







# Predictors of Gastrostomy Tube Placement in Head and Neck Cancer Patients at a Rural Tertiary Care Hospital

Libby R. Copeland-Halperin, MD<sup>1</sup> Prashanthi Divakar, MD<sup>2</sup> Talia Stewart, MD, MHS<sup>3</sup> Falen Demsas, MD<sup>4</sup> Joshua J. Levy, BA<sup>5</sup> John F. Nigriny, MD<sup>6</sup> Joseph A. Paydarfar, MD<sup>6</sup>

| Reconstr Microsurg Open 2023;8:e1-e11.

Address for correspondence Libby R. Copeland-Halperin, MD, 1001 Fifth Avenue, New York, NY 10028 (e-mail: lcopelandhalperin@drcopeland.com).

### **Abstract**

Background Head and neck cancer is a leading cause of cancer. Treatment often requires surgical resection, free-flap reconstruction, radiation, and/or chemotherapy. Tumor burden and pain may limit swallowing and impair nutrition, increasing complications and mortality. Patients commonly require gastrostomy tubes (G-tube), but predicting which patients are in need remains elusive. This study identifies predictors of G-tube among head and neck cancer patients undergoing immediate free-flap reconstruction.

Methods Institutional Review Board approval was obtained. Retrospective database review was performed of patients at 18 years of age or older with head and neck cancer who underwent resection with immediate free-flap reconstruction from 2011 to 2019. Patients who underwent nonfree-flap or delayed reconstruction or with mortality within 7 days postoperatively were excluded. Patient demographics and comorbidities, tumor/treatment characteristics, and need for G-tube were analyzed to identify univariate and multivariate predictors.

Results In total, 107 patients were included and 72 required G-tube placement. On multivariate analysis, tracheostomy (odds ratio [OR]: 81.78; confidence interval [CI]: 7.43–1,399.92; p < 0.01), anterolateral thigh flap reconstruction (OR: 16.18; CI: 1.14– 429.66; p = 0.04), and age 65 years or younger (OR: 9.35; CI: 1.47–89.11; p = 0.02) were predictors of G-tube placement.

Conclusion Head and neck cancer treatment commonly involves extensive resection, reconstruction, and/or chemoradiation. These patients are at high risk for malnutrition and need G-tube. Determining who requires a pre- or postoperative G-tube remains a challenge. In this study, the need for tracheostomy or ALT flap reconstruction and age 65 years or younger were predictive of postoperative G-tube placement. Future research will quide a multidisciplinary perioperative pathway to facilitate the optimization of nutrition management.

### **Keywords**

- ► head and neck cancer
- ► gastrostomy tube predictors
- ► delayed reconstruction
- ► free-flap reconstruction
- ► malnutrition
- ► flap-related complications

received February 22, 2022 accepted after revision September 29, 2022

DOI https://doi.org/ 10.1055/s-0043-1760757. ISSN 2377-0813.

© 2023. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (https://creativecommons.org/ licenses/by-nc-nd/4.0/)

Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA

<sup>&</sup>lt;sup>1</sup>New York, New York

<sup>&</sup>lt;sup>2</sup>Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, New York

<sup>&</sup>lt;sup>3</sup> Department of Surgery, MetroHealth Medical Center, Cleveland, Ohio

<sup>&</sup>lt;sup>4</sup>Department of Surgery, The Massachusetts General Hospital, Boston, Massachusetts

<sup>&</sup>lt;sup>5</sup>Department of Biomedical Sciences, Geisel School of Medicine, Hanover, New Hampshire

<sup>&</sup>lt;sup>6</sup>Department of Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire

Head and neck cancer is the sixth most common cancer worldwide. 1,2 Treatment often requires surgical resection and free-flap reconstruction, as well as radiation and/or chemotherapy. Tumor burden and associated pain may limit swallowing, resulting in impaired nutrition. The extent of resection, reconstruction type, and need for chemotherapy and/or radiation therapy may cause further impairment. Up to 50% of head and neck cancer patients are malnourished at initial presentation. 5,6 Malnutrition increases the risks of infection, poor wound healing, perioperative morbidity, and mortality and may also decrease the effectiveness of chemoradiation therapy. 4,7,8

While up to 46% of patients with head and neck cancer will require gastrostomy tube (G-tube) placement for adequate nutrition during their treatment course, predicting which patients are in need remains elusive. Previous studies exploring predictors of G-tube placement in head and neck cancer patients are limited by the inclusion of patients undergoing nonsurgical treatment, smaller resections or resections not requiring free-flap reconstruction, or delayed reconstruction, as well as small sample sizes and inclusion of a limited number of predictors. This study aims to identify predictors of G-tube placement among patients with head and neck cancer undergoing immediate free-flap reconstruction through a review of our institutional experience in a rural tertiary care hospital.

# **Methods**

Institutional Review Board approval was obtained. Retrospective review of the electronic medical record was performed of all adult patients (age greater than 18 years) with cancer of the head and neck who underwent resection with immediate free-flap reconstruction at a large rural tertiary care hospital between 2011 and 2019. Exclusion criteria were patients with tumors not involving the head and neck region, patients who underwent nonfree-flap or delayed reconstruction, or patients with mortality within 7 days of surgery.

Study data were collected and managed using REDCap electronic data capture tools hosted at Dartmouth-Hitchcock Medical Center. REDCap is a secure, web-based software platform designed to support data capture for research studies. <sup>13,14</sup> The following information was extracted from the medical record: patient demographics and comorbidities, nutrition metrics, prior treatments, tumor characteristics, quality measures, preoperative surgical data, postoperative swallowing assessment, G-tube data, and complications.

Patient demographics included age (at time of surgery), gender, and body mass index (BMI) on the day of surgery and 1 month postoperatively. The presence or absence of specific comorbidities included the American Society of Anesthesiologists Classification, diabetes, coronary artery disease or peripheral vascular disease, and current tobacco and/or current alcohol use.

Nutrition assessment included the presence or absence of malnutrition as documented in the electronic medical record, weight loss, dysphagia, albumin and prealbumin values, and preoperative speech language pathologist (SLP) evaluation, if performed. Treatment factors included the presence or absence of prior treatment for head and neck cancer including radiation, chemotherapy, and/or surgery, as well as postoperative radiation and/or chemotherapy. Tumor characteristics included tumor node metastasis stage and primary tumor location. Quality measures included the presence or absence of preoperative nutrition and/or palliative care assessment and postoperative nutrition assessment.

Specific surgical data included ablative (three surgeons) and reconstruction surgeons (four surgeons), type of resection and reconstruction, need for tracheostomy, and timeframe for removal of oro/nasogastric feeding tube, if placed. Postoperative data included SLP evaluation, if performed, and pertinent results and recommendations. Gastrostomy tube data included the need for preoperative or postoperative G-tube within 3 months of surgery (to allow sufficient time for postoperative edema to resolve and initiation of adjuvant therapy, if indicated). If a G-tube was placed postoperatively, specific data on timeframe and service consulted for placement (interventional radiology or general surgery at our institution) were collected. Thirty-day complications related to the surgical resection/reconstruction or G-tube were analyzed.

We sought to develop statistical models that could integrate information across 41 clinical variables to predict whether: (1) a G-tube would be placed or (2) whether placement was pre- or postoperative (in this case, data were subset to patients with either pre- or postoperative placement). Additionally, whether the G-tube was placed preoperatively, postoperatively, or not at all was used as an additional covariate for the prediction of factors pertaining to: (3) G-tube complications (in this case, data were subset to patients with either pre- or postoperative G-tube placement) and (4) surgical complications.

For all four outcomes, univariable analyses were conducted using logistic regression. When predictors exhibited significant bias (e.g., complete separation of the outcome by predictor or insufficient information), we opted for biasreducing logistic regression models. For each predictor and outcome, we report a univariable odds ratio (OR), where an OR above 1 indicated a positive relationship with the outcome, while below 1 indicated a negative relationship. For the univariable analyses, we adjusted *p*-values using false discovery rate adjustment for multiple comparisons to control for Type-I error.

Given the high dimensionality of the data and the desire to eliminate the potential for collinearity in the data, which would lead to reporting of insignificant effects by reducing the number of clinical features evaluated at the same time, and to control for potential confounders and repeated measurements nested within resection and reconstruction surgeons, we fit hierarchical Bayesian multivariable logistic regression models with Horseshoe LASSO penalization. <sup>15</sup> This reduced the number of predictors from 41 to 14 for each analysis by selecting predictors with the greatest magnitude effect estimates, while also controlling for age and

gender. Bayesian approaches were optimal here to assist with model convergence and reduce bias through the selection of weakly regularizing priors, making effect estimates conservative. 16 We controlled for clustered data by modeling resection and reconstruction surgeon as cross-classified random effects. We then fit hierarchical Bayesian regression without the LASSO penalty with the remaining predictors to derive final multivariable associations. We report multivariable ORs and corresponding credible intervals (akin to confidence intervals, CI). Statistical significance was communicated using the probability of direction (pd, strongly correlated to the *p*-value). <sup>17</sup> Two-sided statistical tests were conducted through the calculation of  $p = 2^*(I - pd)$  as the measure of statistical significance. Additionally, we compared different subgroups of patients based on their BMI whether they had a G-tube placed and if the placement was pre- or postoperative using estimated marginal means.

