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Prognostic factors associated with achieving total oral diet after glossectomy with microvascular free tissue transfer reconstruction

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Keywords

Glossectomy; microvascular free tissue transfer; swallowing; squamous cell carcinoma

Introduction

Based on National Comprehensive Cancer Network guidelines, primary surgical management followed by adjuvant therapy remains the standard of care in the multidisciplinary management of advanced oral cavity tongue squamous cell carcinoma (SCC)[1]. Additionally, salvage glossectomy is used to treat recurrent base of tongue squamous cell carcinoma after definitive chemoradiotherapy. Depending on the extent of tongue removal, deficiencies in speech and swallowing may result. The goal of reconstruction for glossectomy deformities, therefore, is preservation or maximization of post-operative function [2,3]. Oral cavity glossectomy defects limited to less than half the tongue volume can often be effectively managed by secondary intention healing, primary closure, or skin or biologic grafting. Larger volume glossectomies involving at least half of the tongue, or those including mandibulectomy, require more extensive reconstructive procedures to re-establish bulk and shape of the tongue and to preserve the mobility of any remaining native tissues [4–8]. While microvascular free tissue transfer (MVFTT) has established itself as the gold standard in reconstruction of these defects, research on

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functional outcomes following these procedures has often been hindered by low patient numbers and limited follow-up due to mortality and the relatively low incidence of disease. Additionally, the specific question of swallowing outcome following glossectomy with MVFTT has often been focused on total glossectomy deformities without comparisons with other tongue defects [5, 9–10].

As patient expectation of achieving post-operative oral intake is an important aspect of pre-operative counseling and education, greater understanding of long-term swallow outcomes in this patient population is needed. Therefore, the authors sought to accomplish two goals: 1) Detail the rate of and time to achievement of a total oral diet in patients with tongue SCC undergoing any extent of glossectomy requiring MVFTT, and 2) Identify prognostic factors related to achieving a total oral diet in this patient population.

Methods

Following Institutional Review Board approval from the Baylor College of Medicine and the Medical University of South Carolina (MUSC), records of all patients who underwent any extent of glossectomy requiring MVFTT for oncologic purposes at MUSC from January 1, 2010 through June 30, 2015 were reviewed. Patients undergoing definitive surgical resection for oral tongue SCC and salvage glossectomy for recurrent base of tongue SCC were included. Patients less than 18 years of age and those that underwent glossectomy for other non-tongue oral cavity or oropharyngeal primary disease were excluded.

Independent variables collected included sociodemographics, medical comorbidities, prior cancer treatment history, pre-operative diet, gastrostomy tube (G-tube) presence, tumor characteristics, surgical details, and post-operative course including adjuvant treatments rendered and complications encountered. Human papillomavirus (HPV) and p16 status were not routinely tested on all tumors during the study period and thus were not recorded. The Head and Neck Charlson Comorbidity Index (HN-CCI) was used to assess the overall comorbidity burden [11]. A HN-CCI score of 1, 2, and 3 corresponded to having one, two, and three or more of the following comorbidities: congestive heart failure, cerebrovascular disease, chronic pulmonary disease, ulcer disease, liver disease, and diabetes. Tumor characteristics recorded included the American Joint Committee on Cancer (AJCC) TNM 7th edition staging system for carcinoma of oral cavity or oropharynx; unilateral, midline, or bilateral extent of tongue involvement; and extension of tumor to other adjacent upper aerodigestive tract subsites. Surgical details included MVFTT donor site, extent of glossectomy performed (Figure 1), and whether the hypoglossal nerve required sacrifice. Surgical complications recorded included fistula formation and flap failure.

MVFTT at the authors' institutions is planned for any patient requiring resection of greater than or equal to half of the oral tongue and/or tongue base volume, and in any composite resection of tongue and mandible. Flap donor site choice is based on surface area and volume of tissue removed, with forearm-based flaps indicated for tongue resections no larger than a hemiglossectomy; anterolateral thigh (ALT), anteromedial thigh (AMT) parascapular, or latissimus flaps for larger soft tissue deficits; and fibula or osteocutaneous parascapular flaps for composite wounds.

Dependent variables gathered included maximal postoperative diet achieved and/or gastrostomy tube use at last follow-up with either the head and neck surgeon, reconstructive surgeon, radiation oncologist, or speech pathologist. Our primary endpoint was the rate of achievement of a total oral diet. A total oral diet was defined as the ability to aliment orally without tube feedings regardless of type of oral consistency. This included regular diet and abnormal diet with liquids or soft foods per os (PO). Any G-tube usage was considered failure to achieve total PO diet. Diet information was gathered from patient interview on serial clinical visit documentation or from modified barium swallow results when available. Patients expected to achieve nutrition per os (PO) within 2 weeks of surgery had a temporary nasogastric feeding tube placed postoperatively; otherwise, a G-tube was placed at time of surgery. Patients with a nasogastric tube who could not be advanced to total oral diet after 4 weeks ultimately underwent G-tube placement. Our secondary endpoint was time to achievement of a total oral diet. Time to achievement of total oral diet was calculated based on the date of reconstruction to the date of first clinical documentation either on follow-up or on radiographic imaging. All patients underwent modified barium swallow study to assess for aspiration following surgery prior to PO trials and received pre-operative and post-operative counseling by head and neck trained speech pathologists.

