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Prognostic Factors Associated with Achieving Total Oral Diet Following Osteocutaneous Microvascular Free Tissue Transfer Reconstruction of the Oral Cavity

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Abstract

Introduction: Osteocutaneous microvascular free tissue transfer (OMFTT) is the current standard in reconstruction of large bony defects of the oral cavity. Although being able to swallow ranks as a top priority for patients undergoing OMFTT, factors associated with achieving an oral diet following surgery remain unclear. We sought to describe the rate of total oral diet achievement, and to identify possible pre-, intra-, and post-operative factors associated with achievement in patients undergoing OMFTT.

Methods: Retrospective review between January 1, 2010 and March 31, 2018 at two tertiary academic centers.

Results: 249 patients (67% male, mean age 58 years) met inclusion criteria, with a median follow up of 15 months. Overall, 142 (57%) of patients achieved a total PO diet post-operatively, with median time to achievement of 3.2 months. Multivariate analysis identified that lack of concurrent glossectomy (SHR 1.72 [1.09-2.70], $p=0.02$), N0/1 disease (SHR 1.92 [1.16-3.13], $p=0.011$), avoidance of post-operative fistula formation (SHR 1.96 [1.22-3.23], $p=0.005$), preoperative G-tube independence (SHR 3.33 [1.69-6.25], $p<0.001$), and successful dental rehabilitation (SHR 2.08 [1.43-3.03], $p<0.001$) are independently associated with total oral diet achievement.

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Conclusions: Bony resections not requiring glossectomy, limited nodal disease burden, preoperative gastrostomy-independence, avoidance of post-operative fistula, and dental rehabilitation are independently associated with achievement of total oral diet following OMFTT reconstruction of the oral cavity. Counseling patients on associated risk factors is important in guiding post-treatment expectations. Minimization of post-operative fistula, and maximization of dental rehabilitation may significantly improve total oral diet achievement in this patient population.

Keywords

Oral cancer; head and neck cancer; Microvascular free tissue transfer; Swallowing; Squamous cell carcinoma

Introduction

Since the advent of microvascular surgery in the 1960s¹, one of the most significant advancements has been the identification of reliable donor sites for vascularized osteocutaneous flaps, integral in the reconstruction of large composite oral cavity maxillo-mandibular deformities. Use of the fibula, scapula, radius, iliac crest, and even rib for osteocutaneous microvascular free tissue transfer (OMFTT) has now become standard for restoration of form and function for these maxillo-mandibular defects following oncologic or traumatic etiologies²⁻⁵. OMFTT has been found to be superior to soft tissue-only microvascular free tissue transfer in terms of both aesthetic result and swallowing^{6,7}. Through OMFTT, surgeons have the ability to not only resurface mucosal defects and reconstitute segmental bony deformities, but also can facilitate dental restoration through prosthetic rehabilitation or osseointegrated implants^{8,9}.

While numerous studies have investigated risk factors for OMFTT failure and complications in the head and neck, few studies have characterized predictors of poor swallowing outcomes¹⁰⁻¹². To date, most studies evaluating swallowing outcomes following OMFTT have been limited by small population size, lack of differentiation in outcome between oncologic and benign pathologies, and analysis of only single OMFTT donor sites, which limits generalizability of the data¹³⁻¹⁷. Specifically, with OMFTT for oral cavity maxillo-mandibular reconstruction, objective data for counseling patients on expected post-operative swallow function, including achievement of a total oral diet for nutrition, is lacking. Therefore, the authors sought to accomplish two goals: 1) Detail the rate of and time to lifetime achievement of a total oral diet in patients undergoing OMFTT of the oral cavity, 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, a review of consecutive patients undergoing OMFTT reconstruction for oral cavity maxillo-mandibular defects between January 1, 2010 to March 31, 2018 was conducted. Our groups maintain a de-identified patient database of microvascular free tissue transfer outcomes, with results published in the literature on

elderly, laryngectomy, and glossectomy swallowing outcomes^{18–20}. Time periods examined between the studies have differed, and due to de-identification, exact numbers of patients shared between the works is impossible to quantify. Patients less than 18 years of age were excluded.