Age and preoperative BMI were dichotomized by clinically relevant ranges (< or  $\ge$  65 years and  $\le$  18.5 or  $\ge$  30, respectively). Malnutrition, prealbumin, dysphagia, and weight loss were excluded due to excessive missingness, where they could not be imputed. All methods were implemented using the logistf, brms, emmeans, and bayestestR packages of the R statistical software, v3.6. 18-22

## **Results**

One hundred seven patients were included (mean age 60 years; ►Table 1). Seventy-two (67%) required a G-tube pre- or postoperatively, with 73.6% of these patients undergoing preoperative placement. The most common primary tumor location was oral cavity (79%), followed by oropharynx (10%). Among all patients, 28 (26%) had T2 tumors. The majority of patients (85%) did not undergo formal preoperative nutrition assessment. Forty-eight patients (45%) had dysphagia preoperatively and 38 (79%) of these ultimately required a G-tube: 17 (35%) underwent preoperative placement, while 21 (44%) required a postoperative G-tube. Thirty-six patients reported weight loss preoperatively and 28 (78%) of these required a G-tube: 12 (33%) preoperatively and 16 (44%) postoperatively.

Nearly all patients (93%) who underwent at least a subtotal glossectomy and 61% who underwent a segmental mandibulectomy required a postoperative G-tube. Eighty-seven (81%) patients required tracheostomy at the time of surgery and 61 (70%) of these patients required a G-tube pre- or postoperatively. Reconstruction was performed with anterolateral thigh (ALT) (45%), radial forearm (RF) (2% osteocutaneous and 33% fasciocutaneous), and fibula (22%) free flaps. Patients undergoing ALT or fibula flaps had higher rates of postoperative G-tubes than those undergoing fasciocutaneous RF (68 and 61% vs. 40%, respectively; ►Table 2).

Among all patients, 51 (48%) experienced a head and neck-related postoperative complication. These included wound dehiscence (n = 15), surgical site infection (n = 17), leak (n=3), hematoma (n=2), flap-related complications (i.e., flap congestion and/or ischemia; n = 9), and other (n=23). Complication management required readmission

**Table 1** Patient demographics among 107 patients eligible for inclusion

	Overall (%)	Gastrostomy tube (%)	No gastrostomy tube (%)	<i>p</i> -Value
Number of patients	107	72	35	
Preoperative body mass in	dex	•	•	·
< 18.5	18 (17.0)	17 (23.9)	1 (2.9)	
18.5–30	15 (14.2)	10 (14.1)	5 (14.3)	
> 30	73 (68.9)	44 (62.0)	29 (82.9)	
Age	59.51 (11.33)	59.64 (10.48)	59.26 (13.08)	0.88
> 65	32 (29.9)	21 (29.2)	11 (31.4)	0.99
ASA class		•	•	0.39
1	1 (0.9)	1 (1.4)	0 (0.0)	
2	22 (20.6)	14 (19.4)	8 (22.9)	
3	80 (74.8)	54 (75.0)	26 (74.3)	
4	3 (2.8)	3 (4.2)	0 (0.0)	
5	1 (0.9)	0 (0.0)	1 (2.9)	
Comorbidities				
None	25 (23.4)	13 (18.1)	12 (34.3)	0.11
CAD/PVD	26 (24.3)	4 (5.6)	3 (8.6)	0.86
Current tobacco use	43 (40.2)	18 (25.0)	8 (22.9)	1.00
Current alcohol use	41 (38.3)	33 (45.8)	10 (28.6)	0.13
Diabetes	7 (6.5)	29 (40.3)	12 (34.3)	0.70

Abbreviations: ASA, American Society of Anesthesiologists classification; CAD/PVD, coronary artery disease/peripheral vascular disease.