Statistical Methods:

Descriptive statistics (frequencies, percentages, medians ranges) were calculated to summarize patients' characteristics and clinical variables. Swallowing outcome was grouped into two dichotomous categories: achievement of total oral diet and inability to achieve total oral diet as defined as any G-tube use. To examine the effect of possible clinical factors on outcome, time to achievement of total oral diet was analyzed and plotted using the competing risk method, as described by Gray [11], where death was treated as a competing risk. Patients who were alive but did not achieve total oral diet were considered censored at the last time of follow-up. A subdistribution hazard model by the Fine-Gray method [13] was also performed to include all individual significant variables into a single multivariable model for the competing risk analysis. Subdistribution hazard ratios and 95% conference intervals were calculated. *P*-values less than 0.05 were considered statistically significant. All analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Of the 214 patients who underwent MVFTT following glossectomy during the study period, 14 were excluded secondary to incomplete tumor staging, metastatic disease, perioperative death, or premature loss of follow up with no diet route able to be deduced. The remaining 200 patients (69% male, mean age of 60 years) met full inclusion criteria and were analyzed (Table 1). Median length of follow-up was 14 months (interquartile range [IQR] 7–28 months). Most patients were in good health with a HN-CCI score of 0 (74%), and no patient had 3 or more (severe) HN-CCI-relevant comorbidities. 147 (74%) patients presented with advanced T-stage (3 or 4) disease while 113 (57%) presented with nodal metastasis. Inability to tolerate a regular diet affected 115 (58%) patients pre-operatively, and 50 (25%) patients had a G-tube for nutritional supplementation prior to disposition for surgery. 70 (35%) patients had previous exposure to definitive radiation therapy with or without chemotherapy.

Defect classifications are depicted in Figure 1. Resection of partial or hemi-oral cavity tongue occurred in 77 (39%) patients. The remaining population underwent resection of at least half of the base of tongue (with or without hemi oral cavity tongue) (23%), subtotal glossectomy (9%), or total glossectomy (12%). Thirty-five (17%) patients underwent composite resection. The most common flap donor sites utilized were the ALT, latissimus, scapula and AMT flaps (66%), followed by radial or ulnar forearm flaps (22%). Fibula free flap accounted for 12% of cases. Overall flap success rate was 96%.

Achievement of total oral diet:

Total oral diet was achieved in 97 (49%) patients at last follow-up, while 31 (16%) were partially G-tube dependent, and 72 (36%) were entirely feeding tube dependent for nutrition. In patients that achieved a total oral diet, the median time to achievement was 31 days (IQR 9 – 209 days).

Table 2 details the achievement of total oral diet based on patient or treatment characteristics. For patients who had a preoperative G-tube, 18% were able to achieve a total oral diet compared to a rate of 59% in patients that did not require preoperative G-tube. Rate of total oral diet achievement was higher in patients with no prior radiation history (59% vs. 29%, $p<0.001$), no chemotherapy history (55% vs. 32%, $p=0.002$), no smoking history (63% vs 46%, $p=0.014$), and in those who were overweight (BMI ≥ 25 kg/m^2) compared to normal or underweight patients (69% vs. 40%, $p<0.001$).

Regarding extent of glossectomy, 64% of patients that underwent hemi-oral cavity glossectomy achieved a total oral diet compared to only 24% of those who had a subtotal or greater extent of tongue resection ($p<0.001$). Total oral diet achievement rates for patients with base of tongue resection (with or without oral-cavity hemiglossectomy) and composite resection were 46% and 49%, respectively. With respect to free flap donor site, 73% of patients who had radial or ulnar forearm MVFTT achieved total PO. Achievement rates were 63% for fibula free flap reconstructions, and 38% for bulkier reconstructions such as ALT, parascapular, and latissimus dorsi flaps.

Prognostic factors for achieving a total oral diet:

Results of univariate analysis identifying prognostic factors associated with achievement of total oral diet are demonstrated in Table 2. Total oral diet achievement was found to be significantly associated with overweight BMI status, lack of smoking, radiation, or chemotherapy history, normal pre-operative diet, early oncologic stage, unilateral tongue tumors; forearm flap donor site use, resection limited to oral cavity hemiglossectomy only, preservation of the hypoglossal nerve, and absence of adjuvant chemoradiation administration. Overweight BMI status, lack of prior radiation history, resection limited to oral cavity hemiglossectomy only and absence of adjuvant chemoradiation administration were found to be independently associated with achievement of total oral diet on multivariate analysis (Figure 2, Table 2).

Discussion

Chronic dysphagia following surgical management of tongue cancer with MVFTT remains a treatment-related morbidity with substantial influence on quality-of-life. While this is well known, few studies have examined post-reconstructive functional outcomes as it relates to the extent of glossectomy. Chang et al. recently examined glossectomy defect size on swallowing outcomes after MVFTT and found that resections greater than partial or hemiglossectomy had significantly worse swallow function with scores reflective of being partially or fully G-tube dependent [6]. Unfortunately, the authors were not able to report G-tube dependence rates for each defect type, and due to the defect classifications used, analysis of tongue base resection was limited. As the pendulum swings back to primary surgical management of p16 negative tongue base squamous cell carcinomas, and as salvage surgical resection for locally recurrent p16 positive tongue base squamous cell carcinoma increases, the assessment of the impact of tongue base resection and reconstruction on swallow function becomes more important [14,15]. Our study sought to detail total oral diet achievement as a surrogate for swallow function in patients undergoing glossectomy with MVFTT, and to specifically analyze base of tongue resection compared to the more common oral cavity tongue defect in a large series.