Measures and study variables:

Independent variables collected included sociodemographics, comorbidities as scored by the Head and Neck Charlson Comorbidity Index (HNCCI)^{21,22}, indication for surgery, prior cancer treatment history, pre-operative diet, gastrostomy tube (G-tube) presence, tumor characteristics, surgical details, and post-operative course including adjuvant treatments rendered, complications encountered, and dental rehabilitation. Tumor characteristics were described according to the American Joint Committee on Cancer (AJCC) TNM 7th edition. Surgical details included OMFTT donor site, type of mandibulectomy performed, whether concurrent glossectomy was performed (hemiglossectomy, subtotal, or total glossectomy), and length of surgery. Mandibulectomy was grouped according to the Shaw classification²³. Shaw type 1 were lateral mandibulectomy defects, type 2 hemimandibulectomy, type 3 anterior, and type 4 subtotal. Surgical complications included fistula, malocclusion, and total flap failure. Dental rehabilitation was documented as denture fabrication, palatal augmentation prosthetic, or osseointegrated implant placement with prosthetic placement.

OMFTT of the oral cavity at the authors' institutions is planned for composite defects of the maxilla or mandible resulting in more than 2 centimeters of bone loss, or loss of integral bony support of the lower or mid face including the mandibular symphysis or premaxilla. Choice of OMFTT donor site harvested was based on surgeon preference, with all reconstructions performed by the senior authors (EMG, JDH, ATH, JMS). Post-operative nutrition was administered by nasogastric tube in all patients expected to achieve a total oral diet within 2 weeks of surgery, otherwise a G-tube was placed. All patients underwent modified barium swallow study to assess for aspiration following surgery prior to oral trials, and received pre- and post-operative counseling by head and neck trained speech pathologists.

Dependent variables included maximal post-operative diet achieved and/or G-tube use at last follow-up. The primary endpoint was the rate of achievement of a total oral diet, which was defined as the ability to sustain complete nutritional needs orally without G-tube assistance, and included regular or abnormal diets (e.g. mechanically altered, liquid, or syringe feeding). Partial or total G-tube dependence was considered failure to achieve total oral diet. The secondary endpoint assessed was time to achievement of a total oral diet. Time to achievement of oral diet was calculated from the date of reconstruction to the date of first clinical documentation either on follow-up or on radiographic imaging.

Statistical Methods:

Patient characteristics and clinical variables were summarized with descriptive statistics. Patients were grouped based on the primary outcome into two groups: those that achieved total oral diet or those that did not, defined as any G-tube use. Time to achievement of total oral diet was analyzed and plotted via the competing risk method to examine the effect of

possible clinical factors on diet outcome, in which death was treated as a competing risk²⁴. Patients who at last follow-up were alive but did not achieve total oral diet were considered censored. The Fine-Gray method was used to create a subdistribution hazard model to include all individual significant variables into a single multivariable model for the competing risk analysis²⁵. Subdistribution hazard ratios and 95% confidence intervals were calculated. *P* values less than .05 were considered statistically significant. SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used for all analyses.

Results

260 patients underwent OMFTT for oral cavity maxillomandibular reconstruction during the study time period. Eleven patients were excluded due to premature loss of follow up with no diet route able to be deduced, leaving 249 for review (Table 1). 168 (67%) were male, with mean age of 58 and median follow-up length of 15 months (interquartile range [IQR] 9.6-24.7 months). The most common indication for surgery was cancer (73%), followed by osteoradionecrosis or other post-oncologic treatment reconstruction (18%), and lastly benign pathology (9%). 180 (72%) patients were active or prior smokers, 84 (34%) underwent prior radiation, and 64 (26%) underwent prior chemotherapy. A large majority of patients underwent OMFTT for mandibular reconstruction (93%), while 18 patients (7%) had maxillary reconstruction. Most patients were in poor health pre-operatively with a mean HN-CCI score of 3.6. Pre-operatively, 57 (23%) patients had a G-tube, with 27 (11%) patients being completely G-tube dependent for nutrition.