ρ4

**Table 2** Patient tumor and treatment characteristics

Radiation     20 (18.7)     14 (70%)     6 (30%)     0.98       Surgery     26 (24.2)     13 (50%)     13 (50%)     0.06       Chemotherapy     10 (21.2)     9 (57%)     3 (25%)     0.78       T-Stage*     28 (26.2)     20 (71%)     8 (29%)	Prior treatment(s)	Overall	Gastrostomy tube	No gastrostomy tube	p-Value	
Chemotherapy     12 (11.2)     9 (75%)     3 (25%)     0.78       T-Stage³     0.07       1     10 (9.3)     3 (30%)     7 (70%)     1       2     28 (26.2)     20 (71%)     8 (29%)     1       3     23 (21.5)     16 (70%)     7 (30%)     1       4     46 (43.0)     33 (72%)     13 (28%)     1       N-Stage³     0.07     0     52 (48.6)     30 (58%)     22 (42%)     0       1     13 (12.1)     8 (62%)     5 (38%)     1     1       2     36 (33.6)     28 (78%)     8 (22%)     1       3     6 (5.6)     6 (100%)     0 (0%)     0.55       4     4.3.7     3 (75%)     1 (25%)     0.72       Nasal cavity     4 (3.7)     3 (75%)     1 (25%)     0.72       Oropharynx     1 (10.3)     8 (73%)     3 (27%)     1       Resection surgeon     40 (37.4)     29 (73%)     11 (28%)     0.01       Resection surgeon 1     40 (37.4)     29 (73%)	Radiation	20 (18.7)	14 (70%)	6 (30%)	0.98	
T-Stage*     0.07       1     10 (9.3)     3 (30%)     7 (70%)     1       2     28 (26.2)     20 (71%)     8 (29%)     1       3     23 (21.5)     16 (70%)     7 (30%)     1       4     46 (43.0)     33 (72%)     13 (28%)     1       N-Stage*     0.07     0     52 (48.6)     30 (58%)     22 (42%)     1       1     13 (12.1)     8 (62%)     5 (38%)     1     1       2     36 (33.6)     28 (78%)     8 (22%)     1       3     6 (5.6)     6 (100%)     0 (0%)     1       4     4 (3.7)     3 (10%)     0 (0%)     0.55       Tumor location     1     4 (5.7)     3 (75%)     1 (25%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)     1     1       Oral cavity     8 (7.5)     4 (50%)     3 (27%)     1     2     0.01       Resection surgeon     10 (10.3)     8 (73%)     4 (50%)     1     1     0.01	Surgery	26 (24.3)	13 (50%)	13 (50%)	0.06	
10 (9.3)   3 (30%)   7 (70%)	Chemotherapy	12 (11.2)	9 (75%)	3 (25%)	0.78	
2 2 (2 (2 )   2 (2 (7 )   8 (2 9 %)   (2 )     3 3 (2 )   16 (7 0 %)   7 (3 0 %)   (3 )     4 4 (4 3 0)   3 3 (7 2 %)   13 (2 8 %)   (3 )     N-Stage*   0.07   0   52 (4 8 .6)   30 (5 8 %)   22 (4 2 %)   (3 )     1 1 (1 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1	T-Stage <sup>a</sup>		•		0.07	
33   23 (21.5)   16 (70%)   7 (30%)   10 (20%)     4   46 (43.0)   33 (72%)   13 (28%)   10 (20%)     N-Stage*   0.07   0   52 (48.6)   30 (58%)   22 (42%)	1	10 (9.3)	3 (30%)	7 (70%)		
46 (43.0)   33 (72%)   13 (28%)     N-Stage*   0.07     0   52 (48.6)   30 (58%)   22 (42%)     1   13 (12.1)   8 (62%)   5 (38%)     2   36 (33.6)   28 (78%)   8 (22%)     3   6 (5.6)   6 (100%)   0 (0%)   0.55     Metastases   3 (2.8)   3 (100%)   0 (0%)   0.55     Tumor location     Hypopharynx   4 (3.7)   3 (75%)   1 (25%)   0.72     Nasal cavity   8 (7.5)   4 (50%)   4 (50%)   0.72     Oral cavity   84 (78.5)   57 (68%)   27 (32%)   0.72     Oral cavity   84 (78.5)   57 (68%)   27 (32%)   0.72     Oral cavity   84 (78.5)   57 (68%)   27 (32%)   0.72     Resection surgeon   40 (37.4)   29 (73%)   11 (28%)   0.01     Resection surgeon 1   40 (37.4)   29 (73%)   11 (28%)   0.82     Resection surgeon 3   15 (14.0)   4 (27%)   11 (73%)   0.82 <td colsp<="" td=""><td>2</td><td>28 (26.2)</td><td>20 (71%)</td><td>8 (29%)</td><td></td></td>	<td>2</td> <td>28 (26.2)</td> <td>20 (71%)</td> <td>8 (29%)</td> <td></td>	2	28 (26.2)	20 (71%)	8 (29%)	
N-Stage®     52 (48.6)     30 (58%)     22 (42%)     1       1     13 (12.1)     8 (62%)     5 (38%)     2       2     36 (33.6)     28 (78%)     8 (22%)     3       3     6 (5.6)     6 (100%)     0 (0%)     0.55       Metastases     3 (2.8)     3 (100%)     0 (0%)     0.55       Tumor location       Hypopharynx     4 (3.7)     3 (75%)     1 (25%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     27 (32%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     27 (32%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     27 (32%)     0.72       Nasal cavity     8 (7.5)     8 (7.8)     2 (73%)     11 (28%)       Oropharynx     11 (21)     8 (7.5)     2 (73%)     11 (28%)     0.01       Resection surgeon 1     8 (6 (3.6)	3	23 (21.5)	16 (70%)	7 (30%)		
0     52 (48.6)     30 (58%)     22 (42%)     1       1     13 (12.1)     8 (62%)     5 (38%)     -       2     36 (33.6)     28 (78%)     8 (22%)     -       3     6 (5.6)     6 (100%)     0 (0%)     0.55       Metastases     3 (2.8)     3 (100%)     0 (0%)     0.55       Tumor location       Hypopharynx     4 (3.7)     3 (75%)     1 (25%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)     0.72       Oral cavity     84 (78.5)     57 (68%)     27 (32%)     0.01       Oral cavity     84 (78.5)     57 (68%)     27 (32%)     0.01       Resection surgeon     11 (10.3)     8 (73%)     3 (27%)     1.00       Resection surgeon 1     40 (37.4)     29 (73%)     11 (28%)     0.01       Resection surgeon 2     52 (48.6)     39 (75%)     13 (25%)     0.82       Resection surgeon 3     8 (7.4)     4 (27%)     11 (73%)     0.82	4	46 (43.0)	33 (72%)	13 (28%)		
1   13 (12.1)   8 (62%)   5 (38%)	N-Stage <sup>a</sup>	•	•	•	0.07	
2   36 (33.6)   28 (78%)   8 (22%)     3   6 (5.6)   6 (100%)   0 (0%)   0.55     Metastases   3 (2.8)   3 (100%)   0 (0%)   0.55     Tumor location     Hypopharynx   4 (3.7)   3 (75%)   1 (25%)   0.72     Nasal cavity   8 (7.5)   4 (50%)   4 (50%)	0	52 (48.6)	30 (58%)	22 (42%)		
3   6 (5.6)   6 (100%)   0 (0%)      Metastases   3 (2.8)   3 (100%)   0 (0%)   0.55     Tumor location     Hypopharynx   4 (3.7)   3 (75%)   1 (25%)   0.72     Nasal cavity   8 (7.5)   4 (50%)   4 (50%)      Oral cavity   84 (78.5)   57 (68%)   27 (32%)      Oropharynx   11 (10.3)   8 (73%)   3 (27%)      Oropharynx   11 (10.3)   8 (73%)   3 (27%)      Oropharynx   40 (37.4)   29 (73%)   11 (28%)      Resection surgeon   40 (37.4)   29 (73%)   11 (28%)      Resection surgeon 1   40 (37.4)   29 (73%)   13 (25%)      Resection surgeon 2   52 (48.6)   39 (75%)   13 (25%)      Reconstruction surgeon 3   15 (14.0)   4 (27%)   11 (73%)      Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)      Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)   <	1	13 (12.1)	8 (62%)	5 (38%)		
Metastases     3 (2.8)     3 (100%)     0 (0%)     0.55       Tumor location       Hypopharynx     4 (3.7)     3 (75%)     1 (25%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)	2	36 (33.6)	28 (78%)	8 (22%)		
Tumor location       Hypopharynx     4 (3.7)     3 (75%)     1 (25%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)	3	6 (5.6)	6 (100%)	0 (0%)		
Hypopharynx     4 (3.7)     3 (75%)     1 (25%)     0.72       Nasal cavity     8 (7.5)     4 (50%)     4 (50%)       Oral cavity     84 (78.5)     57 (68%)     27 (32%)       Oropharynx     11 (10.3)     8 (73%)     3 (27%)       Resection surgeon     < 0.01	Metastases	3 (2.8)	3 (100%)	0 (0%)	0.55	
Nasal cavity   8 (7.5)   4 (50%)   4 (50%)      Oral cavity   84 (78.5)   57 (68%)   27 (32%)      Oropharynx   11 (10.3)   8 (73%)   3 (27%)      Resection surgeon   40 (37.4)   29 (73%)   11 (28%)      Resection surgeon 1   40 (37.4)   29 (73%)   13 (25%)      Resection surgeon 2   52 (48.6)   39 (75%)   13 (25%)      Resection surgeon 3   15 (14.0)   4 (27%)   11 (73%)      Reconstruction surgeon 1   8 (7.5)   6 (75%)   2 (25%)      Reconstruction surgeon 2   56 (52.3)   36 (64%)   20 (36%)      Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)      Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)      Resection type     Bucal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55 <	Tumor location		•		1	
Oral cavity     84 (78.5)     57 (68%)     27 (32%)       Oropharynx     11 (10.3)     8 (73%)     3 (27%)       Resection surgeon       Resection surgeon 1     40 (37.4)     29 (73%)     11 (28%)       Resection surgeon 2     52 (48.6)     39 (75%)     13 (25%)       Resection surgeon 3     15 (14.0)     4 (27%)     11 (73%)       Reconstruction surgeon 3     8 (7.5)     6 (75%)     2 (25%)       Reconstruction surgeon 1     8 (7.5)     6 (75%)     2 (25%)       Reconstruction surgeon 2     56 (52.3)     36 (64%)     20 (36%)       Reconstruction surgeon 3     41 (38.3)     29 (71%)     12 (29%)       Reconstruction surgeon 4     2 (1.9)     1 (50%)     1 (50%)       Resection type     Buccal     14 (13.1)     8 (57%)     6 (43%)     0.57       Hemiglossectomy     30 (28.0)     22 (73%)     8 (27%)     0.55       Subtotal or total glossectomy     22 (20.6)     21 (95%)     1 (5%)     < 0.01       Marginal mandibulectomy     14 (13.1)     9 (64%)     5 (35%)	Hypopharynx	4 (3.7)	3 (75%)	1 (25%)	0.72	
Oropharynx     11 (10.3)     8 (73%)     3 (27%)       Resection surgeon       Resection surgeon 1     40 (37.4)     29 (73%)     11 (28%)       Resection surgeon 2     52 (48.6)     39 (75%)     13 (25%)       Resection surgeon 3     15 (14.0)     4 (27%)     11 (73%)       Reconstruction surgeon 3     8 (7.5)     6 (75%)     2 (25%)       Reconstruction surgeon 1     8 (7.5)     6 (64%)     20 (36%)       Reconstruction surgeon 2     56 (52.3)     36 (64%)     20 (36%)       Reconstruction surgeon 3     41 (38.3)     29 (71%)     12 (29%)       Reconstruction surgeon 4     2 (1.9)     1 (50%)     1 (50%)       Resection type       Buccal     14 (13.1)     8 (57%)     6 (43%)     0.57       Hemiglossectomy     30 (28.0)     22 (73%)     8 (27%)     0.55       Subtotal or total glossectomy     22 (20.6)     21 (95%)     1 (5%)     < 0.01	Nasal cavity	8 (7.5)	4 (50%)	4 (50%)		
Resection surgeon     < 0.01       Resection surgeon 1     40 (37.4)     29 (73%)     11 (28%)       Resection surgeon 2     52 (48.6)     39 (75%)     13 (25%)       Resection surgeon 3     15 (14.0)     4 (27%)     11 (73%)       Reconstruction surgeon       Reconstruction surgeon 1     8 (7.5)     6 (75%)     2 (25%)       Reconstruction surgeon 2     56 (52.3)     36 (64%)     20 (36%)       Reconstruction surgeon 3     41 (38.3)     29 (71%)     12 (29%)       Reconstruction surgeon 4     2 (1.9)     1 (50%)     1 (50%)       Resection type       Buccal     14 (13.1)     8 (57%)     6 (43%)     0.57       Hemiglossectomy     30 (28.0)     22 (73%)     8 (27%)     0.55       Subtotal or total glossectomy     22 (20.6)     21 (95%)     1 (5%)     < 0.01	Oral cavity	84 (78.5)	57 (68%)	27 (32%)		
Resection surgeon 1   40 (37.4)   29 (73%)   11 (28%)     Resection surgeon 2   52 (48.6)   39 (75%)   13 (25%)     Resection surgeon 3   15 (14.0)   4 (27%)   11 (73%)     Reconstruction surgeon     Reconstruction surgeon 1   8 (7.5)   6 (75%)   2 (25%)     Reconstruction surgeon 2   56 (52.3)   36 (64%)   20 (36%)     Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)     Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)     Resection type     Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Oropharynx	11 (10.3)	8 (73%)	3 (27%)		
Resection surgeon 2   52 (48.6)   39 (75%)   13 (25%)     Resection surgeon 3   15 (14.0)   4 (27%)   11 (73%)     Reconstruction surgeon     Reconstruction surgeon 1   8 (7.5)   6 (75%)   2 (25%)     Reconstruction surgeon 2   56 (52.3)   36 (64%)   20 (36%)     Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)     Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)     Resection type     Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01					< 0.01	
Resection surgeon 3     15 (14.0)     4 (27%)     11 (73%)       Reconstruction surgeon       Reconstruction surgeon 1     8 (7.5)     6 (75%)     2 (25%)       Reconstruction surgeon 2     56 (52.3)     36 (64%)     20 (36%)       Reconstruction surgeon 3     41 (38.3)     29 (71%)     12 (29%)       Reconstruction surgeon 4     2 (1.9)     1 (50%)     1 (50%)       Resection type       Buccal     14 (13.1)     8 (57%)     6 (43%)     0.57       Hemiglossectomy     30 (28.0)     22 (73%)     8 (27%)     0.55       Subtotal or total glossectomy     22 (20.6)     21 (95%)     1 (5%)     < 0.01	Resection surgeon 1	40 (37.4)	29 (73%)	11 (28%)		
Reconstruction surgeon     0.82       Reconstruction surgeon 1     8 (7.5)     6 (75%)     2 (25%)       Reconstruction surgeon 2     56 (52.3)     36 (64%)     20 (36%)       Reconstruction surgeon 3     41 (38.3)     29 (71%)     12 (29%)       Reconstruction surgeon 4     2 (1.9)     1 (50%)     1 (50%)       Resection type       Buccal     14 (13.1)     8 (57%)     6 (43%)     0.57       Hemiglossectomy     30 (28.0)     22 (73%)     8 (27%)     0.55       Subtotal or total glossectomy     22 (20.6)     21 (95%)     1 (5%)     < 0.01	Resection surgeon 2	52 (48.6)	39 (75%)	13 (25%)		
Reconstruction surgeon 1   8 (7.5)   6 (75%)   2 (25%)     Reconstruction surgeon 2   56 (52.3)   36 (64%)   20 (36%)     Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)     Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)     Resection type     Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Resection surgeon 3	15 (14.0)	4 (27%)	11 (73%)		
Reconstruction surgeon 2   56 (52.3)   36 (64%)   20 (36%)     Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)     Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)     Resection type     Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Reconstruction surgeon		'		0.82	
Reconstruction surgeon 3   41 (38.3)   29 (71%)   12 (29%)     Reconstruction surgeon 4   2 (1.9)   1 (50%)   1 (50%)     Resection type     Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01     Marginal mandibulectomy   14 (13.1)   9 (64%)   5 (35%)   1.00     Segmental or hemimandibulectomy   33 (30.8)   24 (73%)   9 (27%)   0.56     Tongue base resection   5 (4.7)   4 (80%)   1 (20%)   0.90     Radical tonsillectomy   13 (12.1)   10 (77%)   3 (23%)   0.64     Soft palate   19 (17.8)   15 (79%)   4 (21%)   0.36	Reconstruction surgeon 1	8 (7.5)	6 (75%)	2 (25%)		
Reconstruction surgeon 4     2 (1.9)     1 (50%)     1 (50%)       Resection type       Buccal     14 (13.1)     8 (57%)     6 (43%)     0.57       Hemiglossectomy     30 (28.0)     22 (73%)     8 (27%)     0.55       Subtotal or total glossectomy     22 (20.6)     21 (95%)     1 (5%)     < 0.01	Reconstruction surgeon 2	56 (52.3)	36 (64%)	20 (36%)		
Resection type     Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Reconstruction surgeon 3	41 (38.3)	29 (71%)	12 (29%)		
Buccal   14 (13.1)   8 (57%)   6 (43%)   0.57     Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Reconstruction surgeon 4	2 (1.9)	1 (50%)	1 (50%)		
Hemiglossectomy   30 (28.0)   22 (73%)   8 (27%)   0.55     Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Resection type	•	•		1	
Subtotal or total glossectomy   22 (20.6)   21 (95%)   1 (5%)   < 0.01	Buccal	14 (13.1)	8 (57%)	6 (43%)	0.57	
Marginal mandibulectomy   14 (13.1)   9 (64%)   5 (35%)   1.00     Segmental or hemimandibulectomy   33 (30.8)   24 (73%)   9 (27%)   0.56     Tongue base resection   5 (4.7)   4 (80%)   1 (20%)   0.90     Radical tonsillectomy   13 (12.1)   10 (77%)   3 (23%)   0.64     Soft palate   19 (17.8)   15 (79%)   4 (21%)   0.36	Hemiglossectomy	30 (28.0)	22 (73%)	8 (27%)	0.55	
Segmental or hemimandibulectomy   33 (30.8)   24 (73%)   9 (27%)   0.56     Tongue base resection   5 (4.7)   4 (80%)   1 (20%)   0.90     Radical tonsillectomy   13 (12.1)   10 (77%)   3 (23%)   0.64     Soft palate   19 (17.8)   15 (79%)   4 (21%)   0.36	Subtotal or total glossectomy	22 (20.6)	21 (95%)	1 (5%)	< 0.01	
Tongue base resection   5 (4.7)   4 (80%)   1 (20%)   0.90     Radical tonsillectomy   13 (12.1)   10 (77%)   3 (23%)   0.64     Soft palate   19 (17.8)   15 (79%)   4 (21%)   0.36	Marginal mandibulectomy	14 (13.1)	9 (64%)	5 (35%)	1.00	
Radical tonsillectomy   13 (12.1)   10 (77%)   3 (23%)   0.64     Soft palate   19 (17.8)   15 (79%)   4 (21%)   0.36	Segmental or hemimandibulectomy	33 (30.8)	24 (73%)	9 (27%)	0.56	
Soft palate 19 (17.8) 15 (79%) 4 (21%) 0.36	Tongue base resection	5 (4.7)	4 (80%)	1 (20%)	0.90	
	Radical tonsillectomy	13 (12.1)	10 (77%)	3 (23%)	0.64	
Hard palate 1 (0.9) 1 (100%) 0 (0%) 1 00	Soft palate	19 (17.8)	15 (79%)	4 (21%)	0.36	
[ - (0.5) [ - (0.5)]	Hard palate	1 (0.9)	1 (100%)	0 (0%)	1.00	
Maxillectomy 7 (6.5) 1 (14%) 6 (86%) 0.01	Maxillectomy	7 (6.5)	1 (14%)	6 (86%)	0.01	
Maxillectomy with orbital exoneration 5 (4.7) 4 (80%) 1 (20%) 0.90	Maxillectomy with orbital exoneration	5 (4.7)	4 (80%)	1 (20%)	0.90	
Pharyngectomy 20 (18.7) 16 (80%) 4 (20%) 0.28	Pharyngectomy	20 (18.7)	16 (80%)	4 (20%)	0.28	
Supracricoid or hemi laryngectomy 4 (3.7) 4 (100%) 0 (0%) 0.38	Supracricoid or hemi laryngectomy	4 (3.7)	4 (100%)	0 (0%)	0.38	
Total pharyngolaryngectomy     3 (2.8)     3 (100%)     0 (0%)     0.55	Total pharyngolaryngectomy	3 (2.8)	3 (100%)	0 (0%)	0.55	

