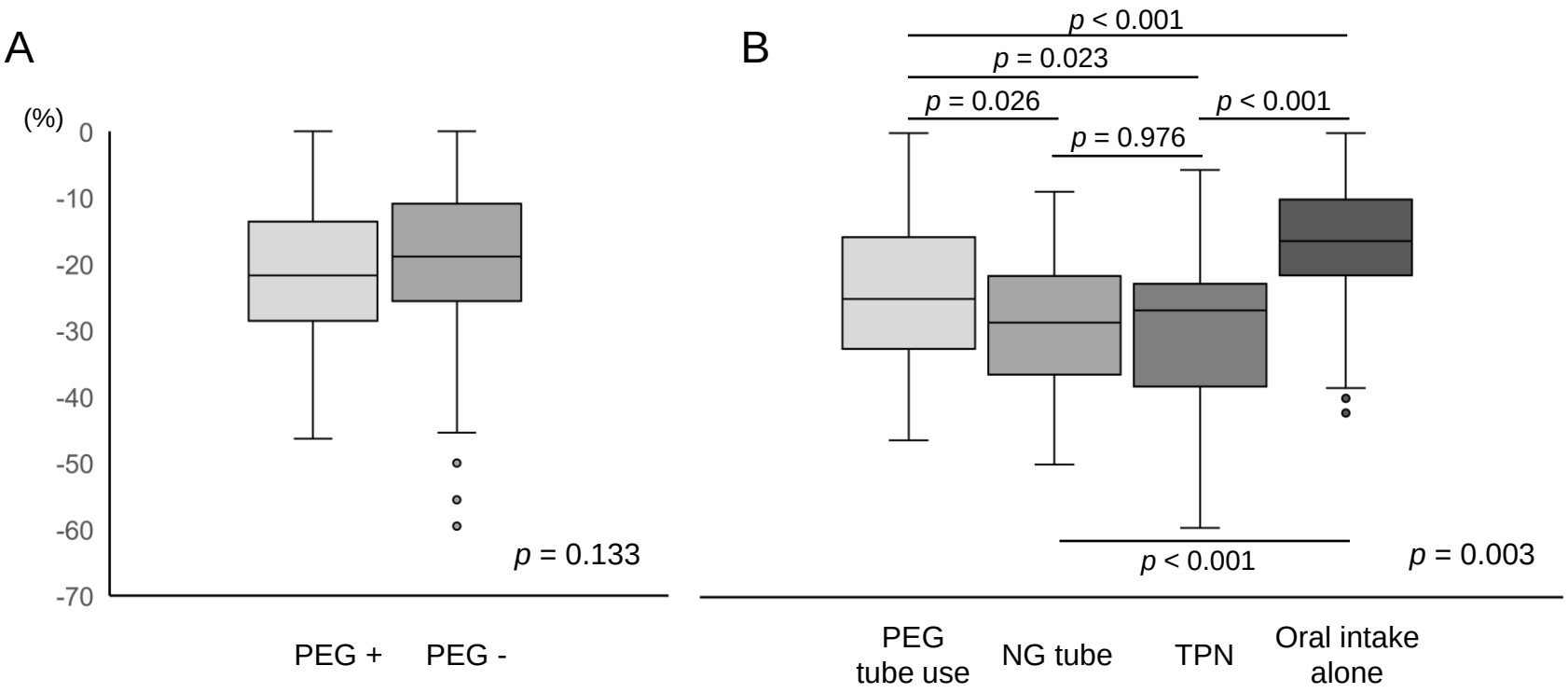
A
(%)
0
-10
-20
-30
-40
-50
-60
-70
p = 0.133
PEG +
PEG -
B
p < 0.001
p = 0.023
p = 0.026
p < 0.001
p = 0.976
p < 0.001
p = 0.003
PEG tube use
NG tube
TPN
Oral intake alone

Figure 3

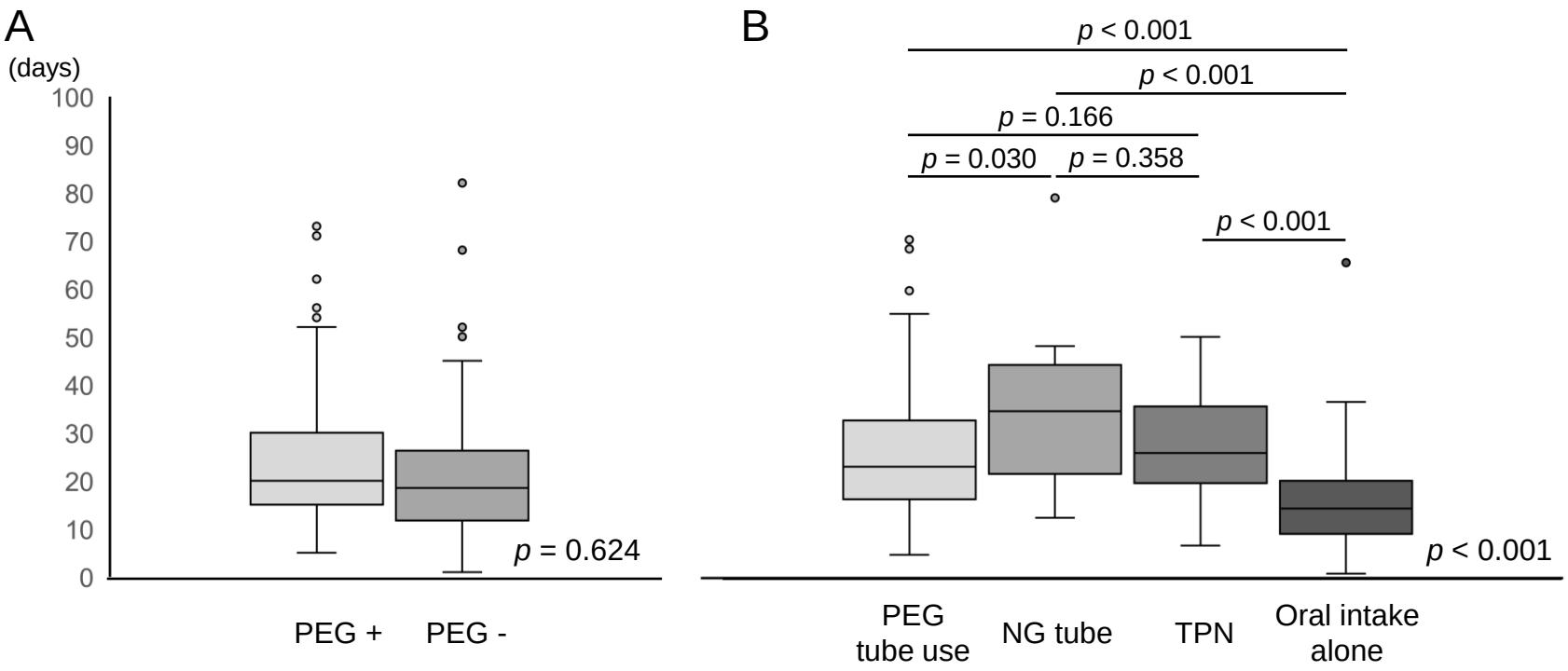
A
(days)
100
90
80
70
60
50
40
30
20
10
0
p = 0.624
PEG +
PEG -
B
p < 0.001
p < 0.001
p = 0.166
p = 0.030
p = 0.358
p < 0.001
p < 0.001
PEG tube use
NG tube
TPN
Oral intake alone

Figure 4