The average length of surgery including defect creation and OMFTT was 11.7 ± 4.8 hours. Median length of hospitalization was 10 days (IQR 8-15 days), with 86% of patients being discharged home. Patients undergoing OMFTT for malignancy predominantly demonstrated advanced T-stage (3 or 4) disease on final pathologic analysis (87%). In patients with composite mandibular OMFTT reconstructions, 80% incurred Shaw type I or type II deformities. 105 (42%) patients underwent concurrent glossectomy, of which 87 (35%) had a hemiglossectomy or lesser resection, and 18 (7%) had a subtotal or total glossectomy. Post-operative fistulae occurred in 26 (10%) of patients, malocclusion in 32 (13%), and total flap failure in 10 (4%).

Achievement of total oral diet and associated prognostic factors

A total of 142 (57%) patients achieved a total oral diet following OMFTT, while 44 (17%) were partially G-tube dependent, and 65 (26%) were totally G-tube dependent. Median time to achievement of a total oral diet was 3.2 months (IQR 0.5-7.2 months). Table 2 details factors analyzed for achievement of total oral diet. Univariate analysis revealed preoperative G-tube use to be significantly associated with failure to achieve a total PO diet compared to patients without a G-tube (18% vs. 69%; SHR 0.17, $p < 0.001$). Rate of total oral diet achievement was higher in patients who were able to be discharged home post-operatively (61% vs. 33%; SHR 2.17, $p < 0.010$), had no prior radiation history (63% vs. 45%; SHR 1.56, $p = 0.018$), no smoking history (67% vs 53%; SHR=1.47, $p = 0.031$), and in those who were normal, overweight, or obese (BMI ≥ 20 kg/m²) compared to underweight patients (61% vs. 28%; SHR 2.70, $p < 0.005$).

Regarding extent and site of OMFTT, only 39% of those who required concurrent glossectomy achieved a total oral diet compared to 69% of patients that underwent segmental mandibulectomy alone and 78% that underwent composite maxillectomy ($p<0.001$). Extent of mandibulectomy separated into Shaw type I/II (lateral defects) and Shaw type III/IV (anterior or subtotal) demonstrated rates of total oral diet achievement of 58% and 38%, respectively, but this did not achieve significance (SHR=1.69, $p=0.088$). Comparing fibula and all other OMFTT donor sites, no significant difference in total oral diet achievement rates was identified (58% vs. 55%; SHR=1.08, $p=0.683$).

Post-operatively, fistula formation was found to significantly negatively affect the ability to achieve a total oral diet with a 38% rate of achievement compared to 59% in those without a fistula (SHR=0.48, $p=0.011$). Adjuvant radiation therapy and malocclusion was not found to be associated with rate of oral diet achievement. In patients with an oncologic indication for surgery, any recurrence of disease whether local, regional, or distant, significantly decreased oral achievement rates (41% vs. 65%; SHR=0.50, $p<0.001$). Dental rehabilitation either by osseointegrated implants or denture prosthetic fabrication was achieved in 61 (24%) patients with significantly better total oral diet rates achieved compared to those who did not receive dental restoration (89% vs. 47%; SHR=2.98, $p<0.001$).

On multivariate analysis, only N0/1 disease (SHR=1.92, $p=0.011$), avoidance of postoperative fistula formation (SHR=1.96, $p<0.005$), preoperative G-tube independence (SHR=3.33, $p<0.001$), lack of concurrent glossectomy (SHR=1.72, $p=0.017$) and dental rehabilitation (SHR=2.08, $p<0.001$) were identified as significant independent prognostic factors contributing to achievement of a total oral diet following OMFTT.