Table 2 (Continued)

Prior treatment(s)	Overall	Gastrostomy tube	No gastrostomy tube	<i>p</i> -Value
Retromolar trigone	12 (11.2)	8 (67%)	4 (33%)	1.00
Lip	5 (4.7)	2 (40%)	3 (60%)	0.40
Neopharynx <sup>b</sup>	2 (1.9)	1 (50%)	1 (50%)	1.00
Free flap type				
Anterolateral thigh	48 (44.9)	37 (77%)	11 (23%)	0.08
Fasciocutaneous radial forearm	35 (32.7)	19 (54%)	16 (46%)	0.08
Osteocutaneous radial forearm	2 (1.9)	1 (50%)	1 (50%)	1.00
Fibula	24 (22.4)	17 (71%)	7 (29%)	0.86
Rectus abdominis	1 (0.9)	1 (100%)	0 (0%)	1.00
Tracheostomy needed	87 (81.3)	68 (78%)	19 (22%)	< 0.01
G-tube placement				
Preoperative	n/a	53	n/a	n/a
Postoperative	n/a	19	n/a	n/a
Postoperative G-tube complication	in 30 d			
Yes	7 (6.5)	7 (100%)	0 (0%)	
No	60 (56.1)	59 (98%)	1 (2%)	
Unknown	40 (37.4)	6 (15%)	34 (85%)	
Type of G-tube complication				
Malfunction	1 (0.9)	1 (100%)	0 (0%)	1.00
Dislodged	3 (2.8)	3 (100%)	0 (0%)	0.55
G-tube placement	·			•
Preoperative	n/a	53	n/a	n/a
Postoperative	n/a	19	n/a	n/a
Postoperative head and neck complication within 30 d	51 (47.7)	40 (78%)	11 (22%)	0.03
Type of head and neck complication	1		•	
Wound dehiscence	15 (14.0)	14 (93%)	1 (7%)	0.04
Surgical site infection	17 (15.9)	16 (94%)	1 (6%)	0.02
Intraoral leak	3 (2.8)	2 (67%)	1 (33%)	1.00
Hematoma	2 (1.9)	2 (100%)	0 (0%)	0.82
Flap congestion or ischemia	9 (8.4)	8 (89%)	1 (11%)	0.28
Other	23 (21.5)	15 (65%)	8 (35%)	1.00

Abbreviations: G-tube, gastrostomy tube; n/a, not available.

in nine patients, operative management in 30 patients, and nonoperative management in 26 patients.