Functional outcome studies for swallowing have employed various objective and subjective measures. Videofluoroscopic studies, diet type tolerance, clinical grading systems, and surveys provide a heterogeneous account of swallow function in small case series [16]. Multi-institutional or large series studies often use G-tube dependence rates as a surrogate marker for swallow dysfunction [9, 16]. The ability to achieve a total oral diet with any consistency and thus be G-tube independent constitutes an important initial functional goal in patient recovery. While studies have sought to describe the rate of achievement of a total oral diet in this population, these analyses have been methodically limited by their failure to account for death as a competing event. On the other hand, by using a competing events analytic method, our study considers time to event for achieving oral diet while recognizing competing mortality risks, thereby producing more interpretable estimates of achieving oral intake. Overall, we found that 97 (49%) patients achieved a total oral diet after MVFTT for glossectomy deformities with 48 (49%) of these patients reaching this goal within 30 days postoperatively. Although many factors demonstrated a significant relationship with achievement of total oral diet on univariate analysis, multivariate analysis revealed only overweight BMI, prior radiation history, resection limited to oral cavity hemiglossectomy only, and adjuvant chemotherapy administration to be independently associated with total oral intake achievement.

The association between smaller extent of glossectomy with higher rate of achieving a complete oral diet is well-documented in the literature [5, 17–18]. In the present study, patients who underwent hemiglossectomy with MVFTT demonstrated a 2.4 times higher likelihood of achieving a total oral diet compared to those with a subtotal or total glossectomy. These results are similar to other reports in the literature in which total oral achievement rates have ranged from 75–100% for hemiglossectomy or smaller resections and 13–55% for larger glossectomies [10, 16, 19–20]. With respect to composite resections, 49% achieved a total oral diet which was significantly worse than those after partial or hemiglossectomy but comparable to cohorts with larger resections. This performance pattern is congruent with prior studies in which patients with composite resections performed worse on swallow function than with isolated glossectomies, but there was no impact by flap selection [6, 20].

While these results are intuitive, the relationship between tongue base resection and swallow function has been less studied. The important role of the tongue base in propulsion of food to the esophagus makes its removal especially concerning, and yet, tongue base resections are becoming more prevalent in the modern era of transoral robotic surgical approaches and as the significance of p16 negative tumors become more understood [14, 21]. Reconstructive algorithms using MVFTT have been devised by many authors to attempt to limit ensuing swallow dysfunction following tongue base resection, but often in the setting of concordant oral cavity tongue removal [2–3, 22–23]. Due to the relative recency of more specific tongue base ablative procedures, many glossectomy reports in the literature often combine patients with tongue base resections either with oral cavity tongue resections or with subtotal/total glossectomies [6, 10, 24]. This may lead to under or over estimation of the functional outcome in these patients. To better assess how patients with tongue base resections fare compared to other glossectomy subtypes undergoing MVFTT, we sub-categorized patients with base of tongue resections, separating out those with concurrent extensive oral cavity tongue resections or composite surgeries. Patients with base of tongue resection overall demonstrated worse swallowing outcomes compared to those who had a partial or hemiglossectomy and were 0.53 times less likely to achieve a total oral diet. This performance, however, was not statistically significant on multivariate analysis (p=0.27, HR 0.71 [0.39–1.30]), and may be a positive indicator that MVFTT techniques abrogate the deleterious effect of tongue base resection on swallowing at least to some degree. It has been reported that approximately 55–71% of patients who undergo total glossectomy with or without laryngeal preservation are at least partially G-tube dependent on long term follow-up, indicating poor swallow function in the majority of cases [5,9]. As expected, our results demonstrate that subtotal and total glossectomy (p=0.04, HR 0.41 [0.18–0.97]), and composite resection (p=0.01, HR 0.47 [0.27–0.81]) resulted in significantly worse achievement of PO compared to hemiglossectomy with 76% of these patients requiring at least partial G-tube supplementation. These results demonstrate a distinction in the ability of MVFTT to aid patients in achievement of PO; those with tongue base resection alone or with hemi-oral tongue resection incur the most benefit while larger resections carry lesser potential. It is likely that the tongue base and oral cavity tongue properties are mutually integral to overall function and that loss of a certain total volume of musculature ultimately results in the distinction between success and failure to achieve PO. These results do not mean to undermine the necessity of MVFTT in larger tongue resections, though, as the authors still recommend performance for its other benefits including faster healing time, potentially quicker transition to adjuvant therapy, and reducing fistula rates [25–26].

The ideal MVFTT donor site used for reconstruction of glossectomy defects is often surgeon or institution-dependent and based on the extent of glossectomy. While comparisons of donor sites on glossectomy reconstruction have not been studied extensively, some authors have advocated an algorithmic approach of donor site selection based on the defect size with bulkier flaps recommended for subtotal or total glossectomies, and thin, more pliable flaps for smaller resections [6, 27]. Even with these recommendations, no clear reconstructive protocol detailing MVFTT donor site choice has been described in a prospective, randomized manner, or correlated with functional outcome [5, 28–30]. In general, at the authors' institutions, glossectomy defects that entail less than half of the oral cavity tongue are reconstructed with forearm-based free flaps, while defects that require more surface area and bulk are reconstructed with anterolateral thigh or subscapular system flaps. Adjunct procedures to maximize swallow function such as hyoid suspension or lingual re-innervation are often utilized when possible on a case-by-case basis. In comparing flap selection, total oral diet after bulkier flap reconstruction (ALT, parascapular) was achieved in 38% of patients, whereas 73% achieved a similar outcome following reconstruction with a forearm-based flap. Multivariate analysis of MFVTT donor site demonstrated this to be a significant difference in ability to achieve a total PO diet, but ultimately this may be due to its surrogacy as a marker of amount of tongue resected. Our results differ from reports by Rihani et al. [5] and de Vicente et al. [28] who demonstrated no difference in swallow function or G-tube dependence based on free flap soft tissue donor site. Compared to forearm-based free flaps, anterolateral thigh flaps carry less donor site morbidity while maintaining versatility in design as it can be harvested as a thin fasciocutaneous free flap or a thick myocutaneous flap [4].