Discussion

OMFTT has become an integral reconstructive modality for head and neck surgeons managing oncologic and traumatic deformities of the oral cavity. While complex three-dimensional osseous defects can be addressed with OMFTT to restore the form of the maxillomandibular complex, there remains a paucity of literature regarding the functional outcomes of these patients^{26,27}. As the association between functional status, quality-of-life and overall survival in head and neck cancer patients has been well documented, it is of paramount importance that functional outcome data in this cohort be elucidated²⁸. Unfortunately, data reporting in this area remains sparse for a variety of reasons. In a systematic review of 8 retrospective and 2 prospective studies looking at functional outcomes following OMFTT, the authors observed a lack of quality data due to small sample sizes and heterogeneity in inclusion criteria, defects, and functional outcome measurements and instruments used¹³.

In this study, 57% of patients ultimately achieved a total oral diet, with 17% remaining partially G-tube dependent and 26% totally G-tube dependent for nutritional needs. Of those achieving a total oral diet, 68 (48%) were cleared for an unrestricted diet while 74 (52%) tolerated a mechanically altered diet. Cordeiro et al, in a review of 133 patients undergoing OMFTT of the mandible, found that 45% were able to achieve a total unrestricted oral diet, 50% a mechanically altered or liquid diet, and only 5% requiring enteral feeding¹⁶.

Similarly, Sukaraba et al and Camuzard et al, in reviews of 101 and 72 patients undergoing fibula free flap reconstruction of the mandible, found 4-7% rates of gastrostomy tube dependence^{17,29}. While our rate of total oral diet achievement is lower compared to these studies, it should be noted that only 0-8% of their patients had a documented history of prior radiotherapy, and oral diet outcome was reported in only 44-94% of their patient population due to issues including loss to follow up and mortality, possibly resulting in observer bias. Additionally, factors such as concurrent glossectomy, post-operative radiation therapy, extent of bony resection, and variation in OMFTT are either incomplete or not reported, making our results difficult to compare with the published literature.

While robust oral diet and swallow function data may be lacking in the current literature, quality of life measurements following OMFTT are becoming more prominent. Recently, Petrovic et al reported on long term physician-reported functional outcomes in 25 patients following fibula free flap reconstruction of the mandible, and found that only 64% of patients had restoration of function compared to normal³⁰. Loss in function was mainly attributed to loss of dentition, malocclusion, trismus, and post-radiotherapy effects. These findings highlight the importance in documenting post-treatment function in these patients to provide clinicians with information to counsel patients pre-operatively on expectations and goals of therapy.

While numerous factors were found to be associated with failure to achieve a total oral diet on univariate analysis, only N2 disease, post-operative fistula formation, preoperative G-tube use, concurrent glossectomy, and failure to undergo dental rehabilitation proved to be independently associated following multivariate analysis. Regarding pre-operative G-tube use, numerous prior studies have shown that pre-treatment and post-treatment function are correlated. Chen et al in a study of 120 patients undergoing chemoradiation for stage III/IV head and neck cancer found significantly higher rates of G-tube dependence at 6 and 12 months post-treatment in those with pre-treatment G-tube placement³¹. Similarly, a recent study of 59 patients undergoing radiotherapy for head and neck cancer revealed a higher incidence of long term G-tube dependence in patients who received G-tubes pre-treatment versus those that did not³².

Our finding of N2 disease being associated with failure to achieve total oral diet has support in the literature as advanced nodal burden has previously been shown to correlate with poor post-treatment functional status. Wopken et al in a systematic review of 32 studies reporting on tube feeding dependence >6 months after chemoradiation for head and neck cancer revealed advanced nodal stage to be a significant prognostic factor³³. While it is unclear why advanced nodal disease results in inability to achieve a total oral diet, it may be attributable to a combination of factors including more extensive surgery and wider field adjuvant radiotherapy affecting the tongue, salivary tissue, and even pharyngeal constrictors.