Among patients who received a G-tube, four (4%) experienced a gastrostomy tube-related complication (one malfunction and three dislodgements). Only one patient required operative management after a dislodged G-tube.

### **Factors Associated with G-Tube Placement**

On univariate analysis, risk factors for any G-tube placement included nodal stage greater than N1 (p = 0.02;  $p_{adj} = 0.17$ ),

undergoing subtotal or total glossectomy (p = 0.01;  $p_{\rm adi}$  = 0.17), and need for tracheostomy (p < 0.01;  $p_{\rm adj}$  < 0.01). After adjusting for confounders via multivariate analysis, tracheostomy (OR: 81.78; [CI: 7.43–1,399.92]; p < 0.01), ALT flap reconstruction (OR: 16.18; [CI: 1.14-429.66]; p = 0.04), and age 65 years or older (OR: 9.35; [CI: 1.47–89.11]; p = 0.02) were predictors of G-tube placement.

On univariate analysis, factors protective against requiring a G-tube included prior surgical treatment (p = 0.03;  $p_{\text{adj}} = 0.23$ ), undergoing maxillectomy (p = 0.02;  $p_{\text{adj}} = 0.17$ ), and fasciocutaneous RF flap reconstruction (p = 0.05;

<sup>&</sup>lt;sup>a</sup>Based on tumor node metastasis (TNM) classification.

<sup>&</sup>lt;sup>b</sup>Among two patients who underwent total laryngectomy and developed recurrent disease in the neopharynx requiring resection of the neopharyx.

 $p_{\rm adj} = 0.28$ ). After adjusting for confounders via multivariate analysis, undergoing maxillectomy (OR: 0.00; [CI: 0.00–0.10]; p < 0.01) or neopharynx resection (OR: 0.00; [CI: 0.00–0.47]; p = 0.02) (in patients who developed recurrence following a total laryngectomy) were protective against requiring a G-tube (**>Table 3**).

# Factors Associated with Preoperative versus Postoperative G-Tube Placement

From the univariate analysis, among patients who required a G-tube, only tumor stage greater than T2 (p=0.02;  $p_{\rm adj}=0.37$ ) was associated with preoperative (versus postoperative) placement. In contrast, BMI of 30 or greater (p=0.023;  $p_{\rm adj}=0.37$ ) and ablative surgeon (p=0.02;

**Table 3** Predictors of preoperative or postoperative gastrostomy tube placement versus no gastrostomy tube based on multivariable analysis

	OR (Confidence interval)	<i>p</i> -Value	
Age (y)			
≥ 65	9.35 (1.47–89.11)	0.02	
Body mass index			
< 18.5 vs. ≥ 18.5	8.51 (0.74–190.71)	0.10	
18.5–30 vs. < 18.5	0.06 (0.00-4.09)	0.21	
18.5–30 vs. ≥ 30	2.35 (0.21–32.02)	0.48	
≥ 30 vs. ≤ 18.5	0.03 (0.00-1.06)	0.05	
≥ 30 vs. < 30	0.22 (0.04–1.03)	0.06	
Comorbidities			
Diabetes	0.04 (0.00-1.04)	0.05	
Prior treatment(s)			
Surgery	0.30 (0.04–2.58)	0.26	
Tumor TNM stage			
N-stage > 1	1.02 (0.12-9.46)	1.00	
Resection type			
Hemiglossectomy	1.55 (0.28-8.98)	0.63	
Lip	0.02 (0.00-3.61)	0.13	
Maxillectomy	0.00 (0.00-0.10)	< 0.01	
Maxillectomy with orbital exoneration	1.12 (0.01–253.69)	0.99	
Neopharynx <sup>a</sup>	0.00 (0.00-0.47)	0.02	
Subtotal or total glossectomy	9.80 (0.40-635.65)	0.19	
Free flap type			
Anterolateral thigh	16.18 (1.14–429.66)	0.04	
Fasciocutaneous radial forearm	0.46 (0.07–3.19)	0.44	
Tracheostomy needed	81.77 (7.43–1,399.92)	< 0.01	

Abbreviations: OR, odds ratio; TNM, tumor node metastasis stage. <sup>a</sup>Among two patients who underwent total laryngectomy and developed recurrent disease in the neopharynx requiring resection of the neopharyx.  $p_{\rm adj}\!=\!0.37$ ) were predictive of postoperative placement. After adjusting for confounders via multivariate analysis among those who underwent G-tube placement, only tumor stage greater than T2 (OR: 59.84; [CI: 2.76–2,746.66];  $p\!=\!0.01$ ) was associated with preoperative placement. The need for repeat surgical resection was associated with postoperative placement (OR: 0.08; [CI: 0.00–1.25];  $p\!=\!0.07$ ), though this did not reach statistical significance ( $\sim$  **Table 4**).

# Factors Associated with Head and Neck Surgical Complications and G-Tube Complications

From the univariate analysis, only the need for a postoperative G-tube (vs. no G-tube) was associated with a head and neck surgical complication within 30 days (OR: 3.90; [CI: 1.57-9.68]; p < 0.01). After adjusting for confounders via multivariate analysis, postoperative G-tube (vs. no G-tube; OR: 4.71; [CI: 1.53-15.93]; p < 0.01), tongue base resection (OR: 19.28; [CI: 1.29-391.42]; p = 0.03), and the presence of a hypopharyngeal tumor (OR: 32.18; [CI: 1.08-1,854.10]; p = 0.05) were associated with head and neck surgical complications. From both univariate (p = 0.02;  $p_{\rm adj} = 0.8$ ) and multivariate analyses (OR: 152.39; [CI: 2.35-11,577.95]; p = 0.02), only the presence of a hypopharyngeal tumor was associated with gastrostomy tube-related complications ( $\blacktriangleright$  **Tables 5** and **6**).

### **Discussion**

Head and neck cancer is one of the most common cancers worldwide. Treatment often entails extensive surgical resection with free-flap reconstruction and potentially chemotherapy and/or radiation therapy. Many patients suffer from malnutrition preoperatively, which can be exacerbated during treatment. This malnutrition increases the risks of perioperative complications (including wound dehiscence or delayed wound healing and surgical site infections), delayed adjuvant therapy, and mortality. Gastrostomy tube placement may provide supplemental nutritional support during the perioperative period and long term, if needed.

Predicting which patients will benefit from a G-tube remains a clinical challenge. Prior studies are limited by small sample sizes and inclusion of patients undergoing only nonsurgical treatments, treatment of benign disease, small resections amenable to less extensive reconstructions, and/or patients delayed or secondary reconstructions, and heterogeneous analysis that limits statistical validity. 10.23,24 To better address this question, we conducted a retrospective review of the EMR at a large, rural, tertiary care hospital. All patients undergoing resection of head and neck cancers with immediate free-flap reconstruction were included, while those undergoing delayed or secondary reconstruction, only nonsurgical treatments, or those undergoing reconstruction with nonfree-flap techniques were excluded.