Prior radiation therapy has been previously reported to negatively affect swallow function [22, 31–32], and this was found to hold true in our patient population. It is not unexpected that with preexisting swallowing dysfunction, salvage surgeries creating further motor and sensory deficits can compound the issue and limit available compensatory mechanisms. Interestingly, adjuvant radiation therapy was not found to be a negative prognosticator for total oral achievement in our present study, differing from prior literature reports [6, 23, 33–34]. Most of these studies focused mainly on qualitative aspect of swallowing such as degree of tongue mobility and type of diet consistency (liquids, softs, solids) tolerated. Fujiki et al. [35] demonstrated adjuvant radiation was associated with high short-term G-tube dependence but at one-year post-treatment, dependency rates returned to pre-therapy levels. With our time-to-event analysis, our results suggest that in the absence of prior radiation, adjuvant radiotherapy alone does not impact a patient's ability or cause delay in achievement of a total oral diet. This finding may be due to primary radiation treatment causing more intrinsic tongue and pharyngeal injury without benefit of new vascularized tissue compared to adjuvant treatment after MVFTT. While not able to be proven or investigated in this study, MVFTT techniques may abrogate adjuvant radiation effects due to their improved vascularity [36]. It is possible that in cases of salvage glossectomy for recurrent base of tongue SCC, the targets during prior radiation therapy have encompassed areas of the oropharynx and hypopharynx, resulting in more radiation dosage on pharyngeal constrictors and other anatomical structures in proximity responsible for the pharyngolaryngeal phase of swallowing compared to radiation delivered in the adjuvant setting [37].

There has been no prior study demonstrating adjuvant chemoradiation (as opposed to adjuvant radiation alone) as an independent factor in PO achievement after MVFTT for oral cavity cancer. While our results show an independent association between adjuvant chemotherapy and decreased oral intake ability following postoperative chemotherapy, the exact mechanism of this association is not able to be discerned. It is likely that this relationship is mediated by acute cytotoxic effects such as mucositis, gastrointestinal discomfort, dysgeusia and anorexia which may develop into chronic maladaptive oral avoidance or aversion. Adjuvant chemotherapy has been associated with persistent dysphagia and prolonged gastrostomy tube dependence in patients after transoral robotic surgery [38,39]. It has also been shown to increase G-tube usage and duration of dependency in organ preservation protocols for treatment of oropharyngeal carcinoma [40–41]. In a systematic review of patients with oral or oropharyngeal squamous cell carcinoma treated with primary surgery and MVFTT with or without adjuvant therapy, small sample sizes precluded inferences on impact of adjuvant chemotherapy or chemoradiotherapy on dysphagia [42].

Interestingly, our study discovered that overweight BMI was found to have an independent significant impact on total PO diet achievement in glossectomy patients undergoing MVFTT. In the glossectomy population, underweight status has been reported as an independent risk factor for postoperative dysphagia requiring G-tube use after MVFTT [23]. While our study found no difference in outcomes between underweight and normal weight patients, overweight and obese patients had significantly higher total PO diet rates following treatment. This finding is supported in the oropharyngeal cancer literature. McRackan et al. [43] reported improved swallowing outcomes and overall survival compared to those with lower BMI after chemoradiation therapy in patients with oropharyngeal cancer and BMI $\geq$ 25. Reasons for this finding are not understood but could be related to BMI representing an overall nutritional status of the patient. Better nutritional status and reserves may allow for patients to better withstand the potentially cachectic effects of cancer and its therapy. Additionally, specifically regarding MVFTT, sufficient fat volume is often required to reconstruct a protuberant shape or supply sufficient bulk in the neo-tongue needed for tongue function. The added bulk supplied to the neotongue often atrophies during radiotherapy, and the greater volume present with a higher BMI may allow more preserved post-treatment neo-tongue volume and function.

While this study does represent one of the largest cohorts of patients undergoing glossectomy with MVFTT, it does have limitations, including its retrospective study design that restricts ability to identify causal inferences and relies on the accuracy of prior documentation. Choice of flap donor site was primarily left to the reconstructive surgeon which poses a selection bias risk. Adjunct surgical techniques such as laryngeal suspension, usage of innervated flaps, and palatal prosthesis placement have been described to enhance functional results, but these factors were not standardized in performance and thus were not accounted for in our analysis. Due to the lack of uniformly collected prospective objective measures, we only examined the ability to achieve a total oral diet as the primary functional outcome and were not able to assess standardized measures such as the MD Anderson Dysphagia Index (MDADI). Quality-of-life remains a multifaceted issue, and factors such as type of PO diet consistency tolerated and speech intelligibility – which was not assessed in the present study – remain important parameters that deserve further investigation. Nevertheless, the ability to achieve a total oral diet and remain G-tube independent is a binary measurement that enabled comparison to literature outcomes and is useful in preoperative patient counseling and postoperative expectation management.