The effect of glossectomy on swallow function has been well documented, with studies demonstrating association of tongue resection volume on swallow dysfunction and G-tube dependence^{34,35}. Our group has recently published on total oral diet following microvascular free tissue transfer reconstruction of glossectomy defects, finding that patients undergoing composite resection of the mandible and tongue performed significantly worse than more

limited glossectomies alone (49% vs. 64% total oral diet achievement)²⁰. This result points to the probable cooperative nature of the oromandibular complex in swallow function, highlighted by this study's observation of only a 39% rate of total oral diet achievement following OMFTT for composite defects of the mandible and tongue, compared to 69% in those without glossectomy.

Dental rehabilitation following OMFTT reconstruction of the oral cavity can be achieved by prosthetic fabrication, fixed in place either by adhesive, attachment to surrounding dentition, or by osseointegrated implants. While it is known that jaw-related post-treatment complications such as trismus and malocclusion result in lower quality-of-life³⁶, our findings, to the authors' knowledge, are the first to demonstrate an independent association between dental rehabilitation and achievement of a total oral diet in this patient population. In total, 61 (24%) patients achieved dental rehabilitation either by adhesive or clasp based prosthetic (77%), palatal augmentation prosthetic (5%), or osseointegrated implant-based prosthetic (18%). Literature regarding the overall rate of dental rehabilitation in patients undergoing OMFTT is limited, but our rate of 24% compares favorably to reported rates of 21-30%³⁷⁻³⁸. Reasons for failure to achieve dental rehabilitation, aside from disease-related mortality, have been reported to include effacement of the oral vestibule, mal-alignment of the maxillomandibular complex, and reconstruction plate or screw interference with osseointegrated implant placement³⁸. There were no implant failures in our study population. Even though there is a lack of literature on dental rehabilitation and oral diet, it is important to note that there is considerable data on the safety of osseointegrated implant placement into OMFTT sites, with implant success rates ranging between 81-97%^{8,39-42}, and OMFTT donor sites showing similar implant acceptance rates^{40,43}. Unfortunately, with the current data, it not possible to determine a causal relationship between dental rehabilitation and achievement of total oral diet, especially considering other social, behavioral, or compliance factors were not able to be measured. However, with dental rehabilitation in any form demonstrating an independent significant effect on achievement of total oral diet following OMFTT, the authors recommend aggressive intervention by oral maxillofacial surgery and maxillofacial prosthodontics colleagues, and future prospective investigations to delineate factors, whether medical, surgical, or social, which may maximize patient access to dental restoration.

Post-operative fistula formation proved to be a significant independent predictor of failure to achieve a total oral diet in our study, and while intuitive, it is a novel finding in this patient population. It is likely that patients who experience this complication often require prolonged periods of oral or neck wound care and enteral feeding, resulting in a possible delay to return of oral function. While there is very little literature regarding potential causative factors associated with fistula following OMFTT, there has been ample literature published regarding pharyngocutaneous fistula following total laryngectomy, which may shed some light in the present context. Medical comorbidities including chronic anemia, congestive heart failure, diabetes, liver disease, and preoperative radiation have all been associated with the development of fistula following total laryngectomy due to their effects on wound healing^{44,45}. Overall, adverse post-operative events in our study are comparable to those found in the literature. A review of 368 patients that underwent OMFTT of the head

and neck revealed rates of 9.8% for flap failure and 8.4% for fistula⁴⁶. These values were 4.0%, and 10.4% in our study, respectively.