Analysis of 107 patients meeting inclusion criteria found that undergoing tracheostomy or ALT flap reconstruction and age 65 years or older were significantly associated with G-tube placement, while undergoing a maxillectomy or neopharynx resection (in patients who previously

**Table 4** Predictors of preoperative versus postoperative gastrostomy tube placement based on multivariable analysis

OR (Confidence p-Value interval) Age (y) > 65 0.4(0.03-4.27)0.46 Body mass index  $< 18.5 \text{ vs.} \ge 18.5$ 2.75 (0.67-12.13) 0.17 18.5-30 vs. < 18.5 0.28 (0.01-4.90) 0.40 18.5-30 vs. > 30 1.60 (0.08-26.77) 0.72  $\geq$  30 vs.  $\leq$  18.5 0.09 0.17(0.02-1.30)> 30 vs. < 300.48(0.12-1.86)0.29 Prior treatment(s) Chemotherapy 7.65 (0.18-405) 0.29 5.47 (0.23-146.36) Radiation 0.33 Surgery 0.08(0.00-1.25)0.07 **Tumor location** Hypopharynx 0.13 (0.00-16.99) 0.42 Nasal cavity 0.18(0.00 - 8.47)0.45 1.40 (0.04-36.73) Oropharynx 0.84 T-stage  $> 2^a$ Stage > 2 59.84 (2.76-2,746.66) 0.01 Resection type **Buccal** 5.30 (0.45-78.12) 0.20 Lip 3.53 (0.09-142.24) 0.49 Partial supracricoid or 3.92 (0.08-185.72) 0.48hemilaryngectomy Segmental or 2.57 (0.40-18.62) 0.35 hemimandibulectomy 1.86 (0.18-16.39) 0.57 Soft palate Free-flap type Rectus abdominis 13.66 (0.19-1,581.79) 0.23

Abbreviations: OR. odds ratio.

underwent total laryngectomy and developed recurrent disease requiring resection of the neopharynx) were associated with lack of G-tube placement. These findings are consistent with previous studies. 10 Patients undergoing subtotal or total glossectomy were more likely to require a G-tube on univariate analysis. Patients undergoing oral tongue resection have worse swallowing function due to prolonged oral preparatory time, slowed oral transit time, and increased oral residue. 25,26 Specifically, resection of over 25% of the tongue base is associated with the inability to trigger a pharyngeal swallow, resulting in postsurgical aspiration.<sup>27,28</sup> While undergoing total laryngopharyngectomy was not associated with the need for G-tube, this was likely due to the small sample size (three patients) for this analysis.

Tracheostomies are associated with impaired swallowing and as many as 93% of patients experience dysphagia follow-

**Table 5** Predictors of gastrostomy tube-related complications based on multivariable analysis

	-				
	OR (Confidence interval)	<i>p</i> -Value			
Age (y)					
≥ <b>65</b>	6.39 (0.43–105.53)	0.18			
Body mass index	Body mass index				
$< 18.5 \text{ vs.} \ge 18.5$	0.65 (0.08-4.30)	0.69			
18.5–30 vs. < 18.5	1.10 (0.02–59.18)	0.95			
18.5–30 vs. ≥ 30	0.33 (0.00–19.56)	0.65			
≥ <b>30</b> vs. ≤ <b>18.5</b>	3.30 (0.16-85.88)	0.45			
$\geq$ 30 vs. $<$ 30	2.15 (0.29–20.84)	0.48			
Comorbidities					
None	6.35 (0.22–177.41)	0.27			
CAD/PVD	9.12 (0.64–140.3)	0.11			
Current tobacco use	0.10 (0.00-1.68)	0.11			
Prior treatment(s)					
None	5.98 (0.18-208.53)	0.31			
Surgery	0.06 (0.00-3.56)	0.17			
Tumor location					
Hypopharynx	152.39 (2.35–11,600)	0.02			
Nasal cavity	0.21 (0.00–16.90)	0.55			
Oropharynx	0.19 (0.00-11.20)	0.42			
Tumor stage <sup>a</sup>					
N-stage > 1	0.13 (0.01–1.68)	0.12			
Resection type					
Marginal mandibulectomy	0.20 (0.00–11.35)	0.49			
Neopharynx <sup>b</sup>	6.44 (0.04–1,224.97)	0.49			
Pharyngectomy	4.28 (0.12-133.91)	0.41			
Radical tonsillectomy	8.85 (0.13-581.56)	0.31			
Segmental or hemimandibulectomy	0.62 (0.03–9.94)	0.76			
Free-flap type					
Anterolateral thigh	4.66 (0.33–109.15)	0.28			

Abbreviations: CAD/PVD, coronary artery disease/peripheral vascular disease; OR, odds ratio.

ing tracheostomy.<sup>29</sup> While some patients are at risk for dysphagia due to factors that result in their requiring a tracheostomy, tracheostomies also independently impair swallowing. Several mechanisms explain this phenomenon. These include neurophysiologic mechanisms involving failure of the glottic closure reflex, disruption of coordination between respiratory and digestive systems resulting in insufficient subglottic pressure, and absent cough reflex.<sup>30</sup>

<sup>&</sup>lt;sup>a</sup>Based on tumor node metastasis stage.

<sup>&</sup>lt;sup>a</sup>Based on tumor node metastasis stage.

<sup>&</sup>lt;sup>b</sup>Among two patients who underwent total laryngectomy and developed recurrent disease in the neopharynx requiring resection of the neopharyx.

**Table 6** Predictors of head and neck-related surgical complications based on multivariable analysis

	OR (Confidence interval)	<i>p</i> -Value		
Age (y)				
≥ 65	1.39 (0.44–4.53)	0.58		
Body mass index				
< 18.5 vs. ≥ 18.5	0.40 (0.14–1.16)	0.09		
18.5–30 vs. < 18.5	3.06 (0.44–21.67)	0.27		
18.5–30 vs. ≥ 30	0.61 (0.13–2.75)	0.52		
≥ 30 vs. ≤ 18.5	5.04 (0.99–27.63)	0.05		
≥ 30 vs. < 30	2.02 (0.89-4.73)	0.08		
Comorbidities				
CAD/PVD	1.66 (0.49–5.87)	0.42		
Prior treatment(s)				
Chemotherapy	0.26 (0.03–1.99)	0.18		
Tumor location				
Hypopharynx	32.18 (1.08–1,854.1)	0.05		
Nasal cavity	10.69 (0.37–332.84)	0.17		
Oropharynx	0.17 (0.01–1.52)	0.12		
Tumor stage				
Metastases	0.04 (0.00-1.02)	0.05		
Resection type				
Marginal mandibulectomy	0.58 (0.14–2.46)	0.47		
Maxillectomy	0.07 (0.00-1.06)	0.06		
Maxillectomy with orbital exoneration	6.65 (0.08–1,153.31)	0.43		
Tongue base resection	19.28 (1.29–391.42)	0.03		
Free-flap type				
Anterolateral thigh	2.43 (0.79-8.05)	0.13		
Osteocutaneous radial forearm	0.06 (0.00–2.18)	0.13		
Timing of gastrostomy tube				
Any vs. none	1.80 (0.83-4.13)	0.14		
Preoperative vs. none	1.24 (0.24-6.50)	0.79		
Postoperative vs. none	4.71 (1.53–15.93)	< 0.01		
Postoperative vs. preoperative	3.79 (0.85–18.62)	0.09		

Abbreviations: CAD/PVD, coronary artery disease/peripheral vascular disease; OR, odds ratio.

Even temporary tracheostomy can impair swallowing, as can how a patient progresses to decannulation.<sup>31</sup>

Reconstruction choice plays an important role in the ability to successfully swallow postoperatively and the type of reconstruction depends on several factors, including the extent of resection, history of radiation, patient comorbidities, and ability to undergo a lengthy operation. While some studies have demonstrated superior swallowing func-

tion with free-flap reconstruction over pedicled flaps, others have found no difference. 32-34 In one study, patients who underwent RF reconstruction reported the best outcomes in terms of postoperative swallowing and mastication ability. This is consistent with our finding that fasciocutaneous RF flap reconstruction was associated with not needing a G-tube, likely due to the thin and pliable nature of RF flaps and their use in patients undergoing comparatively smaller resections. Due to the small sample size, a separate analysis of osteocutaneous RF flaps could not be performed. In contrast, ALT flaps were predictive of needing a G-tube, likely due to the bulkiness of ALT flaps that may impede swallowing. Additionally, the need for a bulkier or larger flap may reflect the extent of the ablative defect.

As with extent and location of primary tumor resection, undergoing bilateral (versus unilateral) neck dissection has been associated with increased incidence of G-tube placement, though data are not definitive. 11,36 The need for radiation or prior radiation has also been associated with impaired swallowing. Through direct tissue damage and resultant edema, pseudomembrane formation, and fibrosis, radiation causes xerostomia, mucositis, odynophagia, and dysgeusia, which lead to increased oral and pharyngeal transit times, lower oral pharyngeal swallowing efficiency, greater pharyngeal residual, and strictures. 28,37-39 Radiation to the pharyngeal constrictors and supraglottic and glottic larynx increases the risk of dysphagia. 34,40 Some effects may be temporary, while others are sustained. 41,42 In one review of head and neck cancer patients, 61% of patients receiving either chemoradiation or radiation alone required feeding tube placement and 41% continued to require their G-tube 1 year following treatment. 43 Surprisingly, we found preoperative chemoradiation therapy was not associated with the need for G-tube, though this may be due to the small sample size. Due to limitations of the EMR and retrospective methodology of our study, we were unable to analyze the effect of postoperative radiation on swallowing function and the need for prolonged G-tube placement. However, the need for postoperative radiation is likely an important determinant.