Conclusion

Swallow dysfunction is a significant morbidity following glossectomy in the treatment of oral cavity tongue carcinoma. Approximately half of patients that undergo glossectomy with MVFTT reconstruction achieve a total oral diet, with most attaining this goal within 30 days. Independent prognostic factors for achieving a total oral diet include overweight BMI, lack of prior radiation history, resection limited to oral cavity hemiglossectomy only, and absence of adjuvant chemotherapy administration. Patients should be appropriately counseled of these factors with emphasis placed on aggressive swallow rehabilitation in the post-treatment setting. Further work in the optimization of patient nutrition prior to surgical therapy may be warranted to improve functional outcomes post-therapy.

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Highlights

- About half of patients achieve a total oral diet after MVFTT reconstruction following glossectomy
- Resections of subtotal glossectomy or greater have worse total oral achievement
- Forearm-based free flaps had superior outcomes but may be surrogate marker for resection extent
- Normal or low BMI, prior radiation, and adjuvant chemoradiation were negative prognostic factors

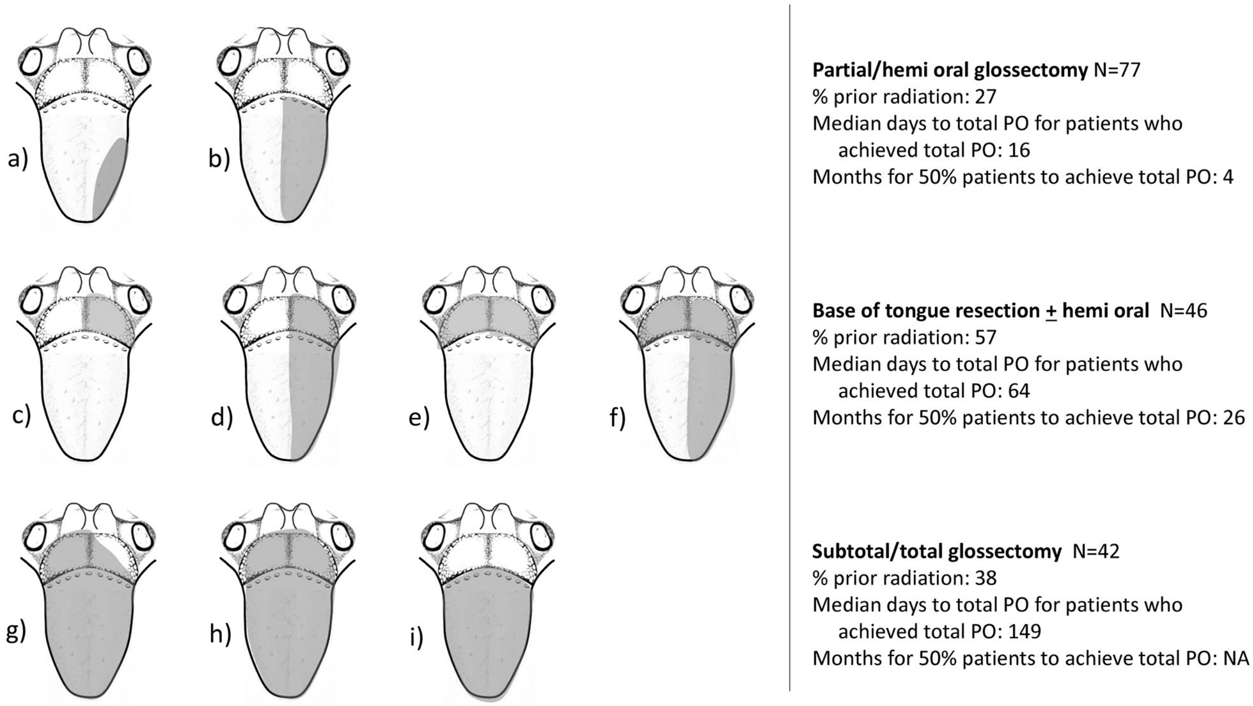
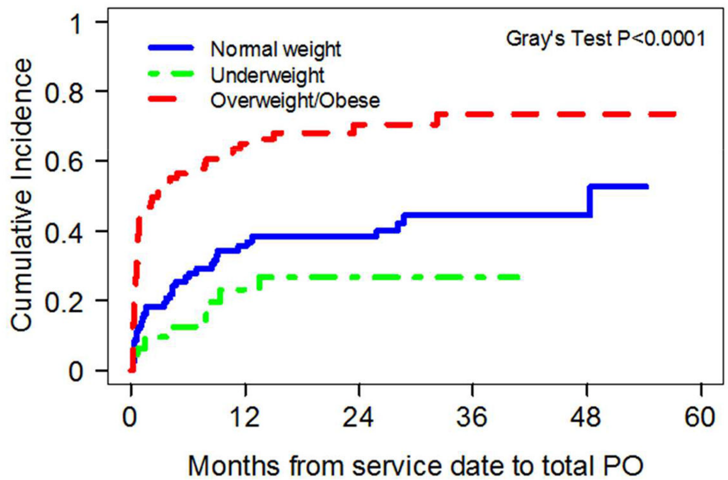