While this study, to the authors' knowledge, represents one of the largest identifying prognostic factors associated with achievement of an oral diet following OMFTT of the oral cavity, there are still numerous limitations. Retrospective studies are inherently prone to confounding and recall bias, and are subject to the completeness of the medical record. For example, timing of patient follow up and recording of the data in the medical record may result in an artificially prolonged length of time before recognition of total oral diet achievement in our patient population. Flap donor sites were chosen according to attending surgeon preference, introducing the potential for selection bias. Objective measures of aesthetic outcome, speech intelligibility, and swallow function were not implemented in our study, and will be necessary in future prospective work in this area. While this limits the conclusions we can draw, the surrogacy of G-tube dependence with swallow dysfunction is well-documented^{47,48}, making the achievement of a total oral diet a significant marker in functional outcome. Strengths of this work include its large study population, the ability to gather data from readily available institutional records rather than separately populated national databases, and our use of a competing events analytic method. Utilizing a time to event analysis for achieving total oral diet while taking into account the competing risk of mortality, censoring those datapoints, allows a more accurate estimate of patients able to achieve oral intake, and better analysis of their associated prognostic factors. Ultimately, these findings allow the clinician more information to counsel patients on their risks and likelihood of achieving an oral diet, and potentially intervene earlier to improve functional outcomes in this cohort.

Conclusion

OMFTT is the standard method of restoring form and function for bony defects of the oral cavity, but only 57% of patients ultimately achieve a total oral diet following treatment. Preoperative G-tube independence, N0/1 disease, lack of concurrent glossectomy, avoidance of post-operative fistula, and dental rehabilitation were found to independently predict achievement of a total oral diet following OMFTT, and should be counseled to patients pre-operatively. While strides are being made to more accurately characterize functional outcomes following OMFTT, further work needs to be done to obtain a better understanding of this unique patient cohort.

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Research Highlights

1. In patients undergoing OMFTT, 57% achieve total oral diet.
2. Those undergoing concurrent glossectomy have worse total oral diet achievement.
3. N0/N1 stage and preop G tube independence are positive predictors of total oral diet achievement.
4. Dental rehab and avoidance of postop fistula are positive predictors of total oral diet achievement