G-tubes may be placed preoperatively, at the time of resection/reconstruction, or postoperatively. Earlier placement can reduce weight loss and hospitalization and improve outcomes in head and neck cancer patients.<sup>44,45</sup> However, the short interval from initial consultation to surgery at high-volume centers often makes preoperative G-tube placement not feasible. Case reports of tumor seeding along the gastrointestinal tract from pre-resection G-tube placement have been reported, though high-level evidence to support a causative mechanism is lacking. 46 The interval between initial consultation and surgical intervention varies, and it may not be feasible to place a G-tube preoperatively. Coordinated G-tube placement at the resection/reconstruction may be beneficial, though limits the benefits of preoperative nutritional optimization. Postoperative placement necessitates an additional procedure with the associated potential for morbidity, may disrupt the recent surgical site, and delay hospital discharge, adjuvant

therapy, and recovery.<sup>7,47,48</sup> Ultimately, a multidisciplinary approach to the initial evaluation of head and neck cancer patients may facilitate evaluation and perioperative optimization of nutritional status.

Gastrostomy tubes can improve nutritional status and reduce surgical complications. On multivariate analysis, postoperative G-tube (versus not needing a G-tube), tongue base resection, and presence of a hypopharyngeal tumor were associated with head and neck-related surgical complications. Undergoing postoperative versus preoperative G-tube placement was not associated with an increased risk of surgical complications, though analysis may be limited by the interval between preoperative placement and surgery, as well as the small sample size.

G-tubes are not without risk and tube dislodgement or malfunction, infection, hemorrhage, aspiration pneumonia, bowel injury, long-term dependence, and poor quality of life have all been described in the literature.  $^{46,49-52}$  In our study, patients with hypopharyngeal tumors who underwent G-tube placement experienced more gastrostomy tube-related complications. However, this trend in this small subset (n=4 patients) may be confounded by the presence of prior treatment, need for tracheostomy, and lower BMI in all four of these patients.

Our study has several limitations. We did not explicitly model interactions within the data or estimate nonlinear effects, for which application of a machine learning model would be of great benefit. We included many predictors for univariable analysis as an exploratory analysis. However, many univariable associations became insignificant after multiple comparisons adjustment and unintuitive associations may be attributed to the lack of confounding adjustment. While multivariable methods reduced the potential for confounding and overcame multiple comparisons issues, there are documented limitations for the predictor selection method (LASSO; e.g., potential exclusion of highly correlated variables). Although many univariable associations were deemed insignificant, either through multiple comparisons adjustment or multivariable analyses, these findings do not necessarily preclude the importance of univariable findings in an exploratory context (e.g., resection type may be a relevant G-tube predictor despite being selected out from the multivariable analysis). Application of Bayesian analyses in the univariable setting can also reduce the potential for Type I error.

Additionally, EMR review introduces risks of missing or incomplete documentation, patients lost to follow-up, and oversimplifies complex clinical decision-making. For instance, while low BMI, dysphagia, and weight loss have been linked to the need for G-tube, preoperative dysphagia was subjectively reported by patients in our study and the degree of weight loss was variable and inconsistently documented, limiting analysis of these variables. <sup>10</sup> Additionally, patients did not routinely undergo preoperative albumin or prealbumin testing. Although low serum albumin has been associated with an increased risk of needing a G-tube, the utility of individual laboratory values in determining nutritional status is debated. <sup>23,53–55</sup>

Lack of randomization, in terms of both G-tube placement and ablative and reconstructive surgeons, introduces selection bias in deciding which patients undergo surgical resection with free-flap reconstruction, as well as who undergoes G-tubes placement and at what time. To this end, we attempted to control for surgeons through hierarchical modeling to report associations independent of the ablative and reconstructive surgeons. The lack of formal recommendations to guide G-tube placement leaves surgeons to decide based on past experiences, resulting in inherent selection biases. In our study, preoperative G tubes were predominantly placed in patients with tumor stages greater than T2, which indicates a larger tumor requiring a larger resection and reconstruction. Randomization and post-hoc statistical adjustment can minimize these biases in prospective cohort studies.56

Our study findings may not be generalizable to other institutions. At our institution patients are generally unable to be discharged with nasogastric tubes in place, which is not the case at many institutions. Therefore, patients unable to maintain sufficient oral nutritional intake postoperatively undergo G-tube placement. As such, some patients may have required G-tubes for only brief periods. While we attempted to analyze data on the duration of G-tube need, this was limited by missing data and patients lost to follow-up. Not all patients can tolerate a nasogastric tube, however, and this should also be considered when deciding on the need for a G-tube.

Follow-up was limited to 3 months postoperatively. While adjuvant treatments are often started within this timeframe, this short follow-up may not adequately capture the need for postoperative radiation or the long-term sequelae of these treatments on swallowing function. In addition, some patients who require a temporary G-tube during adjuvant therapy can ultimately resume independent nutritional intake and have their G-tubes removed. The purpose of this study, however, was to identify patients who required a G-tube for any duration during the immediate perioperative period.

Our study includes only patients undergoing free-flap reconstruction, a subset of patients where the decision to place a G-tube remains unclear. There is evidence to suggest improved swallowing outcomes with free flap (versus pedicled) reconstruction. These patients are more likely to be younger and have fewer comorbidities, making them candidates for free-flap reconstruction and potentially better able to tolerate impaired oral intake than older and more frail patients. Additionally, smaller resections amenable to smaller reconstructions are less likely to significantly impact swallowing function.

### Conclusion

Head and neck cancer is increasingly prevalent and treatment commonly involves extensive resection, reconstruction, and/or chemoradiation. These patients are at high risk for malnutrition and need for G-tube. Determining who requires a pre- or postoperative G-tube remains a challenge. In this study, the need for tracheostomy or ALT flap reconstruction and age 65 years or older were predictive of

postoperative G-tube placement. Future research will guide a multidisciplinary perioperative pathway with nutritionists, SLPs, palliative care clinicians, and ablative and reconstructive surgeons to facilitate the optimization of nutrition management pre- and postoperatively.

#### Note

All authors contributed to this research and development of this manuscript. The content is solely the responsibility of the author(s) and does not necessarily represent the official views of the NIH.

### Funding

Data analysis was performed with the help of statisticians with the support of the Dartmouth Clinical and Translational Science Institute, under award UL1TR001086 from the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH).

### Conflict of Interest

None declared.

### References

- 1 Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, Grandis JR. Head and neck squamous cell carcinoma. Nat Rev Dis Primers 2020:6(01):92
- 2 Pfister DG, Spencer S, Adelstein D, et al. Head and neck cancers, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2020;18(07):873-898
- 3 Alshadwi A, Nadershah M, Carlson ER, Young LS, Burke PA, Daley BJ. Nutritional considerations for head and neck cancer patients: a review of the literature. J Oral Maxillofac Surg 2013;71(11): 1853-1860
- 4 Lo Nigro C, Denaro N, Merlotti A, Merlano M. Head and neck cancer: improving outcomes with a multidisciplinary approach. Cancer Manag Res 2017;9:363-371
- 5 Steer B, Loeliger J, Edbrooke L, Deftereos I, Laing E, Kiss N. Malnutrition prevalence according to the GLIM criteria in head and neck cancer patients undergoing cancer treatment. Nutrients 2020;12(11):3493
- 6 Gorenc M, Kozjek NR, Strojan P. Malnutrition and cachexia in patients with head and neck cancer treated with (chemo)radiotherapy. Rep Pract Oncol Radiother 2015;20(04):249-258
- 7 Mays AC, Worley M, Ackall F, D'Agostino R Jr, Waltonen JD. The association between gastrostomy tube placement, poor postoperative outcomes, and hospital re-admissions in head and neck cancer patients. Surg Oncol 2015;24(03):248-257
- 8 Assenat E, Thezenas S, Flori N, et al. Prophylactic percutaneous endoscopic gastrostomy in patients with advanced head and neck tumors treated by combined chemoradiotherapy. J Pain Symptom Manage 2011;42(04):548-556
- 9 Ahmed KA, Samant S, Vieira F. Gastrostomy tubes in patients with advanced head and neck cancer. Laryngoscope 2005;115(01): 44-47
- 10 Mays AC, Moustafa F, Worley M, Waltonen JD, D'Agostino R Jr. A model for predicting gastrostomy tube placement in patients undergoing surgery for upper aerodigestive tract lesions. JAMA Otolaryngol Head Neck Surg 2014;140(12):1198-1206
- 11 Wermker K, Jung S, Hüppmeier L, Joos U, Kleinheinz J. Prediction model for early percutaneous endoscopic gastrostomy (PEG) in head and neck cancer treatment. Oral Oncol 2012;48(04): 355-360