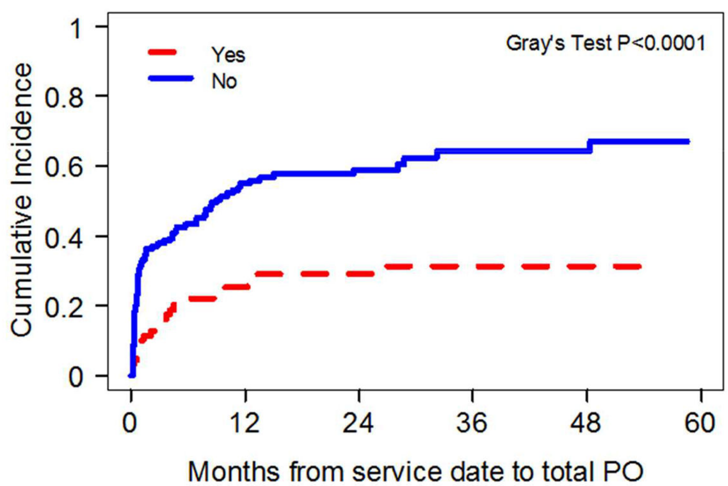
Figure 1.

Illustrative representation of extent of glossectomy categories. a.) partial glossectomy involving less than half the oral tongue; b.) hemi oral glossectomy; c–d.) ≤1/2 base of tongue without and with hemi oral tongue; e–f.) ≥1/2 base of tongue without and with hemi oral tongue, respectively; g.) subtotal glossectomy; h.) total glossectomy; i.) entire oral tongue resection; i.) composite resection with mandibulectomy. Not pictured: ventral oral tongue and composite resection with concurrent mandibulectomy.

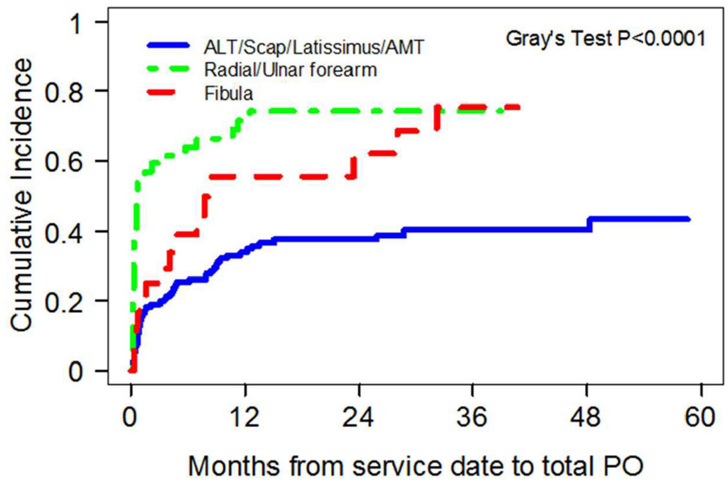
A. BMI (kg/m²)