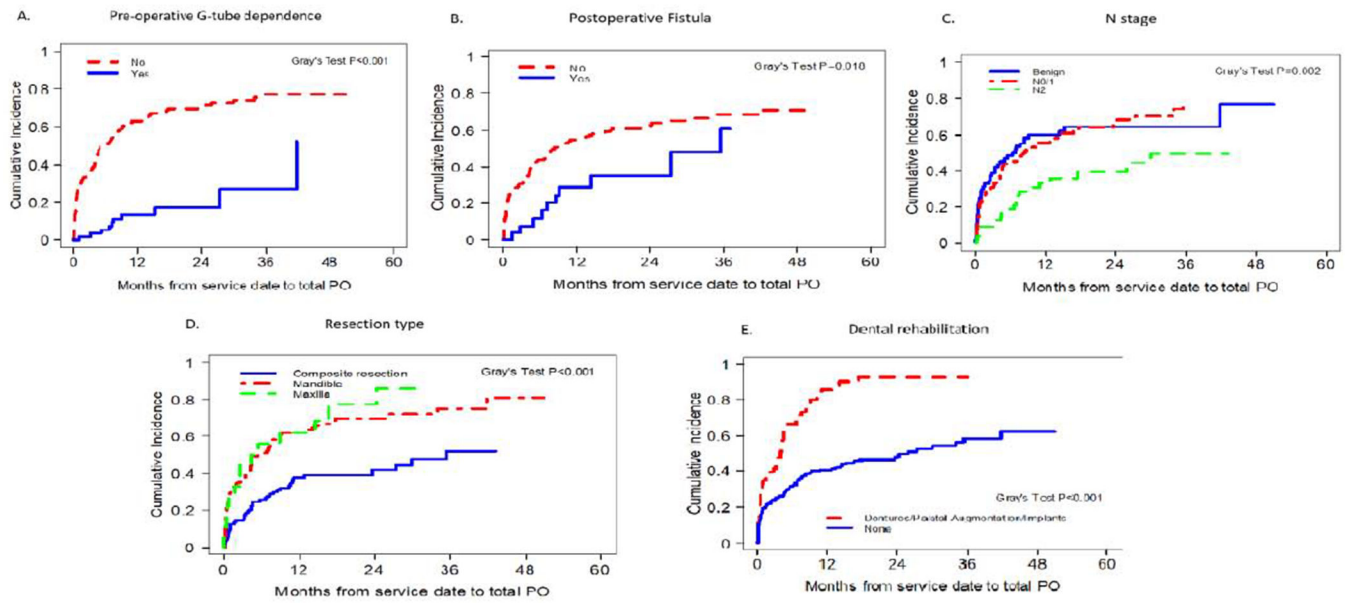


Figure 1. Competing risk plots of factors significantly correlated with total oral diet achievement after osteocutaneous microvascular free tissue transfer of the oral cavity

Table 1.

Characteristics of patients undergoing osteocutaneous microvascular free tissue transfer reconstruction of the oral cavity.

Characteristics		N (%)
No. patients		249
Median follow-up time in months (IQR)		15 (9.6-24.7)
HNCCI (mean +/- STD)		3.6 (1.6)
Sex		
	Female	81 (33)
	Male	168 (67)
Mean age (years)		58.0 ± 14.7
BMI (kg/m ²)		
	Normal weight (20–25)	120 (48)
	Underweight (< 20)	32 (13)
	Overweight/Obese (>25)	97 (39)
Smoking history		
	Non-user	69 (28)
	Former/current user	180 (72)
Prior radiation		
	Yes	84 (34)
	No	165 (66)
Prior chemotherapy		
	Yes	64 (26)
	No	185 (74)
T stage		
	Benign	67 (27)
	0–2	23 (9)
	3–4	159 (64)
N stage		
	Benign	67 (27)
	0-1	127 (51)
	2	55 (22)
AJCC stage (7th ed.)		
	Benign	67 (27)
	I-II	20 (8)
	III-IV	162 (65)
Shaw classification/Bone deficit		
	I (lateral)	177 (71)
	II (Hemi)	22 (9)
	III (anterior)	20 (8)

Table 2.

Univariate and multivariate analyses of factors associated with total oral diet achievement after osteocutaneous microvascular free tissue transfer of the oral cavity

Characteristics		Yes N=142	No N=107	Univariate subdistribution HR	<i>P</i> [*]	Multivariate subdistribution HR	<i>P</i> [*]
		N (%)	N (%)	(95% CI)		(95% CI)	
Sex							
	Male	96 (57)	72 (43)	-	-	-	-
	Female	46 (57)	35 (43)	1.02 (0.71-1.47)	0.899	-	-
HNCCI (mean +/- STD)		3.4 (1.6)	3.8 (1.4)	0.89 (0.80-0.99)	0.030	0.91 (0.79-1.04)	0.155
BMI (kg/m ²)							
	Normal weight (20–25)	68 (57)	52 (43)	-	-	-	-
	Underweight (<20)	9 (28)	23 (72)	0.42 (0.20-0.85)	0.016	0.82 (0.38-1.77)	0.718
	Overweight/Obese (>25)	65 (67)	32 (33)	1.3 (0.93-1.81)	0.127	1.07 (0.73-1.57)	0.618
Disposition							
	Home	130 (61)	83 (39)	-	-	-	-
	Rehab/SNF	12 (33)	24 (67)	0.46 (0.25-0.83)	0.010	0.56 (0.30-1.02)	0.060
Indication							
	Cancer	100 (55)	82 (45)	-	-	-	-
	Benign	19 (86)	3 (14)	2.28 (1.43-3.63)	<0.001	0.51 (0.21-1.25)	0.140
	Post-treatment/ osteoradionecrosis	23 (51)	22 (49)	0.97 (0.60-1.56)	0.888	0.72 (0.35-1.49)	0.372
Smoking history							
	Non-user	46 (67)	23 (33)	-	-	-	-
	Former/current user	96 (53)	84 (47)	0.68 (0.47-0.97)	0.03	0.88 (0.61-1.28)	0.497
Prior radiation							
	Yes	38 (45)	46 (55)	-	-	-	-
	No	104 (63)	61 (37)	1.56 (1.08-2.27)	0.018	1.56 (0.93-2.56)	0.086
T stage							
	1-2	17 (74)	6(26)	-	-	-	-
	3–4	83 (52)	76 (48)	0.57 (0.34-0.94)	0.028	0.77 (0.44-1.35)	0.357
	Benign	42 (63)	25 (37)	0.80 (0.46-1.40)	0.439	-	-
N stage							
	2	21 (38)	34 (62)	-	-	-	-
	0-1	79 (62)	48 (38)	2.12 (1.35-3.33)	0.001	1.92 (1.16-3.13)	0.011
	Benign	42 (63)	25 (37)	1.05 (0.72-1.55)	0.791	-	-
Pre-operative G-tube dependence							
	Yes	10 (18)	47 (82)	-	-	-	-
	No	132 (69)	60 (31)	5.88 (3.23-11.11)	<0.001	3.33 (1.69-6.25)	<0.001
Donor site							
	Fibula	85 (58)	61 (42)	-	-	-	-