- 12 Jack DR, Dawson FR, Reilly JE, Shoaib T. Guideline for prophylactic feeding tube insertion in patients undergoing resection of head and neck cancers. J Plast Reconstr Aesthet Surg 2012;65(05): 610 - 615
- 13 Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)-a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42(02): 377-381
- 14 Harris PA, Taylor R, Minor BL, et al; REDCap Consortium. The REDCap consortium: building an international community of software platform partners. J Biomed Inform 2019; 95:103208
- 15 Carvalho CM, Polson NG, Scott JG. Handling sparsity via the horseshoe. Proceedings of the Twelfth International Conference on Artificial Intelligence and Statistics. PMLR 2009;5:73-80
- Gelman A, Hill J, Yajima M. Why we (usually) don't have to worry about multiple comparisons. J Res Educ Eff 2012;5:189-211
- 17 Makowski D, Ben-Shachar MS, Chen SHA, Lüdecke D. Indices of effect existence and significance in the Bayesian framework. Front Psychol 2019;10:2767
- 18 Ihaka R, Gentleman RR. A language for data analysis and graphics. J Comput Graph Stat 1996;5(03):299-314
- 19 Lenth RV, Buerkner P, Herve M, et al. Estimated marginal means, aka least-squares means. 2021 1.7.0.
- 20 Bürkner P. brms: An R package for Bayesian multilevel models using stan. J Stat Softw 2017;80(01):1-28
- 21 Makowski D, Ben-Sachar MS, Lüdecke D. bayestestR: Describing effects and their uncertainty, existence and significance within the Bayesian framework. J Open Source Softw 2019;4(40):1541
- 22 Heinze G, Schemper M. A solution to the problem of separation in logistic regression. Stat Med 2002;21(16):2409-2419
- 23 Chandler AR, Knobel D, Maia M, et al. Predictive factors for preoperative percutaneous endoscopic gastrostomy placement: novel screening tools for head and neck reconstruction. J Craniofac Surg 2015;26(07):2124-2127
- 24 Scolapio JS, Spangler PR, Romano MM, McLaughlin MP, Salassa JR. Prophylactic placement of gastrostomy feeding tubes before radiotherapy in patients with head and neck cancer: is it worthwhile? J Clin Gastroenterol 2001;33(03):215-217
- 25 Furia CL, Carrara-de Angelis E, Martins NM, Barros AP, Carneiro B, Kowalski LP. Video fluoroscopic evaluation after glossectomy. Arch Otolaryngol Head Neck Surg 2000;126(03):378-383
- 26 Smith JE, Suh JD, Erman A, Nabili V, Chhetri DK, Blackwell KE. Risk factors predicting aspiration after free flap reconstruction of oral cavity and oropharyngeal defects. Arch Otolaryngol Head Neck Surg 2008;134(11):1205-1208
- 27 Fujimoto Y, Hasegawa Y, Nakayama B, Matsuura H. [Usefulness and limitation of crico-pharyngeal myotomy and laryngeal suspension after wide resection of the tongue or oropharynx]. Nippon Jibiinkoka Gakkai Kaiho 1998;101(03):307-311
- 28 Zuydam AC, Rogers SN, Brown JS, Vaughan ED, Magennis P. Swallowing rehabilitation after oro-pharyngeal resection for squamous cell carcinoma. Br J Oral Maxillofac Surg 2000;38 (05):513-518
- 29 Skoretz SA, Anger N, Wellman L, Takai O, Empey A. A systematic review of tracheostomy modifications and swallowing in adults. Dysphagia 2020;35(06):935-947
- 30 Gross RD, Mahlmann J, Grayhack JP. Physiologic effects of open and closed tracheostomy tubes on the pharyngeal swallow. Ann Otol Rhinol Laryngol 2003;112(02):143-152
- 31 Mah JW, Staff II, Fisher SR, Butler KL. Improving decannulation and swallowing function: a comprehensive, multidisciplinary approach to post-tracheostomy care. Respir Care 2017;62(02):
- 32 Hsiao HT, Leu YS, Chang SH, Lee JT. Swallowing function in patients who underwent hemiglossectomy: comparison of primary closure and free radial forearm flap reconstruction with videofluoroscopy. Ann Plast Surg 2003;50(05):450-455

- 33 Hsiao HT, Leu YS, Lin CC. Primary closure versus radial forearm flap reconstruction after hemiglossectomy: functional assessment of swallowing and speech. Ann Plast Surg 2002;49(06): 612-616
- 34 Su WF, Hsia YJ, Chang YC, Chen SG, Sheng H. Functional comparison after reconstruction with a radial forearm free flap or a pectoralis major flap for cancer of the tongue. Otolaryngol Head Neck Surg 2003;128(03):412-418
- 35 You Q, Jing X, Fan S, Wang Y, Yang Z. Comparison of functional outcomes and health-related quality of life one year after treatment in patients with oral and oropharyngeal cancer treated with three different reconstruction methods. Br J Oral Maxillofac Surg 2020;58(07):759-765
- 36 Miyamoto S, Sakuraba M, Nagamatsu S, Kayano S, Kamizono K, Hayashi R. Risk factors for gastric-tube dependence following tongue reconstruction. Ann Surg Oncol 2012;19(07):2320-2326
- 37 Nguyen NP, North D, Smith HJ, et al. Safety and effectiveness of prophylactic gastrostomy tubes for head and neck cancer patients undergoing chemoradiation. Surg Oncol 2006;15(04):199–203
- 38 Bleier BS, Levine MS, Mick R, et al. Dysphagia after chemoradiation: analysis by modified barium swallow. Ann Otol Rhinol Laryngol 2007;116(11):837-841
- 39 Shin YS, Koh YW, Kim SH, et al. Radiotherapy deteriorates postoperative functional outcome after partial glossectomy with free flap reconstruction. J Oral Maxillofac Surg 2012;70 (01):216-220
- 40 Andry G, Hamoir M, Leemans CR. The evolving role of surgery in the management of head and neck tumors. Curr Opin Oncol 2005; 17(03):241-248
- 41 Spijkervet FK, van Saene HK, Panders AK, Vermey A, Mehta DM. Scoring irradiation mucositis in head and neck cancer patients. J Oral Pathol Med 1989;18(03):167-171
- 42 Lalla RV, Peterson DE. Treatment of mucositis, including new medications. Cancer J 2006;12(05):348-354
- Wopken K, Bijl HP, Langendijk JA. Prognostic factors for tube feeding dependence after curative (chemo-) radiation in head and neck cancer: a systematic review of literature. Radiother Oncol 2018;126(01):56-67
- 44 Rutter CE, Yovino S, Taylor R, et al. Impact of early percutaneous endoscopic gastrostomy tube placement on nutritional status and hospitalization in patients with head and neck cancer receiving definitive chemoradiation therapy. Head Neck 2011;33(10): 1441-1447
- 45 Atasoy BM, Yonal O, Demirel B, et al. The impact of early percutaneous endoscopic gastrostomy placement on treatment completeness and nutritional status in locally advanced head and

- neck cancer patients receiving chemoradiotherapy. Eur Arch Otorhinolaryngol 2012;269(01):275-282
- 46 Rahnemai-Azar AA, Rahnemaiazar AA, Naghshizadian R, Kurtz A, Farkas DT. Percutaneous endoscopic gastrostomy: indications, technique, complications and management. World J Gastroenterol 2014;20(24):7739-7751
- 47 Dziegielewski PT, Boyce B, Manning A, et al. Predictors and costs of readmissions at an academic head and neck surgery service. Head Neck 2016;38(Suppl 1):E502-E510
- 48 Mays AC, Bartels HG, Wistermayer PR, et al. Potential for health care cost savings with preoperative gastrostomy tube placement in the head and neck cancer population. Head Neck 2018;40(01):
- 49 Corry J, Poon W, McPhee N, et al. 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 2009;31(07):867-876
- 50 Paleri V, Patterson J. Use of gastrostomy in head and neck cancer: a systematic review to identify areas for future research. Clin Otolaryngol 2010;35(03):177-189
- 51 Hutcheson KA, Barringer DA, Rosenthal DI, May AH, Roberts DB, Lewin JS. Swallowing outcomes after radiotherapy for laryngeal carcinoma. Arch Otolaryngol Head Neck Surg 2008;134(02):178-183
- 52 Mekhail TMA, Adelstein DJ, Rybicki LA, Larto MA, Saxton JP, Lavertu P. Enteral nutrition during the treatment of head and neck carcinoma: is a percutaneous endoscopic gastrostomy tube preferable to a nasogastric tube? Cancer 2001;91(09):1785–1790
- 53 Unal D, Orhan O, Eroglu C, Kaplan B. Prealbumin is a more sensitive marker than albumin to assess the nutritional status in patients undergoing radiotherapy for head and neck cancer. Contemp Oncol (Pozn) 2013;17(03):276-280
- White JVG, Guenter P, Jensen G, Malone A, Schofield MAcademy Malnutrition Work Group A.S.P.E.N. Malnutrition Task Force A.S.P. E.N. Board of Directors. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). JPEN J Parenter Enteral Nutr 2012;36(03):275–283
- 55 Mangar S, Slevin N, Mais K, Sykes A. Evaluating predictive factors for determining enteral nutrition in patients receiving radical radiotherapy for head and neck cancer: a retrospective review. Radiother Oncol 2006;78(02):152-158
- 56 Levy J, Lebeaux R, Christensen B, Tosteson T, Bryan Y. Journey across epidemiology's third variables: an anesthesiologist's guide for successfully navigating confounding, mediation, and effect modification. Reg Anesth Pain Med 2021;46(11):936-940