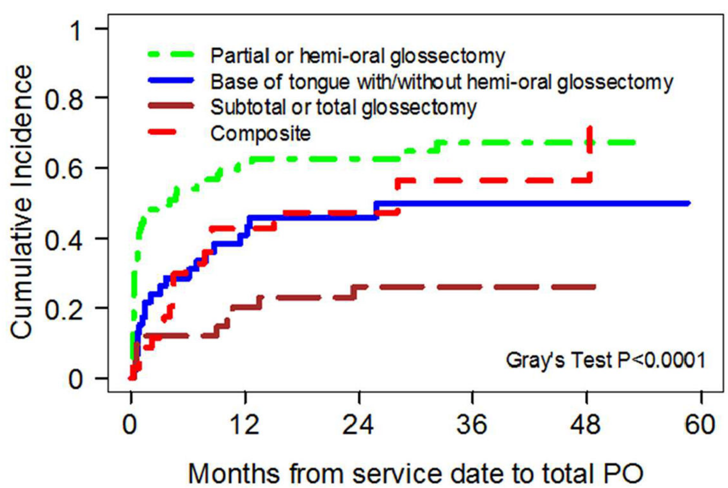
B. Prior radiation



C. Flap donor site



D. Amount of tongue removed



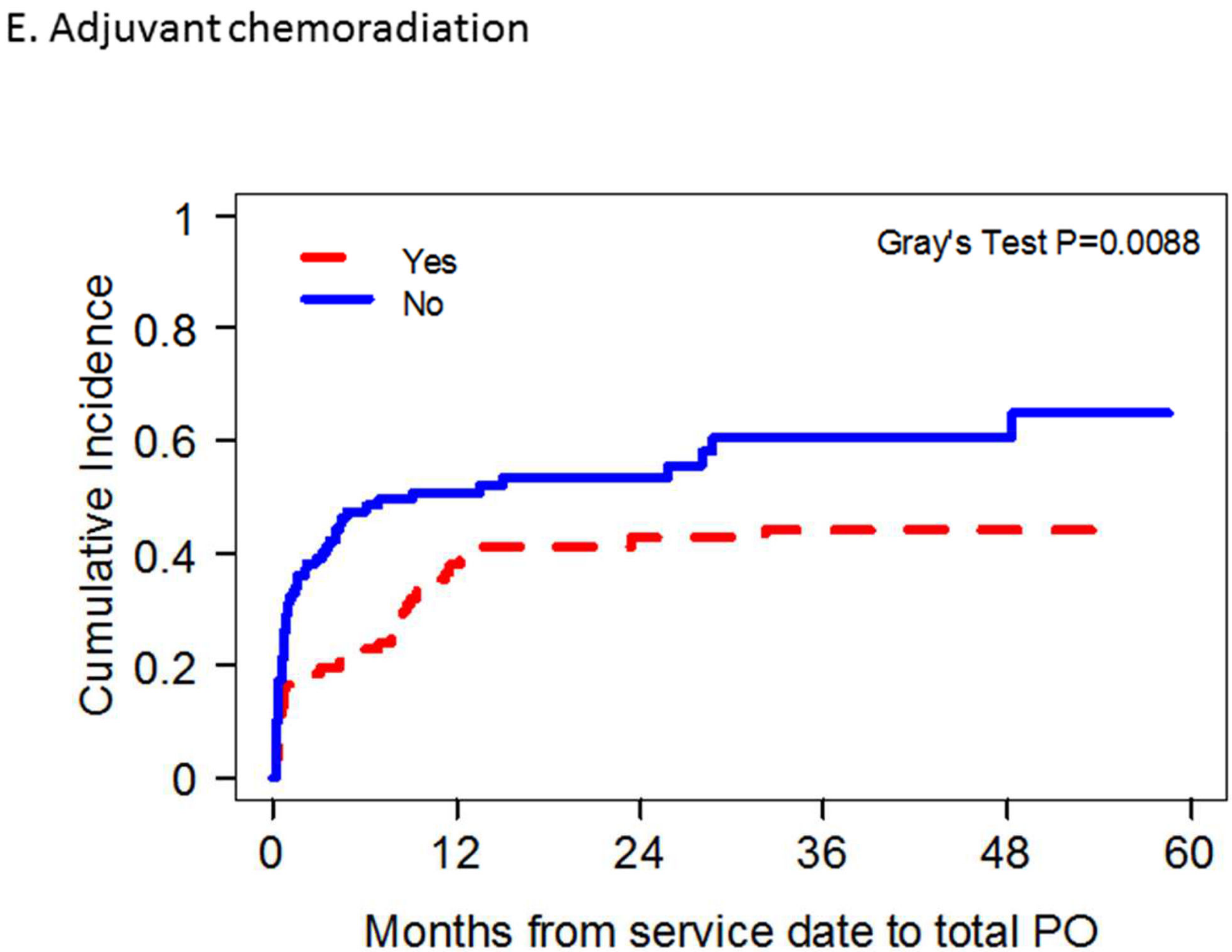


Figure 2.

Competing risk plots of factors significantly correlated with total oral diet achievement after microvascular free tissue transfer (MVFTT) following glossectomy on multivariate analysis.

Table 1.

Demographic and surgical characteristics of patients who underwent glossectomy and microvascular free tissue transfer (MVFTT) reconstruction

Characteristics	**N (%)**
No. patients	200
Median follow-up time in months (IQR)	13.8 (7 – 27.5)
Sex	
Female	62 (31)
Male	138 (69)
Mean age (STD)	59.5 (11.1)
BMI (kg/m^2)	
Normal weight (20–25)	93 (47)
Underweight (≤20)	32 (16)
Overweight/Obese (>25)	75 (37)
Smoking history	
Non-user	33 (17)
Former/current user	167 (83)
Alcohol history	
Non-user	97 (49)
Former/current user	103 (51)
HN-CCI score	
0 (none)	147 (74)
1 (mild)	40 (20)
2 (moderate)	13 (6)
3 (severe)	0 (0)
Prior radiation	
Yes	70 (35)
No	130 (65)
Prior chemotherapy	
Yes	57 (29)
No	143 (71)
T stage	
0–2	53 (26)
3–4	147 (74)
N stage	
0	87 (43)
1	32 (16)
2–3	81 (41)
AJCC stage (7th ed.)	
I-II	29 (15)
III-IV	171 (85)
Tumor laterality	

Characteristics	N (%)
Bilateral	58 (29)
Midline	28(14)
Unilateral	114 (57)
Tumor extension	
Extension to adjacent site	107 (54)
No extension	93 (46)
Preoperative G-tube dependence	
Yes	50 (25)
No	150 (75)
Preoperative diet	
Abnormal (modified PO, any G-tube use)	115 (58)
Normal PO	85 (43)
Flap donor site	
ALT/Scap/Latissimus/AMT	132 (66)
radial/ulnar forearm	44 (22)
fibula	24 (12)
Amount of tongue resected	
Partial or hemi-oral glossectomy	77 (39)
Base of tongue with/without hemi-oral glossectomy	46 (23)
Subtotal or total glossectomy	42 (21)
Composite	35 (17)
Hypoglossal nerve removed	
Yes	68 (34)
No	132 (66)
Postoperative radiation	
Yes	147 (74)
No	53 (26)
Postoperative chemoradiation	
Yes	97 (49)
No	103 (51)
Total PO diet achieved	
Yes	97 (49)
No	103 (51)
Median days to achieve to total PO diet (IQR)	31 (9–209)

Table 2.

Univariate and multivariate analyses on factors associated with total oral diet achievement after microvascular free tissue transfer (MVFTT) reconstruction following glossectomy.