Characteristics		Yes N=142	No N=107	Univariate subdistribution HR	<i>P</i> [*]	Multivariate subdistribution HR	<i>P</i> [*]
		N (%)	N (%)	(95% CI)		(95% CI)	
	Radial forearm/ALT/ scapula	57 (55)	46 (45)	0.93 (0.67-1.30)	0.683	-	-
Resection type							
	Mandible (+) glossectomy	41 (39)	64 (61)	-	-	-	-
	Mandible (-) glossectomy	87 (69)	39 (31)	2.27 (1.59-3.23)	<0.001	1.72 (1.10-2.70)	0.017
	Maxilla alone	14 (78)	4 (22)	1.18 (0.69-2.00)	0.545	0.93 (0.51-1.70)	0.822
Shaw classification							
	I (lateral)/II (hemi)	116(58)	83 (42)	-	-	-	-
	III(anterior)/IV(subtotal)	12 (38)	20 (62)	0.59 (0.32-1.08)	0.088	-	-
Malocclusion							
	Yes	19 (59)	13 (41)	-	-	-	-
	No	123 (57)	94 (43)	1.07 (0.66-1.74)	0.786	-	-
Fistula							
	Yes	10 (38)	16 (62)	-	-	-	-
	No	132 (59)	91 (41)	2.08 (1.19-3.70)	0.011	1.96 (1.22-3.23)	0.005
Dental rehabilitation							
	None	88 (47)	100 (53)	-	-	-	-
	Dentures/Palatal Augmentation/Implants	54 (89)	7 (11)	2.98 (2.14-4.14)	<0.001	2.08 (1.43-3.02)	<0.001
Post-operative chemoradiotherapy							
	Yes	37 (45)	46 (55)	-	-	-	-
	No	105 (63)	61 (37)	1.67 (1.16-2.44)	0.006	1.10 (0.68-1.75)	0.701
Any cancer recurrence							
	Yes	33 (41)	47 (59)	-	-		
	No	109 (64)	60 (36)	2.00 (1.33-2.94)	<0.001	1.45 (0.91-2.33)	0.122

Abbreviations: HR, hazards ratio; CI, confidence interval; HN-CCI, Head and Neck Charlson Comorbidity Index; STD, standard deviation; BMI, body mass index; SNF, skilled nursing facility; G-tube, gastrostomy tube; ALT, anterolateral thigh

* Clinical significance defined as $p < 0.05$. *P*-values were not adjusted for multiple comparisons.