Characteristics	Yes (N=97)	No (N=103)	Univariate Subdistribution HR	p^*	Multivariate Subdistribution HR	p^*
	N (%)	N (%)	(95% CI)		(95% CI)	
Sex						
Female	35 (57)	27 (43)				
Male	62 (45)	76 (55)	0.70 (0.46 – 1.06)	0.096		
Mean age (STD)	59 (12)	60 (10)	1 (0.98 – 1.02)	0.661		
BMI (kg/m^2)						
Normal weight (20–25)	37 (40)	56 (60)			-	
Underweight (≤20)	8 (25)	24 (75)	0.55 (0.26 – 1.15)	0.109	0.70 (0.28 – 1.72)	0.433
Overweight/Obese (>25)	52 (69)	23 (31)	2.44 (1.61 – 3.71)	<0.001	1.6 (1.03 – 2.48)	0.036
Smoking history						
Non-user	21 (64)	12 (36)			-	
Former/current user	76 (46)	91 (55)	0.54 (0.33 – 0.88)	0.014	0.64 (0.39 – 1.07)	0.088
Alcohol history						
Non-user	47 (48)	50 (52)				
Former/current user	50 (49)	53 (51)	0.92 (0.62 – 1.36)	0.671		
HN-CCI score						
0 (none)	67 (46)	80 (54)				
1 (mild)	23 (58)	17 (42)	1.27 (0.80 – 2.01)	0.304		
2 (moderate)	7 (54)	6 (46)	1.18 (0.58 – 2.42)	0.651		
Prior radiation						
Yes	20 (29)	50 (71)			-	
No	77 (59)	53 (41)	2.68 (1.65 – 4.35)	<0.001	3.02 (1.34 – 6.83)	0.008
Prior chemotherapy						
Yes	18 (32)	39 (68)			-	
No	79 (55)	64 (45)	2.17 (1.33 – 3.56)	0.002	0.67 (0.28 – 1.62)	0.375
T stage						
0–2	36 (68)	17 (32)				

Characteristics	Yes (N=97)	No (N=103)	Univariate Subdistribution HR	p^*	Multivariate Subdistribution HR	p^*
	N (%)	N (%)	(95% CI)		(95% CI)	
3–4	61 (42)	86(59)	0.47 (0.31 – 0.71)	<0.001		
N stage						
0	47 (54)	40 (46)				
1	22 (69)	10 (31)	1.61 (0.95 – 2.71)	0.074		
2–3	28 (35)	53 (65)	0.56 (0.36 – 0.89)	0.014		
AJCC stage (7th ed.)						
I-II	21 (72)	8 (28)			-	
III-IV	76 (44)	95 (56)	0.48 (0.30 – 0.78)	0.003	0.92 (0.50 – 1.69)	0.777
Tumor laterality						
Bilateral	16 (28)	42 (72)			-	
Midline	13 (46)	15 (54)	1.85 (0.92 – 3.73)	0.084	1.34 (0.65 – 2.79)	0.429
Unilateral	68 (60)	46 (40)	2.84 (1.69 – 4.78)	<0.001	1.07 (0.54 – 2.11)	0.846
Tumor extension						
Extension to adjacent site	48 (45)	59 (55)				
No extension	49 (53)	44 (47)	1.39 (0.94 – 2.06)	0.103		
Preoperative G-tube dependence						
Yes	9 (18)	41 (82)			-	
No	88 (59)	62 (41)	4.46 (2.31 – 8.64)	<0.001	2.08 (0.95 – 4.56)	0.066
Preoperative diet						
Abnormal[a]	34 (30)	81 (70)			-	
Normal PO	63 (74)	22 (26)	3.78 (2.50 – 5.72)	<.0001	1.53 (0.82 – 2.83)	0.178
Flap donor site						
ALT/Scap/Latissimus/AMT	50 (38)	82 (62)			-	
Radial/ulnar forearm	32 (73)	12 (27)	3.39 (2.10 – 5.47)	<0.001	1.90 (1.13 – 3.19)	0.016
Fibula	15 (63)	9 (37)	2.02 (1.22 – 3.34)	0.007	1.17 (0.63 – 2.16)	0.625
Amount of tongue resected						
Partial or hemi-oral glossectomy	49 (64)	28 (36)			-	
Base of tongue with/without hemi-oral glossectomy	21 (46)	25 (54)	0.53 (0.32 – 0.88)	0.014	0.71 (0.39 – 1.30)	0.269
Subtotal or total glossectomy	10 (24)	32 (76)	0.24 (0.12 – 0.47)	<0.001	0.41 (0.18 – 0.97)	0.043
Composite	17 (49)	18 (51)	0.56 (0.34 – 0.94)	0.027	0.47 (0.27 – 0.81)	0.007

Characteristics	Yes (N=97)	No (N=103)	Univariate Subdistribution HR	p^*	Multivariate Subdistribution HR	p^*
	N (%)	N (%)	(95% CI)		(95% CI)	
Hypoglossal nerve removed						
Yes	22 (32)	46 (68)			-	
No	75 (57)	57 (43)	2.31 (1.47 – 3.64)	<0.001	1.43 (0.85 – 2.42)	0.183
Postoperative radiation						
Yes	72 (49)	75 (51)				
No	25 (47)	28 (53)	1.08 (0.69 – 1.71)	0.730		
Postoperative chemoradiation						
Yes	40 (41)	57 (59)			-	
No	57 (55)	46 (45)	1.68 (1.13 – 2.51)	0.010	1.87 (1.17 – 2.99)	0.009

Abbreviations: HR, hazards ratio; CI, confidence interval; STD, standard deviation; AJCC, American Joint Committee on Cancer; BMI, body mass index; HN-CCI, The Head and Neck Charlson Comorbidity Index; ALT, anterolateral thigh; AMT, anteromedial thigh; Scap, parascapular; PO, per os; G-tube, gastrostomy tube

*Clinical significance defined as $p<0.05$

[a]Abnormal diet defined as modified PO to liquids or soft diet or any G-tube use